EANM'18

Annual Congress of the
European Association of Nuclear Medicine
October 13 – 17, 2018
Düsseldorf, Germany

Abstracts

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Dear colleagues, dear friends,

On behalf of the European Association of Nuclear Medicine, it is my great pleasure and honour to welcome you to the 31st Annual EANM'18 Congress in Düsseldorf, Germany.

The EANM meeting is now definitively the world-reference congress in nuclear medicine. In order to maintain our congress at its excellent level, the meeting will build on the traditions that are highly appreciated by all the attendees, with the expansion of newer features. A specific educational track, implemented with the collaboration of the European School of Multimodality Imaging and Therapy, will include up-to-date teaching sessions, enriched pitfalls seminars and Continuous Medical Education interactive sessions. In all these active learning conferences, attendees will have the possibility to enhance their knowledge of multimodality imaging. A careful evaluation procedure relating to the speakers will be implemented in order to gain feedback and ensure that future interactive sessions continue to enjoy a positive response. With similar pedagogic intent, numerous multidisciplinary joint symposia, organised by several EANM Committees in collaboration with our sister societies, will offer an integrative approach to various topics relevant to the state of the art of our discipline. I would like to take this opportunity to make a special appeal to young specialists, who will probably benefit most from the academic sessions. You represent the future of our discipline and it is you who should begin to shape yourself for a brighter tomorrow in our community!

Of course, all this will not reduce the predominant role of our congress, namely to deliver oral and electronic-poster presentations on the latest achievements in clinical nuclear medicine, science and technology. On the contrary, the oral sessions will be enriched. Rapid Fire sessions will draw attention to the highly rated abstracts in specific comprehensive topics, with a panel of top-level presentations followed by extensive discussions; this will provide attendees with an integrated and coherent view on a wide variety of topics. Furthermore, the concept of featured oral sessions in which an invited speaker places the presentations into a broader perspective will be generalised to all the other oral presentations. The now well-established tracks M2M – Molecule to Man (basic and translational science) and Do.MoRe (radionuclide therapy and dosimetry) promise to promote high-quality research through interaction between basic and translational clinical scientists and to present the latest achievements and developments in the fields of clinical molecular imaging and nuclear medicine therapy. During plenary lectures, distinguished speakers will address the state of the art and new developments in clinical and allied sciences, covering a broad range of topics with the goal of fostering the provision of the best possible care for our patients. In particular, it is a pleasure and an honour for me to announce the contribution to our congress of Prof. Bernard L. Feringa, from Groningen, the Netherlands, Nobel Prize in Chemistry 2016, with a lecture on the *"Fascinating World of Molecules"*.

At the end of the meeting, the traditional Highlights lecture will provide a broad overview of the science presented at EANM'18. I am delighted that two young but very motivated and highly respected members of our European Nuclear Medicine community, Prof. Ken Hermann from Essen, Germany, and Dr. Fijs van Leeuwen from Leiden, the Netherlands, have agreed to take on this task.

For all these reasons, I cordially invite you to EANM'18 to actively participate in our 31st Annual Congress, to meet and interact with friends and colleagues from all over the world, to discuss science, to learn about the exciting developments in nuclear medicine, to break away from the daily routine and to enjoy everything that the city of Düsseldorf has to offer.

Francesco Giammarile,
EANM Congress Chair 2017-2019

Saturday, October 13, 2018

	Plenary Hall	Meeting Room 26	Hall 1			Hall 2	Hall 3	Hall X	Hall Y	Hall 28		
09:00 - 09:30												09:00 - 09:30
09:30 - 10:00						Pre-Symposium 1 Radiopharmacy/ Drug Development Clinical Trial Regulations	Pre-Symposium 2 Bone & Joint / Oncology / GEMO Nuclear Medicine Management of Bone Metastases in the Era of Targeted Treatments	Pre-Symposium 3 Translational Molecular Imaging & Therapy The Role of Molecular Imaging in Radiation Oncology	Pre-Symposium 4 Physics / AAPM Radiomics - Image Derived Parameters in Multimodality Imaging	Pre-Symposium 5 Neuroimaging / INMIND Imaging Neuroinflammation in Neurodegeneration		09:30 - 10:00
10:00 - 10:30												10:00 - 10:30
10:30 - 11:00												10:30 - 11:00
11:00 - 11:30												11:00 - 11:30
11:30 - 12:00		EANM Advisory Council Meeting										11:30 - 12:00
12:00 - 12:30												12:00 - 12:30
12:30 - 13:00												12:30 - 13:00
13:00 - 13:30												13:00 - 13:30
13:30 - 14:00						Pre-Symposium 6 Cardiovascular / Inflammation & Infection / ASNC Recent Imaging Guidelines on Myocardial Amyloidosis, Sarcoidosis and Large Vessel Vasculitis	Pre-Symposium 7 Oncology / Physics Radiomics, AI and Machine Learning in Hybrid Imaging	Pre-Symposium 8 Oncology / Physics Alpha- Endoradiotherapy in Solid Tumours	Pre-Symposium 9 Thyroid / Dosimetry Dosimetry in Thyroid Cancer	Pre-Symposium 10 Drug Development / Neuroimaging Towards New Radiopharmaceuticals for Psychiatry		13:30 - 14:00
14:00 - 14:30			EANM Delegates Assembly									14:00 - 14:30
14:30 - 15:00												14:30 - 15:00
15:00 - 15:30												15:00 - 15:30
15:30 - 16:00												15:30 - 16:00
16:00 - 16:30												16:00 - 16:30
16:30 - 17:00												16:30 - 17:00
17:00 - 17:30			EANM Members Assembly									17:00 - 17:30
17:30 - 18:00												17:30 - 18:00
18:00 - 18:30												18:00 - 18:30
19:30 - 20:30	EANM Opening Ceremony											19:30 - 20:30

Sunday, October 14, 2018

	Plenary Hall	Hall 2	Hall 3	Hall 5	Hall X	Hall Y	Hall 1	Hall 4	Hall 6	Hall 28	Hall A	
08:00 - 08:30	1021 CME 1 Inflammation & Infection Fever of Unknown Origin	1022 Joint Symposium 1 Paediatrics / ESPN The Role of Nuclear Medicine in Paediatric Febrile UTIs	1023 Joint Symposium 2 Oncology / EAU Update on the Use of PET/CT in Testicular Cancer	1024 Technologists' Opening (08:00-08:15) CTE 1 Technologists/ SNMMI Prostate Cancer Imaging and Therapy: Tech Guide Launch	1025 M2M - Featured Session PRRT - Understand & Improve	1026 Do.MoRe SPECT-CT	1027 Pitfalls & Artefacts 1 - ICC* Bone & Joint / Paediatrics Multimodality Imaging in Sports Medicine	1028 Clinical Oncology - Rapid Fire Session 68Ga-PSMA: it is!		1029 Cardiovascular From Myocardial Perfusion to Plaque Imaging	1031 e-Poster Walk 1 Oncology All Around Oncology	08:00 - 08:30
08:30 - 09:00												08:30 - 09:00
09:00 - 09:30												09:00 - 09:30
09:30 - 10:00												09:30 - 10:00
10:00 - 10:30	1021 Plenary 1 incl. Marie Curie Lecture In Vivo Molecular Diagnosis of Cognitive Disorders - A Paradigm Change			1024 (in Plenary Hall) Plenary 1 incl. Marie Curie Lecture In Vivo Molecular Diagnosis of Cognitive Disorders: A Paradigm Change								10:00 - 10:30
10:30 - 11:00												10:30 - 11:00
11:00 - 11:30												11:00 - 11:30
11:30 - 12:00	1027 CME 2 Thyroid New Guidelines in Nuclear Thyroidology	1022 Joint Symposium 3 - Interactive Paediatrics / SIOPEN Interactive Session on Neuroblastoma	1023 Joint Symposium 4 Cardiovascular / ESMI New Approaches for Atherosclerosis Imaging	1024 CTE 2 - Interactive Technologists Radionuclide Therapy - A Multidisciplinary Approach	1025 M2M Therapie Effects, Preclinical	1026 Do.MoRe Dosimetry for ¹⁷⁷ Lu-DOTA- Octreotate Therapy	1027 Pitfalls & Artefacts 2 - ICC* Oncology / Physics Artefacts in Hybrid Imaging	1028 Clinical Oncology - Rapid Fire Session Mix it up, Please!			1031 e-Poster Walk 2 M2M PSMA - e-Walk to Success?	11:30 - 12:00
12:00 - 12:30												12:00 - 12:30
12:30 - 13:00												12:30 - 13:00
13:00 - 14:30					Lunch Symposium	Lunch Symposium	EANM Young Daily Forum		Lunch Symposium	Lunch Symposium		13:00 - 14:30
14:30 - 15:00	1027 CME 3 Cardiovascular SPECT or PET?	1022 Joint Symposium 5 Inflammation & Infection / Cardiovascular / EULAR Guidelines on Vasculitis	1023 Joint Symposium 6 Oncology / ISNS / EHNS What is Changing in the Sentinel Node Procedure?	1024a Mini Course 1 (14:30-15:30) Non-Imaging Nuclear Medicine Diagnostic	1025 M2M PSMA Targeting	1026 Do.MoRe Image Processing / Analysis	1027 Teaching Session 1 - ICC* Neuroimaging Basics of Neuroimaging	1028 Special Symposium 20 Years of PET/CT in Clinical Practice	1029 Thyroid Targeted Imaging of Malignant Thyroid Tumours		1031 e-Poster Walk 3 Do.MoRe Clinical Dosimetry	14:30 - 15:00
15:00 - 15:30												15:00 - 15:30
15:30 - 16:00				1024b Mini Course 2 (15:45-16:45) Lymphoscintigraphy and Sentinel Node								15:30 - 16:00
16:00 - 16:30												16:00 - 16:30
16:30 - 17:00	1027 CME 4 Paediatrics PET/MR in Paediatrics - Sharing Experiences	1022 Joint Symposium 7 Neuroimaging / EAN / SNMMI Clinical Trials in Dementia - Expectations on Molecular Imaging	1023 Joint Symposium 8 Oncology / IASLC New Techniques for Diagnosis and Prognostication of Lung Cancer Patients	1024c Mini Course 3 - Interactive (17:00 - 18:00) PET Patient Preparation: Pitfalls & Artefacts	1025 M2M PSMA - Expanding Effects	1026 Do.MoRe Standardization & Calibration	1027 Teaching Session 2 - ICC* Neuroimaging Lung Anatomy and Patterns of Lung Malignancy	1028 Clinical Oncology PRRT of Neuroendocrine Tumours	1029 Thyroid Endocrine Oncology	1030 Inflammation & Infection New Trends in Imaging Infection & Inflammation	1031 e-Poster Walk 4 Bone & Joint Scintigraphy Bone Imaging	16:30 - 17:00
17:00 - 17:30												17:00 - 17:30
17:30 - 18:00												17:30 - 18:00

Monday, October 15, 2018

	Plenary Hall	Hall 2	Hall 3	Hall 5	Hall X	Hall Y	Hall 1	Hall 4	Hall 6	Hall 28	Hall A	
08:00 - 08:30	607 CME 5 Radiopharmacy / EDQM	602 Joint Symposium 9 Inflammation & Infection / ESVS Inside the Aorta: Vascular Inflammation, Infection and Atherosclerosis	603 Joint Symposium 10 Oncology / ESMO Radioisotope Therapies in Prostate Cancer and Position in Oncological Treatment Paradigms	604 Technologists Oral Presentations 1	605 M2M It's All About Peptides	606 Do.MoRe Radiation Exposure & Protection	607 Pitfalls & Artefacts 3 - ICC* Dosimetry Advantages and Limitations of Voxelized Dosimetry for Intra-Arterial Liver Therapy	608 Clinical Oncology - Rapid Fire Session It's in the Blood!	609 Thyroid Endocrine Molecular Imaging	610 Cardiovascular Integrating Models in MPI - From Injection to Interpretation	611 e-Poster Walk 5 Do.MoRe Instrumentation & Data Analysis	08:00 - 08:30
08:30 - 09:00	Validation of Radionalytical Methods											08:30 - 09:00
09:00 - 09:30												09:00 - 09:30
09:30 - 10:00												09:30 - 10:00
10:00 - 10:30	2021 Plenary 2 To Do, or Not to Do Dosimetry, that is the Question			204 (in Plenary Hall) Plenary 2 To Do, or Not to Do Dosimetry, that is the Question								10:00 - 10:30
10:30 - 11:00												10:30 - 11:00
11:00 - 11:30												11:00 - 11:30
11:30 - 12:00	607 CME 6 Dosimetry Alpha Particle Dosimetry - When, Why and How?	602 Joint Symposium 11 Thyroid / ATA tbc.	603 Joint Symposium 12 Oncology / EORTC Integrating PET into RECIST	604 (in Rooms 31-34) Technologists Technologist e-Poster Walks 1-4		606 Do.MoRe Reconstruction	607 Pitfalls & Artefacts 4 - ICC* Neuroimaging / Physics Amyloid Imaging	608 Clinical Oncology - Rapid Fire Session GIT up!	609 Special Session Tomorrow's Experts Session Best-Ranked Papers from the Under-30s			11:30 - 12:00
12:00 - 12:30												12:00 - 12:30
12:30 - 13:00												12:30 - 13:00
13:00 - 14:30					Lunch Symposium	Lunch Symposium	EANM Young Daily Forum		Lunch Symposium	Lunch Symposium		13:00 - 14:30
14:30 - 15:00	607 CME 7 Radiation Protection / Paediatrics Optimization of Diagnostic Reference Levels in Hybrid Imaging in Paediatric Nuclear Medicine	602 Joint Symposium 13 Neuroimaging / Drug Development / ECNP Imaging Phosphodiesterases (PDEs) - Targets for Drug Development	603 Joint Symposium 14 Oncology / EHA PET/CT Guided Treatment in Hodgkin Lymphoma	604 CTE 3 Technologists / Neuroimaging Nuclear Medicine Imaging in Dementia	605 M2M Antibodies & Peptides: Let's Modify!	606 Do.MoRe Dosimetry in PSMA Therapy - What is the Benefit?	607 Teaching Session 3 - ICC* ESMIT - Modern Insight in Medical Education		609 Thyroid Radiolodine Therapy of Benign Thyroid Diseases	610 Joint Symposium 29 Radiopharmacy / Dosimetry / Radiation Protection / EMA tbc.	611 e-Poster Walk 6 Cardiovascular Different Aspects of Cardiovascular Imaging I	14:30 - 15:00
15:00 - 15:30												15:00 - 15:30
15:30 - 16:00												15:30 - 16:00
16:00 - 16:30												16:00 - 16:30
16:30 - 17:00	2001 CME 8 Oncology Different Strategies in the Management of Hepatic Metastases in NEN	2002 Joint Symposium 15 Cardiovascular / ASNC Detecting Cardiac Microvascular Disease with PET	2003 Joint Symposium 16 Physics / EFOMP / ESR Dedicated and Low Dose Molecular Imaging	2004 CTE 4 Technologists Latest Development in PET/MR	2005 M2M Antibodies and their Fragments	2006 Do.MoRe Alpha-Particle Emitter Dosimetry	2007 Teaching Session 4 - ICC* Lung TNM 8 and Function of the Lung MDM	2008 Clinical Oncology PSMA Ligand Therapy of Prostate Cancer	2009 Thyroid Thyroid Cancer - From Pathology to Personalized Treatment	2010 Neuroimaging - Rapid Fire Session Cognitive Impairment & Neuro-Degeneration	2011 e-Poster Walk 7 Inflammation & Infection Infection & Inflammation	16:30 - 17:00
17:00 - 17:30												17:00 - 17:30
17:30 - 18:00												17:30 - 18:00

Tuesday, October 16, 2018

	Plenary Hall	Hall 2	Hall 3	Hall 5	Hall X	Hall Y	Hall 1	Hall 4	Hall 6	Hall 28	Hall A	
08:00 - 08:30	CME 9 Translational Molecular Imaging & Therapy / Oncology Imaging Targets for Cancer Immunotherapy	Joint Symposium 17 Dosimetry / ICRU Target Practice Conditions for Personalized Treatment Planning in Radionuclide Therapy	Joint Symposium 18 Oncology / JSNM Targeted Alpha Therapy - Prospect of Networking, Partnership, and Logistics	Technologists Oral Presentations 2	M2M AD-PD - It's in the brain!	Do.MoRe Data Analysis - Neurology	Pitfalls & Artefacts 5 - ICC* Thyroid Pitfalls in Parathyroid Detection with Nuclear Medicine Imaging	Clinical Oncology - Rapid Fire Session Prostate - Not Just 68Ga-PSMA	Other Clinical Studies Non Oncology	Cardiovascular Myocardial Imaging with SPECT and PET	e-Poster Walk 8 Paediatrics / Other Clinical Studies Joint Paediatrics / Other Clinical Studies	08:00 - 08:30
08:30 - 09:00												08:30 - 09:00
09:00 - 09:30												09:00 - 09:30
09:30 - 10:00												09:30 - 10:00
10:00 - 10:30	Plenary 3 The Fascinating World of Molecules			Plenary 3 The Fascinating World of Molecules								10:00 - 10:30
10:30 - 11:00												10:30 - 11:00
11:00 - 11:30												11:00 - 11:30
11:30 - 12:00	CME 10 - Interactive Bone & Joint How Much Radiology Do We Need in Bone and Joint Multi-Modality Imaging?	Joint Symposium 19 Neuroimaging / EANO Meningioma	Joint Symposium 20 Cardiovascular / EACVI Quantification of Myocardial Blood Flow	Technologists Oral Presentations 3	M2M Therapie Effects - α Emitters and PDT	Do.MoRe - Rapid Fire Session Quantification & Data Analysis	Pitfalls & Artefacts 6 - ICC* Translational Molecular Imaging & Therapy Is this Uptake Pathological or is it Due to Excretion?	Clinical Oncology - Rapid Fire Session Lung! Lung! Lung!	Thyroid - Featured Session Thyroid Scintigraphy - An Evergreen		e-Poster Walk 9 Neuroimaging Neuroimaging	11:30 - 12:00
12:00 - 12:30												12:00 - 12:30
12:30 - 13:00												12:30 - 13:00
13:00 - 14:30						Lunch Symposium	EANM Young Daily Forum					13:00 - 14:30
14:30 - 15:00	CME 11 Oncology Update on PET/MR in Oncology	Joint Symposium 21 Translational Molecular Imaging & Therapy / AHA Imaging Early Remodelling in Cardiomyopathies - From Preclinical to Clinical	Joint Symposium 22 Thyroid / ETA / EUGOGO Treatment of Graves' Disease (GD) in the Presence of Graves' Ophthalmopathy (GO)	CTE 5 Technologists / ESTRO PET/CT Radiotherapy Planning in Head & Neck Malignancies		Do.MoRe Dosimetry Methodologies - From Images to Absorbed Dose	Teaching Session 5 - ICC* Radiopharmacy Nanomedicine and Radiopharmaceuticals	Clinical Oncology Radioligand Therapy of Neuroendocrine Tumours - Safety & Toxicity		Paediatrics Paediatrics	e-Poster Walk 10 M2M Quality Control & Radiopharmaceutical Aspects	14:30 - 15:00
15:00 - 15:30												15:00 - 15:30
15:30 - 16:00												15:30 - 16:00
16:00 - 16:30												16:00 - 16:30
16:30 - 17:00	CME 12 Oncology PET Guided Biopsy	Joint Symposium 23 EANM/EARL New Developments of EANM Oncology PET/CT Guidelines and Update of the EARL Accreditation Standards	Joint Symposium 24 Thyroid / ETA-CRN Molecular Mechanism of Iodine Resistance and Their Clinical Implications	CTE 6 - Interactive Technologists Renal Imaging	M2M Novel Tracers in Oncology	Do.MoRe Treatment Planning for Y-90 Radioembolisation Therapy	Teaching Session 6 - ICC* Lung Cancer Interactive Session Testing your Knowledge with Live Cases	Clinical Oncology - Rapid Fire Session In the Air and Beyond		Cardiovascular Myocardial Imaging - New Developments with CZT-Cameras	e-Poster Walk 11 Clinical Oncology Oncology Mixer	16:30 - 17:00
17:00 - 17:30												17:00 - 17:30
17:30 - 18:00												17:30 - 18:00

Wednesday, October 17, 2018

	Plenary Hall	Hall 2	Hall 3	Hall 5	Hall X	Hall Y	Hall 1	Hall 4	Hall 6	Hall 28	Hall A	
08:00 - 08:30	1601 CME 13 Neuroimaging / Cardiovascular Myocardial ¹⁸ F-mIBG Imaging in Neurology – Is it Ready for Prime Time?	1602 Joint Symposium 25 Radiation Protection / Dosimetry / Thyroid / ICRP Risk Estimates for Patients Undergoing Molecular Radionuclide Therapy	1603 Joint Symposium 26 Translational Molecular Imaging & Therapy / IFCAIS Computer Assisted Image and Radioguided Intervention in Surgery and Radiology		1605 M2M Neuroinflammation & Brain Imaging	1606 Do.MoRe PET-CT & PET-MR	1607 Pitfalls & Artefacts 7 - ICC* Oncology PSMA Therapy	1608 Clinical Oncology - Rapid Fire Session Women ONLY!			1611 e-Poster Walk 12 Cardiovascular Different Aspects of Cardiovascular Imaging II	08:00 - 08:30
08:30 - 09:00												08:30 - 09:00
09:00 - 09:30												09:00 - 09:30
09:30 - 10:00												09:30 - 10:00
10:00 - 10:30	1701 CME 14 Physics / Dosimetry Quantitative Multimodality Imaging	1702 Joint Symposium 27 Cardiovascular / EACVI The Potential of Dual Isotope Imaging in Nuclear Cardiology	1703 Joint Symposium 28 Oncology / ESTRO PET/CT for Radiotherapy Planning	1704 CTE 7 - Interactive Technologists / Thyroid Thyroid Imaging and Therapy	1705 M2M Radiochemistry is Cool!	1706 Do.MoRe Miscellaneous Topics in Dosimetry			1709 Neuroimaging Dementia	1710 Bone & Joint - Featured Session Bone & Joint Hybrid Imaging	1711 e-Poster Walk 13 Radionuclide Therapy / Thyroid Local and Systemic Therapy of Malignant Tumours	10:00 - 10:30
10:30 - 11:00												10:30 - 11:00
11:00 - 11:30												11:00 - 11:30
11:30 - 12:00	1801 Awards Ceremony (11:45 - 12:15) Plenary 4 - Highlights Lecture (12:15 - 13:15) Closing Ceremony (13:15 - 13:20)			1804 (in Plenary Hall) Awards Ceremony (11:45 - 12:15) Plenary 4 - Highlights Lecture (12:15 - 13:15) Closing Ceremony (13:15 - 13:20)								11:30 - 12:00
12:00 - 12:30												12:00 - 12:30
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16:30 - 17:00												16:30 - 17:00

Oral Sessions

PS1 **Saturday, October 13, 2018, 09:00 - 12:00, Hall 2**

Pre-Congress Symposium 1 - Radiopharmacy / Drug Development: Clinical Trial Regulations

PS01

Clinical Trials and GCP

S. Embacher-Aichhorn; Medical University Innsbruck, CTC, Innsbruck, AUSTRIA.

PS02

Requirements for Radiopharmaceuticals as IMPS in Clinical Trials

I. Peñuelas; Clinica Universidad de Navarra, Radiopharmacy Unit, Nuclear Medicine Department, Madrid, SPAIN.

PS03

Radiopharmaceuticals and Clinical Trials in Europe: Chances and Challenges

C. Decristoforo; Medical University Innsbruck, CTC, Innsbruck, AUSTRIA.

PS05

Regulation of Radiopharmaceutical Preparations for Clinical Trials in EU Countries

C. Rossetti; Niguarda Hospital, Nuclear Medicine, Milan, ITALY.

PS06

Clinical Trials with Radiopharmaceuticals in Collaboration with Pharma Industry

D. Vugts; VU University Medical Center, Dept of Radiology & Nuclear Medicine, Amsterdam, NETHERLANDS.

PS07

Implications of the Updated Clinical Trial Regulation (EU Reg 536/2014) for the Research on Radiopharmaceuticals in a CRO Setting

H. Bergmann; Director Medical Writing, ABX-CRO advanced pharmaceutical services Forschungsgesellschaft mbH, Dresden, GERMANY.

PS2 **Saturday, October 13, 2018, 09:00 - 12:00, Hall 3**

Pre-Congress Symposium 2 - Bone & Joint / Oncology / GEMO: Nuclear Medicine Management of Bone Metastases in the Era of Targeted Treatments

PS09

Bone Oncologist's View - Bone Metastases Therapies in the Era of Targeted Treatments

P. Clézardin; INSERM Laboratory "Pathophysiology, Diagnosis & Treatments of Bone Diseases", Lyon, FRANCE.

PS10

Pathologist's View - Bone Response and Molecular Targets for Imaging

J.-M. Guinebreière; Pathology Department, Institut Curie, Site Hôpital René Huguenin, Saint-Cloud, FRANCE.

PS11

Bone Targeted Tracers

F. Paycha; Service de Medecine Nucleaire, Hopital Lariboisiere, Paris, FRANCE.

PS13

Tumour Targeted Tracers

M. Beheshti; PET - CT Center, Linz, AUSTRIA.

PS14

Quantification

T. Kuwert; Clinic of Nuclear Medicine, University of Erlangen-Nürnberg, Erlangen, GERMANY.

PS15

See the Forest for the Trees - RECIST, PERCIST, iRECIST, and PCWG-2?

E. Lopci; Nuclear Medicine department, Humanitas Clinical and Research Hospital, Milan, ITALY.

PS3 **Saturday, October 13, 2018, 09:00 - 12:00, Hall X**

Pre-Congress Symposium 3 - Translational Molecular Imaging & Therapy: The Role of Molecular Imaging in Radiation Oncology

PS16

Radiation Treatment Planning Using PET and Multimodal Imaging

L. Specht; Rigshospitalet, University of Copenhagen, Department of Oncology, Copenhagen, DENMARK.

PS17

Early Response Assessment in Radiation Therapy

R. Hustinx; University Hospital Center of Liege, Department of Nuclear Medicine and Oncology Imaging, Department of Medical Physics, Liège, BELGIUM.

PS18

Technology Development in Molecular Imaging Guided Radiotherapy

D. Jaffray; Institute of Biomaterials & Biomedical Engineering, University of Toronto, Department of Radiation Oncology, Department of Medical Biophysics, Toronto, CANADA.

PS20

Radiomics for Response Prediction in Radiation Oncology

M. Hatt; Institute of Health & Clinical Sciences, Brest, FRANCE.

PS21**Hypoxia and Resistance to Radiation Therapy**

B. Cornelissen; CRUK/MRC Oxford Institute for Radiation Oncology, University of Oxford, Department of Oncology, Oxford, UNITED KINGDOM.

PS22**Dose Painting by Hypoxia Imaging**

J. Kotzerke; Universitätsklinikum Carl Gustav Carus an der Technischen Universität Dresden, Dresden, GERMANY.

PS4

Saturday, October 13, 2018, 09:00 - 12:00, Hall Y

Pre-Congress Symposium 4 – Physics / AAPM:
Radiomics - Image Derived Parameters in
Multimodality Imaging

PS24**Basic Principles of Radiomics in Multimodality Imaging**

M. Hatt; Institute of Health & Clinical Sciences, Brest, FRANCE.

PS26**Radiomics - Robustness, Reproducibility, Standardisation**

A. Zwanenburg; OncoRay-Center for Radiation Research in Oncology, Dresden, GERMANY.

PS29**Radiomics Based Multi-Parametric Modeling - The Role of Data Mining / Machine Learning**

I. El Naqa; Michigan Medical School, Radiation Oncology, Physics Department, Michigan, UNITED STATES OF AMERICA.

PS31**Potential Role of Radiomics in Clinical Multimodality Imaging Based Research**

C. Cheze Le Rest; University of Poitiers, Faculty of Medicine, Poitiers, FRANCE.

PS5

Saturday, October 13, 2018, 09:00 - 12:00, Hall 28

Pre-Congress Symposium 5 - Neuroimaging / INMiND:
Imaging Neuroinflammation in Neurodegeneration

PS33**Target Identification**

A. M. Villa; University of Milan, Center of Excellence on Neurodegenerative Diseases and Department of Pharmacological and Biomolecular Sciences, Milan, ITALY.

PS34**Ligand Development**

B. Windhorst; VU University Medical Center, Department of Radiology & Nuclear Medicine, Amsterdam, NETHERLANDS.

PS35**Quantification**

R. Boellaard; VU University Medical Centre, Radiology and Nuclear Medicine, Amsterdam, NETHERLANDS.

PS37**Preclinical Studies**

H. Boutin; The University of Manchester, Wolfson Molecular Imaging Centre, Manchester, UNITED KINGDOM.

PS38**Clinical Studies**

A. Jacobs; University of Münster, European Institute of Molecular Imaging, Münster, GERMANY.

PS6

Saturday, October 13, 2018, 13:00 - 16:00, Hall 2

Pre-Congress Symposium 6 - Cardiovascular /
Inflammation & Infection / ASNC: Recent Imaging
Guidelines on Myocardial Amyloidosis, Sarcoidosis and
Large Vessel Vasculitis

PS40**Basis of Myocardial Metabolic Imaging**

R. R. Russell; Rhode Island Cardiovascular Institute, Rhode Island Hospital, The Warren Alpert Medical School of Brown University, Providence, UNITED STATES OF AMERICA.

PS41**Myocardial Amyloidosis - Clinical Perspective**

P. Soman; Division of Cardiology and The Heart and Vascular Institute, University of Pittsburgh Medical Center, Pittsburgh, UNITED STATES OF AMERICA.

PS42**Myocardial Amyloidosis - Imaging Guideline**

S. Dorbala; Cardiovascular Imaging Program, Departments of Medicine (Cardiovascular Division) and Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, UNITED STATES OF AMERICA.

PS43**Myocardial Sarcoidosis - Clinical Perspective**

R. Blankstein; Cardiovascular Imaging Program, Departments of Medicine (Cardiovascular Division) and Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, UNITED STATES OF AMERICA.

PS45**Myocardial Sarcoidosis - Imaging Guideline**

O. Gheysens; Department of Nuclear Medicine and Molecular Imaging, University Hospitals Leuven, Department of Imaging and Pathology, KU Leuven, Leuven, BELGIUM.

PS46**Large Vessel Vasculitis - Clinical Perspective**

D. Blockmans; General Internal Medicine Department, University Hospitals Leuven Leuven, Leuven, BELGIUM.

PS47**Large Vessel Vasculitis - Imaging Guideline**

R. Slart; Department of Nuclear Medicine and Molecular Imaging, University of Groningen, University Medical Center Groningen, Groningen, NETHERLANDS.

PS7

Saturday, October 13, 2018, 13:00 - 16:00, Hall 3

Pre-Congress Symposium 7 - Oncology / Physics: Radiomics, AI and Machine Learning in Hybrid Imaging

PS49**Radiomics, Radiogenomics, AI, Deep-Learning and Machine Learning - Definitions and Imaging Applications**

A. Boss; University Hospital Zurich, Dept. of Diagnostic and Interventional Radiology, Zurich, SWITZERLAND.

PS50**Basic Principles of Radiomics and Machine Learning - What Every Imaging Person should Have Understood by Now**

D. Visvikis; National Institute of Health and Clinical Science, Director Research INSERM, Brest, FRANCE.

PS51**PET-Radiomics - How to Compete with Morphological Imaging**

R. Hustinx; University Hospital Center of Liege, Department of Nuclear Medicine and Oncology Imaging, Department of Medical Physics, Liège, BELGIUM.

PS53**Radiomics and Machine Learning in CT - Oncological Applications**

S. Tanadini-Lang; University Hospital Zurich, Dept. Radiation Oncology, Zurich, SWITZERLAND.

PS54**Radiomics and Machine Learning in MRI - Oncological Applications**

V. Goh; King's College London, Dept. Cancer Imaging, London, UNITED KINGDOM.

PS55**Future Applications for Radiomics, Machine Learning and AI in Hybrid Imaging**

I. Jurisica; Krembil Research Institute, UHN and University of Toronto, Toronto, CANADA.

PS8

Saturday, October 13, 2018, 13:00 - 16:00, Hall X

Pre-Congress Symposium 8 - Oncology / Physics: Alpha-Endoradiotherapy in Solid Tumours

PS56**When do we need Endoradiotherapy, if any?**

P. Albers; Dept. of Urology, University Hospital Düsseldorf, Düsseldorf, GERMANY.

PS57**Tracer Development: When is Specific Specific?**

J. Babich; Radiopharmaceutical Sciences in Radiology, Weil/Cornell College, New York, UNITED STATES OF AMERICA.

PS58**Production of Alpha Emitting Isotopes: Can we get Enough?**

F. Haddad; Arronax Nantes and University of Nantes, Nantes, FRANCE.

PS59**Radio-Hybrid Ligands: Is there an All-Purpose Tracer?**

H.-J. Wester; Pharmaceutical Radiochemistry, TU Munich, Munich, GERMANY.

PS61**Alpha-Radioimmunotherapy, Bigger or Better?**

M. Chérel; Centre de Recherche en Cancérologie et Immunologie Nantes-Angers, University of Nantes, Nantes, FRANCE.

PS62**Endoradiotherapy with Alpha Emitters in NET and Prostate Cancer - Looking for the All-Purpose Isotope**

C. Kratochwil; Dept. of Nuclear Medicine University Hospital Heidelberg, Heidelberg, GERMANY.

PS63**Microenvironmental Reactions in Irradiated Tumours and their Use for Combination Therapy**

F. Herrera; Department of Oncology, University Hospital of Lausanne (CHUV), Lausanne, SWITZERLAND.

PS9

Saturday, October 13, 2018, 13:00 - 16:00, Hall Y

Pre-Congress Symposium 9 - Thyroid / Dosimetry: Dosimetry in Thyroid Cancer

PS65**Terms & Terminology - The Martinique Principles**

M. Luster; Universitätsklinikum Marburg, Nuclear Medicine, Marburg, GERMANY.

PS66**I-131 Therapy of Advanced DTC - Clinical Considerations**

L. Giovanella; Oncology Institute of Southern Switzerland, Nuclear Medicine and PET Centre, Bellinzona, SWITZERLAND.

PS67**Dosimetry in DTC - Physical Considerations and Procedures**

M. Lassmann; University Hospital Würzburg, Department of Nuclear Medicine, Würzburg, GERMANY.

PS69**Pro and Con Discussion - Dosimetrically Determined Activities in Advanced DTC - Pro**

D. Deandreis; University Hospital Turin, Department of Nuclear Medicine, Torino, ITALY.

PS70**Pro and Con Discussion - Dosimetrically Determined Activities in Advanced DTC - Con**

F. Verburg; University Hospital Marburg, Department of Nuclear Medicine, Marburg, GERMANY.

PS10

Saturday, October 13, 2018, 13:00 - 16:00, Hall 28

Pre-Congress Symposium 10 - Drug Development / Neuroimaging: Towards New Radiopharmaceuticals for Psychiatry

PS72**Is There Still a Place for PET Neuroimaging in the Understanding of Psychiatric Diseases?**

I. Rabiner; Imanova - Centre for Imaging Sciences, London, UNITED KINGDOM.

PS73**Contributions of PET Imaging of ABC Transporters at the Blood-Brain Barrier to the Evaluation of Psychotropic Drugs**

N. Tournier; CEA-Service Hospitalier Frédéric Joliot, Orsay, FRANCE.

PS74**Imaging of Serotonin Neurotransmission in Psychiatry**

R. Lanzenberger; Medical University of Vienna, Neuroimaging Labs, Vienna, AUSTRIA.

PS76**Metabotropic Glutamate Receptor Imaging in Psychiatry**

K. van Laere; KU Leuven, Nuclear Medicine Department, Leuven, BELGIUM.

PS77**What can PET Imaging of Synaptic Density Contribute to the Understanding of Neuropsychiatric Pathologies?**

E. Salmon; University of Liège, Cyclotron Research Centre, Liège, BELGIUM.

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Sunday, October 14, 2018, 08:00 - 09:30, Plenary Hall

CME 1 - Inflammation & Infection: Fever of Unknown Origin

OP-002**The Infectiologist's Point of View**

A. McGregor; Department of Infectious Diseases and Tropical Medicine, Northwick Park Hospital, London & Faculty of Medicine, Imperial College London, London, UNITED KINGDOM.

OP-003**Role of Nuclear Medicine in FUO Diagnosis: When and How to Use WBC Scintigraphy**

E. Lazzeri; Regional Center of Nuclear Medicine, Azienda Ospedaliero-Universitaria Pisana, Pisa, ITALY.

OP-004**Role of Nuclear Medicine in FUO Diagnosis: When and How to Use FDG-PET**

L.-F. de Geus-Oei; Leiden University, Leiden, NETHERLANDS.

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Sunday, October 14, 2018, 08:00 - 09:30, Hall 2

Joint Symposium 1 - Paediatrics / ESPN: The Role of Nuclear Medicine in Paediatric Febrile UTIs

OP-006**Imaging Role and Impact on Management of Paediatric Febrile UTIs**

P. Calhau; Hospital Garcia de Horta, Pediatric Department, Almada, PORTUGAL.

OP-007**Cortical Renal Scintigraphy with DMSA in Paediatric Febrile UTIs: Established Use and Future Developments**

I. Roca Bielsa; Hospital Vall D'Hebron, Nuclear Medicine, Barcelona, SPAIN.

OP-008**Radionuclides Studies for Vesico-Ureteric Reflux: What, Why, When**

D. de Palma; ASST-settelaghi, Nuclear Medicine, Varese, ITALY.

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Sunday, October 14, 2018, 08:00 - 09:30, Hall 3

Joint Symposium 2 - Oncology / EAU: Update on the Use of PET/CT in Testicular Cancer

OP-009**Clinical Impact of FDG PET/CT in Germ Cell Tumours - The Urologist's Point of View**

J. Walz; Institut Paoli Calmette, Urology, Marseille, FRANCE.

OP-010**Update on FDG PET/CT for Staging and Restaging of Seminomas**

Y. Lorient; Oncology Department, Gustave Roussy Institute, Paris, FRANCE.

OP-011**Current Status and Future Trends of PET/CT in NonSeminomatous Germ Cell Tumours**

N. Aide; Service de Médecine Nucléaire, Centre Régional de lutte contre le cancer François Baclesse, Caen, FRANCE.

OP-012**Take Home Message**

J. Walz; Institut Paoli Calmette, Urology, Marseille, FRANCE.

OP-013**Take Home Message**

M. Beheshti; PET - CT Center, Linz, AUSTRIA.

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Sunday, October 14, 2018, 08:00 - 09:45, Hall 5

CTE 1 - Technologists / SNMMI: Prostate Cancer Imaging and Therapy: Tech Guide Launch**OP-015****PET-CT Procedures Based on F-18 tracers in Prostate Cancer**

D. Gilmore; Regis College, Medical Imaging, Boston, UNITED STATES OF AMERICA.

OP-016**The Management of a Prostate Cancer Patient**

M. C. Attard; Isala Kliniek, Nuclear Medicine Department, Zwolle, NETHERLANDS.

OP-017**Future Perspectives and Pre-Clinical Studies in Prostate Cancer**

L. Evangelista; Nuclear Medicine and Molecular Imaging Unit, Veneto Institute of Oncology, Padova, ITALY.

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Sunday, October 14, 2018, 08:00 - 09:00, Hall X

M2M - Featured Session: PRRT - Understand & Improve**OP-018****PRRT - Understand & Improve**

M. De Jong; Erasmus MC Rotterdam, Department of Nuclear Medicine, Rotterdam, NETHERLANDS.

OP-019**Efficacy of ^{67}Cu -SARTATE targeted therapy in somatostatin receptor expressing tumours in mice**

E. M. van Dam¹, B. E. Rogers², N. Bandara², D. Tran², C. Mpoy²,

G. Gaehle², C. M. Jeffery¹, J. L. Stoner³, M. J. Harris¹; ¹Clarity Pharmaceuticals, Eveleigh, AUSTRALIA, ²Washington University, St Louis, MO, UNITED STATES OF AMERICA, ³Idaho Accelerator Center, Pocatello, ID, UNITED STATES OF AMERICA.

Introduction: Copper radionuclides have long been touted as an ideal pairing for theranostic PRRT. Whereas copper-64 (^{64}Cu) is a positron-emitter with a good half-life (12.7 h) for use with peptides for PET imaging, copper-67 (^{67}Cu) is a therapeutic radionuclide that has recently been able to be produced in sufficient quantities for clinical use and has a half-life (2.6 days) that makes it suitable for repeat dose studies. A first-in-human PET imaging trial using ^{64}Cu -MeCOSar-octreotate (^{64}Cu -SARTATE) to diagnose SSTR expressing NETs has been completed. Projected dosimetry estimates for a therapeutic dose of ^{67}Cu -SARTATE suggested repeat administrations of ^{67}Cu -SARTATE can safely be given to patients. However, preclinical data on the efficacy of fractionated dosing of ^{67}Cu -SARTATE is lacking. This study aims to determine the optimal dosing regime of ^{67}Cu -SARTATE in a therapeutic mouse model, varying dose levels, frequency, and timing of administration, to gain insight in the optimal dosing regime for ^{67}Cu -SARTATE in patients. **Methods:** Mice were inoculated subcutaneously with A427#7 cells, a cell line that stably overexpresses SSTR2. Once tumours reached $\sim 100\text{mm}^3$, mice were randomised into treatment groups. Mice received either saline, ^{67}Cu -SARTATE or ^{177}Lu -DOTA-octreotate (Lutathera). Tumour volume and body weight was monitored thrice weekly. Mice were euthanized once tumours reached a volume of 4000mm^3 . Tumour volume (mm^3) was calculated as length (mm) x width (mm) x width (mm)/2. Administered activity range of ^{67}Cu -SARTATE or Lutathera was from 5 to 55 MBq. **Results:** The results of the ^{67}Cu -SARTATE dose escalation efficacy study in tumour bearing mice showed all dose levels were well tolerated and no toxicity was observed in any of the groups as assessed by general monitoring of body weight changes. The tumour growth inhibition (TGI) as measured on day 16 after treatment ranged from 45% at 10 MBq of ^{67}Cu -SARTATE to 90% at 55 MBq of ^{67}Cu -SARTATE. In a second study, the efficacy of fractionated administration of ^{67}Cu -SARTATE was assessed. ^{67}Cu -SARTATE was administered at 30 MBq at a single dose on day 1, or as 15 MBq administered on day 1 and 8, or day 1 and 15. There was no significant difference in TGI as measured on day 23, the last day all control mice were alive, between the 3 treatment groups and ranged between 86 and 95%. No significant differences between SARTATE and Lutathera treatments were observed. **Conclusions:** ^{67}Cu -SARTATE has a good efficacy profile and shows promise as a therapeutic agent to treat SSTR2 expressing cancers.

OP-020**Potentiating ^{177}Lu -DOTATATE Therapy By HSP90 Inhibition - First In Vivo Study**

S. Lundsten, D. Spiegelberg, N. Raval, B. Stenerlöw, M. Nestor; Uppsala University, Uppsala, SWEDEN.

Aim: ^{177}Lu -DOTATATE is approved for therapy of gastroenteropancreatic neuroendocrine tumors and has exhibited impres-

sive treatment in the clinic. Onalespib, an HSP90-inhibitor, is currently in clinical trials and previous studies with the compound demonstrated radiosensitizing effects. The aim of this study was to investigate potential radiosensitizing effects and toxicity profiles of ^{177}Lu -DOTATATE together with Onalespib. **Methods:** Effects of Onalespib and/or ^{177}Lu -DOTATATE were initially assessed in somatostatin receptor (SSTR) positive and negative cell lines grown in 3D tumor spheroids. Biodistribution of ^{177}Lu -DOTATATE was assessed in SSTR positive and negative tumor xenografts. An *in vivo* therapy study with SSTR positive xenografted tumors was performed where tumor growth, metastatic burden and toxicity was monitored over time. Metastatic burden was monitored by regularly weighing animals, assessing morphology of organs post-mortem and SPECT/CT imaging to detect SSTR positive lesions. Immunohistochemistry of critical organs and tumors was used to assess short- and long-term toxicity and response to therapy. **Results and discussion:** *In vitro* assays displayed synergistic effects of combining Onalespib and ^{177}Lu -DOTATATE. Biodistribution demonstrated high and specific uptake of ^{177}Lu -DOTATATE in SSTR positive tumors, significantly higher than in SSTR negative tumors. The therapeutic study resulted in significantly reduced tumor growth in the ^{177}Lu -DOTA-TATE and combination groups, with best effect in the combination group. Animal weights indicated no overlapping toxicities. SPECT/CT imaging verified high and specific ^{177}Lu -DOTATATE uptake in SSTR positive tumors, independent of Onalespib treatment. **Conclusions:** This first *in vivo* study of Onalespib as ^{177}Lu -DOTATATE radiosensitizer displays promising results, with reduced tumor growth and low toxicity. This approach could lead to more effective ^{177}Lu -DOTATATE treatments, potentially also reducing radiation exposure and undesirable side effects in normal tissues. By further understanding the mechanisms behind this radiosensitizing effect, the treatment regime can be further optimized.

OP-021

Mapping the Radiobiology of Targeted Radionuclide Therapy in an *in vivo* Model for Neuroendocrine Cancer

D. Feijtel, G. N. Doeswijk, N. S. Verkaik, J. C. Haecck, M. C. Clahsen-van Groningen, M. W. Konijnenberg, D. C. van Gent, M. de Jong, J. Nonnekens; Erasmus MC, Rotterdam, NETHERLANDS.

Aim: Neuroendocrine tumors (NETs) are a relatively rare form of cancer. However, patients are often presented with metastases, making resection as a treatment strategy alone insufficient. In the clinic, localization of NETs has been assessed by targeting the highly expressed somatostatin receptor subtype 2 (SSTR2) on NET cells, with radiolabeled somatostatin analogues. By radiolabeling these analogues (e.g. DOTA-(Tyr3)-octreotate (DOTA-TATE)) with DNA-damaging radionuclides, this imaging modality has been transformed into a strategy to treat the disease: peptide receptor radionuclide therapy (PRRT). PRRT with Lutetium-177-DOTA-TATE proves effective in improving both progression-free and overall survival and quality of life. To further increase the therapeutic efficacy, we set out to deepen the current knowledge on the effects of PRRT on the tumor and dose-limiting organs (bone marrow and kidney). **Materials and**

methods: NCI-H69, a small cell lung cancer cell line that highly expresses SSTR2 was treated *in vitro* with 1MBq/mL ^{177}Lu -DOTA-TATE (molar activity 18.5MBq/0.5 μg), after which cytopsins were assessed for DNA damage markers on multiple timepoints. DNA double strand break (DSB) induction was observed using 53BP1, γH2AX and RAD51 immunofluorescent stainings. NCI-H69 cells were also engrafted subcutaneously on BALB/c-nude mice to assess the ^{177}Lu -DOTA-TATE response *in vivo*. Mice were treated with 30MBq/mouse ^{177}Lu -DOTA-TATE (molar activity 30MBq/0.5 μg), euthanized at different time points until 14 days post-treatment, and tumors, bone marrow and kidneys were isolated for DNA damage response (DDR) analyses. **Results:** Following PRRT we observed differential intensity in DNA damage signaling and subsequent repair in a time-dependent manner. Contrasting the homogeneity of SSTR2 receptor distribution, we observed intra-tumoral heterogeneity in terms of apoptosis and activation of the DDR machinery. The peak of DSB repair was observed at two days after treatment. Resolve of these DSBs are, at least in part, be conveyed by homologous repair, as we observed RAD51 focus formation. Interestingly, acute, but transient damage was observed in bone marrow and kidneys. Possible late effects have not been studied. **Conclusion:** In this study we investigated the radiobiology of PRRT in a preclinical setting on a (sub)cellular level. Our results will contribute to a better understanding of the effects of PRRT on its target and healthy tissue. Repair of DNA damage during the exposure by PRRT forms a crucial element in delivering an efficacious therapy while keeping damage to normal organs controllable. This might potentiate future patient treatment by revealing novel therapeutic windows. If and how intra-tumoral heterogeneity might influence therapy response warrants further investigation.

OP-022

Understanding The Radiobiology Of Targeted Radionuclide Therapy With ^{177}Lu -dotatate

W. Delbart, Z. Wimana, M. Vercruyssen, N. Meuleman, G. Ghanem, P. Flamen; Jules Bordet Institute, Brussels, BELGIUM.

Aim: Several mechanisms affecting radiosensitivity have been investigated, namely proliferation rate, metabolism, cell cycle, DNA repair, the degree of chromatin compaction and oxidative stress. Their importance in radiobiology stems from external beam radiotherapy (EBRT) studies and is mostly related to direct DNA damage. However, when using targeted radionuclide therapy with low-LET β^- emitter (eg. Lutetium-177 (^{177}Lu)), generation of reactive oxygen species is more likely to occur hence also affecting cell redox-balance and viability. Our aim is to investigate these radiosensitivity parameters following ^{177}Lu -DOTATATE treatment in somatostatin receptors (SSTR) expressing tumors. **Materials and methods:** Human cancer cell lines were selected for their different intrinsic radiosensitivities to EBRT: HBL and MM162 (melanoma, radioresistant), COLO-677 and EJM (multiple myeloma, radiosensitive), MIA-PACA-2 and HT-29 (pancreatic and colon neuroendocrine tumor (NET), intermediate radioresistance). SSTR expression was assessed by qRT-PCR and western blot and its functionality by binding/uptake assays with 20kBq

of $^{68}\text{Ga}/^{177}\text{Lu}$ -DOTATATE. Cell lines were treated with different activities of ^{177}Lu -DOTATATE (100–2000 kBq, 2h incubation) and cell viability assessed at three time-points (1–3–6 days) using MTT assay. The different parameters of radiosensitivity were evaluated by means of MTT assay, ^{18}F FDG uptake and qRT-PCR of antioxidant defense enzymes (catalase, glutathione (GSH) peroxidase, GSH reductase). **Results:** SSTR expression and $^{68}\text{Ga}/^{177}\text{Lu}$ -DOTATATE uptake was present in all cell lines with the highest uptake observed in MM162 and was by about 4 folds higher than in EJM and 2 folds higher as compared to the control NET MIA-PACA-2. Cell survival after ^{177}Lu -DOTATATE treatment was time and radioactivity dependent. Six days after incubation it was significantly reduced in all cell lines (COLO-677: $64\pm 9\%$, EJM: $58\pm 4\%$, MIA-PACA-2: $35\pm 15\%$, HBL: $30\pm 4\%$, MM162: $24\pm 6\%$) but was particularly low, if present, in HT-29 ($3\pm 13\%$). Interestingly, the later exhibited two folds higher expression of antioxidant enzymes compared to the most affected cell lines (relative expression for HT-29: 0.006 ± 0.002 vs COLO-677 : 0.003 ± 0.001 and EJM : 0.004 ± 0.002 , $p = 0.03$). In contrast, the other radiosensitivity parameters were not found to be significantly associated with cell survival. **Conclusion:** Our results show the presence and the functionality of SSTR and differences in radiosensitivity parameters in all cell lines. Although all these characteristics are likely to affect response to treatment with ^{177}Lu -DOTATATE, the expression of enzymes linked to antioxidant defenses was the only significant difference between radioresistant and radiosensitive cell lines. Therefore and in this context of metabolic radiotherapy, antioxidant defense mechanisms must be considered along with DNA damage assessment.

OP-023

$^{111}\text{In}/^{177}\text{Lu}$ -DOTA-[Tyr³]-albutate-1, a novel long circulating radiotracer for the somatostatin receptor subtype 2

S. T. van Tiel¹, T. Maina-Nock², B. A. Nock², E. de Blois¹, M. W. Konijnenberg¹, J. Nonnekens¹, G. N. Doeswijk¹, M. R. Bernsen¹, M. de Jong¹; ¹ErasmusMC, Rotterdam, NETHERLANDS, ²NCSR "Demokritos", Athens, GREECE.

Aim: Currently, radiolabelled DOTA-Tyr³-octreotate (DOTA-Tate) is successfully applied in the clinic to image and treat neuroendocrine somatostatin receptor subtype 2 (SSTR₂)-positive tumors. To further improve therapeutic efficacy, the tumor uptake of the radioactive tracer should be enhanced. One way to achieve this is by prolonging the tracer circulation time. Toward this goal, we developed DOTA-albutate-1, a DOTA-Tate derivative coupled to an albumin-binding domain. The aim of this study is to determine the characteristics of the novel $^{111}\text{In}/^{177}\text{Lu}$ -DOTA-albutate-1 analogue. **Material and method:** The IC₅₀ of DOTA-albutate-1 was established using autoradiography on fresh-frozen SST_{2R}-positive tumor sections. In vitro cell-uptakes and internalisation rates for ^{111}In -DOTA-Tate and ^{111}In -DOTA-albutate-1 were determined in H69 human small cell lung cancer cells. A comparative biodistribution study was also performed for both ^{177}Lu -labelled peptides in mice bearing H69 xenografts. Animals ($n=4$ for each time point) were injected intravenously with 0.5 $\mu\text{g}/30$ MBq ^{177}Lu -DOTA-Tate or ^{177}Lu -DOTA-albutate-1 together with gelofusine to reduce renal uptake. Mice were euthanized at

different time points post injection (pi); organs and tumors were collected and percentage injected dose per gram tissue (%ID/g) was determined. **Results:** The IC₅₀ value of DOTA-albutate-1 was 1.2 nM, similar to that of DOTA-Tate (1.5 nM). Both ^{111}In -labelled tracers showed a comparably high internalisation rate, with a higher percentage of radioactivity found in the cell fraction than in the membrane fraction (^{111}In -DOTA-albutate-1 14.0 vs 1.9 % of added radioactivity; ^{111}In -DOTA-Tate 11.0 vs 1.5 % of added radioactivity). ^{177}Lu -DOTA-Tate was cleared rapidly from the circulation, while ^{177}Lu -DOTA-albutate-1 still showed 58% ID/g at 1 h pi and 2 %ID/g at 168 h pi. Tumor uptake and retention differed significantly between ^{177}Lu -DOTA-Tate (5%ID/g at 1 h pi decreasing to <3 %ID/g at 24 h pi) and ^{177}Lu -DOTA-albutate-1 (with the highest uptake of 24%ID/g at 24 h pi reaching 8%ID/g at 168 h pi). The tumor:kidney ratio of ^{177}Lu -DOTA-albutate-1 increased from 0.35 at 1 h to 6.5, whereas for ^{177}Lu -DOTA-Tate this ratio increased from 0.8 to 17. **Conclusion:** ^{177}Lu -DOTA-albutate-1 circulated in blood for a longer period than ^{177}Lu -DOTA-Tate, leading to tumor uptake enhanced by a factor 8 at 24 h; all tissues showed higher radioactivity levels compared to ^{177}Lu -DOTA-Tate. Dosimetry is currently ongoing to investigate bone marrow radiotoxicity risks potentially induced by the prolonged circulation of ^{177}Lu -DOTA-albutate-1.

OP-024

Differences on the Mechanism of Action between the Radiolabeled Somatostatin Receptor Antagonist ^{177}Lu -OPS201 and the Agonist ^{177}Lu -DOTA-TATE: an in vitro Investigation

R. Mansi¹, D. Santoianni-Klauer¹, L. Del Pozzo¹, P. Plas², M. Fani¹; ¹University Hospital Basel, University of Basel, Basel, SWITZERLAND, ²Ipsen, Institut Henri Beaufour, Les Ulis, FRANCE.

Aim: The increased clinical evidences of advantages using radiolabeled somatostatin receptor subtype 2 (sstr2) antagonists instead of agonists in neuroendocrine tumour patients pose several questions on their mechanism of action in cellular level. In order to understand why sstr2-antagonists outperform agonists, we performed comparative *in vitro* studies on cell membranes expressing sstr2. We investigated the binding capacity (K_D and B_{max}) and the ligand-receptor binding kinetics of the radiolabeled sstr2-antagonist ^{177}Lu -OPS201 and sstr2-agonist ^{177}Lu -DOTA-TATE. In addition, we investigated whether the two analogs can be alternatively displaced by each other. **Materials:** ^{177}Lu -OPS201 and ^{177}Lu -DOTA-TATE were studied under identical experimental conditions using HEK-hsstr2 cell membranes. Saturation binding experiments were performed with increased concentrations of each radioligand, ranging from 0.075 to 10 nM, at 37°C. Kinetic experiments were performed using different concentrations of each radioligand, based on their respective K_D . Their association rate was followed up to 4h at 37°C. The dissociation was studied up to 3h, after association of the radioligands for 1h. Displacement experiments were performed with the addition of 1,000-fold excess of either of the competitors, natLu-OPS201 or natLu-DOTA-TATE (nat: natural Lu). The data were analyzed employing the corresponding equations of GraphPad Prism 7 Software. **Results:** ^{177}Lu -OPS201 recognizes

3.7-times higher number of binding sites than ^{177}Lu -DOTA-TATE (B_{max} : 0.261 vs 0.071 nM, respectively), while the K_D values are on a similar level (0.073 ± 0.009 vs 0.112 ± 0.054 nM, respectively). ^{177}Lu -OPS201 associates much faster than ^{177}Lu -DOTA-TATE, reaching a plateau within 15 min ($k_{\text{obs}} = 0.45 \pm 0.08 \text{ min}^{-1}$ for ^{177}Lu -OPS201 and $0.072 \pm 0.008 \text{ min}^{-1}$ for ^{177}Lu -DOTA-TATE). The radioantagonist when bound to sstr2 can only be displaced by agonist in excess up to a certain extend; ^{177}Lu -OPS201 is only displaced by 40% in the presence of 1,000-fold excess of ^{177}Lu -DOTA-TATE within 3h, while it is completely displaced by excess of ^{177}Lu -OPS201 ($T_{1/2} = 49.8 \text{ min}$). The observation is different for the radioagonist when bound to sstr2. ^{177}Lu -DOTA-TATE is completely displaced by both agonist and antagonist, though following different dissociation kinetics. ^{177}Lu -OPS201 displaces completely ^{177}Lu -DOTA-TATE within 24h ($T_{1/2} = 212 \text{ min}$), while ^{177}Lu -DOTA-TATE displaces ^{177}Lu -DOTA-TATE much faster ($T_{1/2} = 6.3 \text{ min}$). **Conclusion:** ^{177}Lu -OPS201 and ^{177}Lu -DOTA-TATE show significant differences in their binding kinetics. The inability of the agonist to completely displace the radioantagonist bound to sstr2 is a first indication that ^{177}Lu -OPS201 binds not only to additional, but also to different, binding sites that are not recognized by ^{177}Lu -DOTA-TATE.

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Sunday, October 14, 2018, 08:00 - 09:00, Hall Y

Do.MoRe: SPECT-CT

OP-025

General Purpose Whole-body Solid State CZT and Standard SPECT/CT Cameras: Characterization and Dual Isotope $\text{Tc}^{99\text{m}}$ / I^{123} Quantitation

J. Kennedy^{1,2}, R. Lugassi¹, Z. Keidar^{1,2}; ¹Rambam - Health Care Campus, HAIFA, ISRAEL, ²Technion – Israel Institute of Technology, Haifa, ISRAEL.

Purpose: To compare performance characteristics between a solid state cadmium zinc telluride (CZT) based whole-body SPECT/CT camera (CZTC) and a standard sodium iodide (NaI) based device (NaIC), including assessment of dual isotope $\text{Tc}^{99\text{m}}$ / I^{123} acquisitions. **Methods:** NEMA (National Electrical Manufacturers Association) measurements of spatial resolution, sensitivity, and energy resolution were compared for CZTC (Discovery 670 CZT) with 5 mm thick detector crystals and NaIC (Discovery 670). CZTC was configured with 50 mm, and then 45 mm long collimator holes (CZTC50 and CZTC45, respectively). Spatial resolution was also estimated at distances 0 to 24 cm from each detector. Image quality was assessed for a NEMA body phantom emulating clinical count rates loaded with a “lung” insert and 6 hot spheres with a 12:1 target-to-background ratio (TBR) of $\text{Tc}^{99\text{m}}$ and of I^{123} . A second phantom trial was performed with the same configuration except the 10, 17, and 28 mm diameter spheres were reloaded to increase the $\text{Tc}^{99\text{m}}$ TBR to 47:1, leaving all other TBRs at 12:1. Assessed phantom parameters included residual error of the lung insert and the mean squared error (MSE) of peak standardized uptake values of each sphere, normalized to remove the effect of recovery coefficients, with respect to the loaded

TBRs. **Results:** Spatial resolution measurements for CZTC50 and CZTC45 were similar ($5.6 \pm 0.4 \text{ mm}$ and $5.3 \pm 0.1 \text{ mm}$, respectively) and significantly superior to NaIC ($7.3 \pm 0.1 \text{ mm}$). CZTC spatial resolution estimates were better than NaIC at all distances. Planar sensitivity of CZTC45 (70.5 cps/MBq per head) was comparable to NaIC (75.9 cps/MBq) and greater than CZTC50 (56.6 cps/MBq). The system energy resolution for CZTC (5.5 %) was superior to NaIC (9.2 %). MSE was larger for CZTC $\text{Tc}^{99\text{m}}$ images compared to NaIC (0.60 vs. 0.40) but smaller for CZTC for I^{123} images (0.10 vs. 0.20) and for CZTC $\text{Tc}^{99\text{m}}$ and I^{123} results of just the 3 reloaded spheres (0.09 vs. 0.21 and 0.02 vs. 0.19). The lung residual error was similar between CZTC and NaIC for $\text{Tc}^{99\text{m}}$ images (59 % vs. 60 %), but lower for the CZTC I^{123} images (39 % vs. 49 %). **Conclusion:** CZTC showed superior spatial and energy resolution compared to NaIC. System planar sensitivities were similar for CZTC45 and NaIC. Image quality for dual energy $\text{Tc}^{99\text{m}}$ / I^{123} was visually similar between CZT and standard cameras. Smaller MSE and lung residual error with CZTC suggests less cross-talk between $\text{Tc}^{99\text{m}}$ and I^{123} peaks, showing potential for superior dual isotope $\text{Tc}^{99\text{m}}$ / I^{123} quantitation.

OP-026

Towards a vendor-independent standard for absolute quantitative SPECT/CT

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Introduction: Absolute quantification of radiotracer distribution using SPECT/CT holds great potential for dosimetry aimed at personalized radionuclide precision treatment. However, its accuracy depends on many parameters. Using phantom measurements, this multi-vendor and multi-center study evaluates the quantitative accuracy and inter-system variation of various SPECT/CT systems as well as the effect of patient size and reconstruction algorithms on recovery coefficients (RC), aiming at defining a new standard for quantitative SPECT. **Methods:** Four state-of-the-art SPECT/CT systems were included: DiscoveryTM NM/CT 670 Pro (General Electric Healthcare), PrecedenceTM 6 (Philips Healthcare), Symbia IntevoTM and SymbiaTM T16 (Siemens Healthineers). RC were determined using three phantoms based on the NEMA IEC body phantom without lung insert simulating body mass indexes (BMI) of 24, 28 and 47 kg/m². The six spheres (0.5–26.5 mL) and background were filled with 0.10 and 0.01 MBq/mL $\text{Tc}^{99\text{m}}$ -pertechnetate, respectively. Volumes of interest (VOI) of spheres were obtained by a 50% region growing method based on maximum voxel value corrected for background activity. RC, defined as imaged activity concentration divided by actual activity concentration, were determined for maximum (RC_{max}) and mean voxel value (RC_{mean}) in the VOI. Accuracy was determined per sphere volume as the RC averaged over all systems. Inter-system variation was expressed as standard deviation (SD). Acquisition settings were standardized

for all systems. Images were reconstructed using vendor specific 3D iterative reconstruction algorithms with institute specific clinical settings. Additionally, all data for the BMI 25 kg/m² phantom were reconstructed with a vendor neutral reconstruction algorithm (Hermes Hybrid Recon™). Image analysis was performed in Python using the SimpleITK framework. **Results:** Accuracy of RC_{mean} decreased from 0.99 to 0.25 with decreasing sphere volume from 26.5 to 0.5 mL, with an average inter-system variation of 0.15 ± 0.08 . For phantoms of BMI 28 and 47 kg/m², accuracy of RC_{mean} decreased for spheres > 1.15 mL, while smaller spheres could not be identified in the images. A large overshoot for RC_{max} was found, reaching 1.39 for the largest sphere. Reconstruction with vendor neutral software improved the accuracy of RC_{mean} up to 30% (inter-system variation: 0.13 ± 0.05) but increased RC_{max} overshoot. **Discussion/Conclusion:** Vendor-neutral reconstruction improves both accuracy and inter-system variation of RC, while phantom size (BMI) impacts only accuracy. We demonstrate the feasibility of absolute SPECT quantification in a multi-center and multi-vendor setting. Our standardized approach for image acquisition, reconstruction and analysis paves the way for a vendor-independent standard for quantitative SPECT.

OP-027

Establishment of Optimized SPECT/CT Protocol for Therapy with ¹⁶¹Tb Demonstrate Improved Image Quality with Monte Carlo Based OSEM Reconstruction

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Introduction: Targeted radionuclide therapy with ¹⁷⁷Lu labeled somatostatin analogues for neuroendocrine tumors or prostate specific membrane antigen ligands for prostate cancer has proven to be efficacious and safe. However, relapse occurs even in cases of complete remission. It is, therefore, important to accomplish high absorbed doses in micrometastases, which ¹⁷⁷Lu may not be optimal for due to the range of its emitted electrons. ¹⁶¹Tb emits a large amount of low energy auger and conversion electrons, which implies that a higher absorbed dose to micrometastases may be achieved. ¹⁶¹Tb also emits gamma photons of energies between 25 and 75 keV, which enables imaging with single photon emission computed tomography (SPECT). ¹⁶¹Tb may be a better alternative than ¹⁷⁷Lu for treating micrometastases, but whether SPECT imaging of ¹⁶¹Tb with sufficient image quality may be done is unknown. The aim of this study was to assess the feasibility of SPECT imaging with ¹⁶¹Tb and to develop and optimize a protocol. **Materials and methods:** Patient-sized Jaszczak and lung phantoms including hollow sphere inserts were filled with ¹⁶¹Tb and imaged with a gamma camera using three different collimators and two emission energy windows. SPECT raw data of various scan times were simulated. Images were reconstructed using three ordered subset expectation maximization (OSEM) algorithms, attenuation corrected (AC), AC

and scatter corrected (ACSC) and the Monte Carlo based Sahl-grenska academy reconstruction code (SARec). Image quality was assessed visually and by calculating signal to background ratio (SBR) and signal to noise ratio (SNR). A line phantom was also filled with ¹⁶¹Tb and used for further development of SARec. **Results:** SARec showed higher SBR and SNR and better visual rendering of the hot spheres than AC and ACSC for most sphere sizes. The LEHR collimator provided high resolution in resulting images and more defined edges of the spheres. The energy window between 67.1 and 82.1 keV provided the best image quality by visual assessment. The imaging time affected the noise and thus SNR. SBR, however was unaffected. **Conclusion:** Attenuation and scatter are inevitable in SPECT imaging of patients. The measurements with the human-sized phantoms demonstrate that gamma camera imaging of ¹⁶¹Tb with good image quality is feasible in patients. A protocol with specified collimator and energy window was developed. Quantitative studies are needed to assess collection time, activity amounts for acceptable statistics and attenuation and scatter characteristics.

OP-028

Quantitative Assessment Of Accuracy And Precision For High Count Rate Spect Imaging Of 99mTc And 177Lu

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Aims: Theranostics applications require SPECT imaging at high count rate. The aim is to characterize the ability of real-time integrated correction methods for high count rate losses in quantitative SPECT imaging with ^{99m}Tc and ¹⁷⁷Lu. **Methods:** Siemens developed a proprietary algorithm that stabilizes the energy response at high count rates and estimates the losses due to dead time for the Symbia Intevo systems in real time ("TrueCalc™"). Count loss information is obtained per projection view and used within the quantitative SPECT reconstruction xSPECT Quant to correct for dead time. We measured activity concentration on 6 Symbia Intevo systems at the factory equipped with both 3/8" and 5/8" detector crystals. The systems were calibrated for quantitative imaging using 3% NIST traceable ⁵⁷Co and ⁷⁵Se point sources for ^{99m}Tc and ¹⁷⁷Lu imaging, respectively. We assessed quantitative accuracy and precision with TrueCalc enabled using a uniformly filled standard quality control cylinder phantom. The activities ranged from 650 MBq - 1 GBq of ^{99m}Tc and from 1 GBq - 7.4 GBq of ¹⁷⁷Lu obtaining incident count rates up to 310 kc/s per detector. Additionally we measured up to 700 kc/s per detector using 7.4 GBq of ^{99m}Tc with and without TrueCalc enabled at various time points while the phantom was decaying to 4 T_{1/2}. We acquired each data set with 24 million counts over 360 degrees using a standard clinical acquisition workflow. Data were reconstructed with xSPECT Quant using the recommended clinical parameters. We recorded the deviation of the average reported activity concentration in a large ellipsoidal VOI from the true activity concentration reported by the cross calibrated dose calibrator. **Results:** For ¹⁷⁷Lu, the average absolute deviation and its uncertainty (1SD) from the true activity concentra-

tion across the 6 systems was $1.4\% \pm 1.1\%$ at low count rates and $2.1\% \pm 1.3\%$ at 310 kc/s with TrueCalc. The ^{99m}Tc measurements resulted in an average deviation of $1.5\% \pm 1.0\%$ at low count rates and $2.5\% \pm 1.1\%$ at 310 kc/s with TrueCalc. The difference to reference at 700 kc/s was -3.0% with TrueCalc enabled and -19.1% without. **Conclusion:** Activity concentration accuracy is within 2.5% when using TrueCalc on the xSPECT Quant platform for count rates up to 310kc/s incident count rate per detector. At 700kc/s the bias reduced from -19.1% without TrueCalc to -3.0% with TrueCalc. Future work will include a population of patients and various studies with other isotopes.

OP-029

Myocardial Blood Flow Quantitation with Comprehensive Image Corrections: Head-to-Head Comparison between Conventional Dual-head SPECT and CZT SPECT

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Aim: The capability of myocardial blood flow quantitation (MBFQ) has been demonstrated by conventional dual-head SPECT (C-SPECT) and CZT SPECT systems recently. However, the difference in measurement of numerical flow value between these systems under the same imaging setting and corrections still need further investigation. **Materials and Methods:** Twenty patients with congestive heart failure (CHF) and a control group of subjects without CHF were included for comparison of rest flow (RMBF) quantified by dynamic SPECT (DySPECT) image data acquired from C-SPECT and CZT-SPECT. The imaging protocol utilized the same imaging setting on both systems, including patient preparation, injection dose of ^{99m}Tc -Sestamibi tracer (20 mCi) and timing, for DySPECT acquisitions on two separate days. Frame-mode of DySPECT data for C-SPECT were acquired in the format of $10 \times 10 \text{ sec} + 5 \times 20 \text{ sec} + 2 \times 60 \text{ sec} + 1 \times 280 \text{ sec}$ (18 dynamic frames in 10 minutes). List mode data of CZT-SPECT were acquired and rebinned to create frame-mode data matching with C-SPECT. All DySPECT images were reconstructed with full physical corrections (attenuation, scatter, resolution and noise) and utilized to quantify flow parameters (K1, k2) with one-tissue kinetic model. RMBF was converted from K1 with additional corrections for rate pressure product and MIBI extraction. Global RMBF values of the same cohorts from C-SPECT and CZT-SPECT were then mutually compared with T-test, linear regression (LR) and Bland-Altman (BA) plots to assess the difference between these two systems. **Results:** Significantly lower global RMBF was found in the CHF group than the control group on either C-SPECT (0.74 ± 0.28 vs 1.14 ± 0.18) or CZT-SPECT (0.71 ± 0.26 vs 1.12 ± 0.15) (all $p < 0.0001$). For the CHF group, no significant difference ($p = 0.0644$) between C-SPECT and CZT-SPECT revealed LR as $y(C) = 1.0412x(\text{CZT})$ ($R = 0.973$) with small systemic difference ($\Delta = 0.03$ ml/min/g, 95% CI: -0.11 - 0.20) in BA plot. For the control group, LR was $y(C) = 1.025x(\text{CZT})$ ($R = 0.8872$) with small systemic difference ($\Delta = 0.02$ ml/min/g, 95% CI: -0.14 - 0.19) in BA plot also showed no significant difference ($p = 0.2114$) between these two systems respectively. **Conclusion:** Under the same

image setting, DySPECT images processed with comprehensive image corrections warrant closely similar flow measurement independent of SPECT systems.

OP-030

Comparison of performances of analogical and digital SPECT/CT imaging systems

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Introduction: Recently, general-purpose whole-body CZT digital SPECT/CT systems have been developed for clinical use. These digital SPECT systems may replace traditional Anger-camera based analogical SPECT systems in near future. In this study, the performance of Discovery NM/CT 670 CZT digital SPECT/CT (GE Healthcare, Tirat Hacarmel, Israel) was compared with the same manufacturer's latest analogical Discovery NM/CT Pro imaging system. The aim was to show the advantages of digital gamma-camera technology. **Materials and methods:** The performance measurements of both imaging systems followed a current NEMA standard [1]. All measurements appropriate for both systems were carried out. ^{99m}Tc isotope was employed and an energy window was $140 \text{ keV} \pm 10\%$ in all relevant tests. In the analogical system (AS), low-energy high-resolution collimators and in the digital system (DS) wide-energy high-resolution collimators were used. When a test can be applied to both gamma-camera detector-heads, or when several equivalent performance figures are achieved, the results are given in ranges (min - max). **Results:** The tests applicable for both imaging systems were selected for comparison. Intrinsic energy-resolution was 9.47 - 9.50% for AS and 6.14 - 6.27% for DS. Integral intrinsic uniformity was 2.48 - 2.95% for AS and 0.87 - 1.00% for DS and differential was 1.11 - 1.54% for AS and 0.67 - 0.86% for DS. Intrinsic maximum count rate in air at 20% energy window was 412.7 - 416.5 kc/s for AS and 355 - 357 kc/s for DS. System spatial-resolution with scatter resulted in 7.8 - 7.85 mm (FWHM) for AS and 7.65 - 7.95 mm (FWHM) for DS without and 6.40 - 6.95 mm (FWHM) with Clarity 2D filter of 40% (Clarity40). The system volume-sensitivity at 20% energy-window was 290856 cps/MBq/cm³ for AS and 364078 cps/MBq/cm³ for DS. SPECT reconstructed spatial-resolution with scatter was 6.55 - 9.90 mm (FWHM) for AS and 6.40 - 10.60 (FWHM) for DS and whole-body system spatial-resolution without scatter was 6.2 - 6.5 mm (FWHM) for AS and 5.5 - 6.4 mm (FWHM) for DS with Clarity40. Discussion and **Conclusions:** DS has superior intrinsic energy-resolution and intrinsic uniformities compared to AS. DS has also better sensitivity and system spatial-resolution especially when Clarity40 was utilized. SPECT spatial-resolutions, however, do not differ between the systems because of the basic filtered back-projection algorithm used to reconstruct the images in accordance with the standard. **References:** [1] NEMA NU 1-2012, Performance Measurements of Gamma Cameras, NEMA Standards Publication, 2012.

OP-031**Learning SPECT detector response for Monte-Carlo simulations**

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Introduction: The use of Artificial Neural Networks (ANN) was investigated to learn detector response in Monte-Carlo (MC) simulation of imaging systems in order to replace computationally costly particle tracking in the detector. The proposed method is applied to speed-up simulation of collimator-detector systems with Angular Response Function (ARF) for SPECT imaging. **Method:** In SPECT MC simulation, the collimator-detector response function (CDRF), which combines the accumulated effects of all interactions in the imaging head, may be approximated with the ARF method [1,2]. It replaces photon tracking inside the imaging head by a tabulated model of the CDRF, build with a histogram (denoted histo-arf) computed from a training simulation. This approach has previously been shown to be efficient and provides variance reduction that greatly speeds up the simulation. One limitation is that computing the tabulated functions is a time-consuming process: about $1e11$ emitted primary photons are required to obtain good statistical uncertainty. We replaced ARF tables with ANN, trained with data obtained from MC simulations. Russian-Roulette was used to decrease data size. Once trained, the nn-arf was used like the histo-arf to estimate the probability of a photon with given incident angles and energy to be detected in each energy window. All development was performed with the open-source Gate/Geant4 platform and will be available in the next release. **Results:** The normalised mean absolute error (MAE) between the reference MC simulation and ARF-based simulation, averaged over all image pixels, was compared for various sizes of the training dataset and binning of the histo-arf. Larger datasets ($> 1e9$) were needed for histo-arf to reach the same precision as nn-arf in all studied test cases. Efficiency distributions of all voxels in the image were computed and showed similar results for both methods, with an average around 2 to 3 orders of magnitude faster than analog MC (tracking particles inside the detector, but not the phantom). **Conclusion:** The proposed ANN-based approach builds ARF tables from less data than conventional methods. It produced results as accurate as histo-arf with slightly better overall efficiency. No binning parameters are required, contrary to histo-arf where results vary depending on such choice. Learning Monte-Carlo detector response with ANN is feasible. The proposed approach is general and may be applied for other types of detectors or MC simulations. **References:** [1]Song, et al. PMB, 50:1791-1804, 2005.[2]Rydeen, et al. EJNMMI 5(1), 2018.

OP-032**Monte-Carlo Simulation and Experimental Validation of a Gamma-Camera Prototype Featuring a Novel Collimation Technique**

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Purpose: Gamma camera imaging is based on the absorptive collimation for determining the direction of incident photons. We propose a new absorptive collimation principle consisting of a rotating cylinder with specially designed slits. The aim is to reach spatial resolutions < 3 mm FWHM with a collimator of comparatively small dimensions (diam. 50 mm, height 80 mm). Evaluating various designs beforehand saves developing time and costs. For this purpose, multiple parameters have been tested in Monte-Carlo simulations (MCS) and their influence on imaging performance has been assessed. Additionally, first experiments have been carried out using a mechanical prototype cylinder and a conventional NaI gamma camera. **Methods:** Using the GATE MCS, a NaI detector and a rotating cylinder were implemented. Nine 140 keV photon point sources were placed at various source-cylinder distances. Simulated cylinder materials were brass, iron, lead, and a tungsten alloy (Densimet). Results were assessed visually (distortions, artefacts) and quantitatively (symmetry of point-spread-function, spatial resolution, system sensitivity). For experimental evaluation, Tc-99m point sources of known activity were placed in front of the rotating cylinder. Obtained images were inspected for artifacts; spatial resolution and system sensitivity were compared to those of standard parallel-hole high-resolution collimators. **Results:** MCS resulted into images with geometric properties as expected. The shape of the point-spread-function depended significantly on the cylinder material chosen. The most symmetric PSF was achieved with the Densimet cylinder resulting in a spatial resolution of < 2 mm @ 10 cm source-cylinder distance and a photon sensitivity of 0.3 cps/MBq. The experiment resulted into images with geometric properties as expected. Photon sensitivity was lower than for the parallel-hole collimator, whereas spatial resolution was higher (smaller FWHM). **Conclusion:** It was shown from simulations, as well as from experiments that the rotating cylinder principle is suitable for gamma camera imaging. For both, MCS and experiments, the rotating cylinder achieved spatial resolutions with smaller FWHM as compared to clinically used parallel-hole collimators. Unfortunately, photon sensitivity was comparably low, as it had been expected. In the future, simulations and experiments based on advanced cylinder designs should be carried out in order to improve the photon sensitivity with an extended slit design.

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Sunday, October 14, 2018, 08:00 - 09:30, Hall 1

Pitfalls & Artefacts 1 - Interactive Clinical Cases: Bone & Joint / Paediatrics: Multimodality imaging in Sports Medicine

OP-033**Role of Bone Scan in Young Athletes**

W. U. Kampen; Nuclear Medicine Spitalerhof, Hamburg, GERMANY.

OP-034**Scintigraphic Evaluation of Back Pain in the Adolescent**

L. Drubach; Boston Children's Hospital / Harvard medical School, Boston, UNITED STATES OF AMERICA.

OP-035**Imaging Strategies in (Adolescent) Sports Injuries**

M. van Gorp; *Rijnstate, Dept. of radiology and nuclear medicine, Arnhem, NETHERLANDS.*

OP-036**Inherited Bone Disorders Versus Acquired Bone Conditions - The Role of Nuclear Medicine**

F. Smit; *Leiden University Medical Center and Alrijne Ziekenhuis, Dept. of nuclear medicine and radiology, Leiden, NETHERLANDS.*

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Sunday, October 14, 2018, 08:00 - 09:00, Hall 4

Clinical Oncology - Rapid Fire Session: 68Ga-PSMA it is!

OP-037**Primary diagnosis of prostate cancer: potential role of ⁶⁸Ga-Prostate Specific Membrane Antigen PET/CT**

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Background: The current study is designed to test the hypothesis that prostate biopsy using ⁶⁸Ga-PSMA PET/Trans Rectal Ultrasound (TRUS) fusion images may have a clinical impact in the subset of patients with a high suspicion of prostate cancer (PCa), a previously negative biopsy and contraindications to or negative multiparametric MRI (mpMRI). **Methods:** This prospective study started in April 2015 and was emended in 2017 to include ⁶⁸Ga-PSMA PET/CT in a selected subgroup of patients: men with persistently elevated PSA and/or PHI (prostate health index) suspicious for PCa, negative digital rectal examination, and at least one negative biopsy were enrolled. The cohort comprised patients with either an equivocal mpMRI (PIRADS v2. ≤2) or an absolute or relative contraindication to mpMRI. All patients underwent whole body ⁶⁸Ga-PSMA PET/CT 60 minutes after radiopharmaceutical injection (185-250MBq). Focal PSMA uptake superior to background activity was considered for the analysis and outlined for target biopsy. Semi-quantitative measures for all lesions comprised SUVmax and SUVratio-to-background. Sensitivities, specificities, and accuracy were calculated compared to histopathology results. **Results:** Overall, 624 consecutive patients were enrolled in our trial; from January to December 2017, 59 cases were referred to ⁶⁸Ga-PSMA PET/CT: 34 patients (57.6%) had already performed mpMRI with either a negative result for PCa (n=10) or positive mpMRI but negative biopsy. In this subset of patients, 42 cases (71%) were addressed to ⁶⁸Ga-PSMA PET/TRUS fusion biopsy that demonstrated the presence of 27 malignant lesions (16 patients): 11 cases with GS 6 (3+3), 14 cases with GS 7 (10 cases GS 3+4; 4 cases GS 4+3), and 2 cases GS 10 (5+5). Average SUVmax for all PCa lesions resulted statistically significantly higher than in benign lesions (P < 0.001). In particular, mean SUVmax values for GS 6, GS 7 and GS 10 resulted 7, 14 and 29, respectively. Also average SUVratio for

PCa lesions resulted statistically significantly higher (P < 0.001) than in benign lesions, with GS 6, GS 7 and GS 10 having a mean SUVratio of 2.5, 5.4 and 9.6, respectively. ROC analysis performed for optimal cut-off points demonstrated that a SUVmax >5.8 and a SUVratio >2.2 could identify clinically significant PCa (GS ≥7) with a sensitivity of 93.7% in both cases. **Conclusions:** In patients with a high suspicion of cancer, despite previously negative biopsy and/or mpMRI, ⁶⁸Ga-PSMA PET/CT is still capable to detect malignant lesions and identify with a high sensitivity clinically relevant PCa.

OP-038**The Role and Impact of 68Ga-PSMA PET/CT in Primary Staging of Prostate Cancer: Preliminary Results in Relation to AJCC Risk Group Staging**

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Purpose: Major changes in 8th edition of AJCC Staging Manual on Prostate cancer (Pca) involve the new histologic grading system and a revision to the prognostic stage grouping; stage-III also includes organ-confined-disease based on PSA, Grade group. PSMA-PET/CT is addressed as a promising method for lymph node and bony staging. Still it is not recommended as part of the current standard of clinical staging. We evaluated the association of initial PSMA-PET/CT findings with prognostic staging according to the 8th edition of the AJCC. **Methods:** 48 patients with newly diagnosed Pca who underwent initial PSMA-PET/CT were reviewed. PSA levels, Gleason scores, Grade, c-TNM, stage groups, therapy decisions were documented. SUVmax of primary tumor (T-SUVmax), metastases, prostate tissue, liver were determined. T-SUVmax/Liver activity (T/L) index was calculated. Final stages according to PSMA-PET/CT were determined. Spread of disease was scored defining 5 regions; 1: prostate, 2: pelvic nodes (PLN), 3: bones, 4: abdominal nodes, 4: distant nodes, 5: visceral organs. A PET regional spread score (PRS) was calculated as the sum of number of involved regions. Correlations between parameters derived from PSMA- PET/CT and PSA at diagnosis, Grade, stage groups, impact of PSMA-PET/CT on staging were evaluated. **Results:** Mean age, PSA were 67.60±8.56 (45-86 years), 43.50±48.08 (4.10-200ng/ml). Mean GS was: 7.38±1.37 (Grade 1-5). Seven patients were stage-group-I, 5 were IIA, 3 group-IIB, 3 IIC, 10 group-IIIA, 3 IIIB, 11 IIIC and 1, 5 patients were group-IVA, IVB respectively, according to the AJCC 8th edition. Mean TSUVmax, T/L index were 13.47±12.93, 2.47±2.24. PSMA- PET/CT indicated prostate confined disease in 22, pelvic disease in 11, metastasis in 15 patients. T-SUVmax, T/L indexes were correlated with PSA, Grade and prognostic stage groups, PRS (Pearson correlation; r:0.534-p<0.001, r:0.515-p<0.001, r:0.400-p=0.006, r:0.665-p<0.001, respectively), (Spearman's rho; r:0.593-p<0.001, r:0.619- p<0.001, r:0.502-p<0.001, r:0.638-p<0.001, respectively). 17 patients; organ-confined high risk disease were upstaged with PSMA-PET/CT (4: IIA-C, 4: IIIA, 2: IIIB, 7: IIIC). Treatment decisions were; operation and PLN dissection in 1 patient, hormone castration (HC) in 2, radiotherapy (RT) and HC in 12, RT, che-

motherapy, HC in 1, HC and chemotherapy in 1patient. **Conclusion:** Sensitive imaging of metastatic disease is essential for patients with high-risk-localized disease, those seeking salvage therapies. Our preliminary results suggest that parameters of initial PSMA-PET/CT correlate with new risk stratification system of 8th edition of AJCC Staging. Moreover, it is notable that most of the patients upstaged on PSMA-PET were consistent with the newly underlined risk-stage group-III.

OP-039

Correlation of SUVmax and ADC values detected by Ga-68 PSMA PET/MRI in primary prostate lesions and their significance in lymph node metastasis

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Aim: Ga-68 PSMA PET is an effective imaging tool for detection of lymph node and organ metastasis in prostate cancer patients. Hybrid PET/MRI systems have recently been shown to be more accurate than multiparametric prostate MRI (mpMRI) in terms of primary prostate lesion detection. In our study, using hybrid PET/MRI we aim (1) to detect the correlation between SUVmax and ADC values of primary prostate lesions and (2) to assess the prognostic value of SUVmax and ADC in terms of lymph node or bone metastasis detection. **Material and Methods:** Patients, who were diagnosed for prostate cancer (Gleason score greater than or equal to 7) with 12-core prostate biopsy were included in our study. All patients had Ga-68 PSMA PET/MRI together with biparametric MRI (bpMRI) sequences for the prostatic bed including T1-weighted (T1W), T2-weighted (T2W), focus diffusion weighted imaging (DWI) (b=50-400-800 and b=50-1400) and ADC mapping. SUVmax, ADCmean and ADCmin were recorded for index lesions of prostate. Presence of lymph node (LN) or bone metastasis was recorded according to whole body Ga-68 PSMA PET/MRI. Spearman correlation analysis, Mann-Whitney U test and ROC analysis were performed for statistical analysis. **Results:** Total 26 prostate cancer patients were included in the analysis. SUVmax was inversely correlated with ADCmean ($p<0.001$, $r=-0.663$ for $b=800$; $p=0.001$, $r=-0.635$ for $b=1400$). SUVmax was significantly higher in patients with LN metastasis ($p=0.004$). Although ADCmean values were lower in patients with LN metastasis, the difference was not statistically significant. In contrast, ADCmin values for $b=800$ were significantly lower in patients with LN metastasis ($p=0.02$). There were only 3 patients with bone metastasis and no significant difference was recorded in SUVmax or ADC values. For presence of LN metastasis, SUVmax cut-off 19.9 has sensitivity and specificity of 77.8% and 76.5%, respectively, whereas ADCmin ($b=800$) cut-off 0.536 has sensitivity and specificity of 75% and 70.6%, respectively. SUVmax/ADCmean ($b=800$) ratio cut-off 27.6 has sensitivity and specificity of 85.7%

and 82.4%, respectively. **Conclusions:** SUVmax and ADCmean values are inversely correlated in primary prostate lesions and presence of both values may add up with each other, thereby increase diagnostic accuracy of hybrid PET/MRI in detection of primary prostate lesions. SUVmax and ADCmin ($b=800$) detected by Ga-68 PSMA PET/MRI are future promising new prognostic values for lymph node metastasis in prostate cancer patients.

OP-040

PET Imaging of Multiple Myeloma: Comparison of ⁸⁹Zr- and ⁶⁴Cu-labeled anti-CD138 Conjugates to ⁶⁴CuCl₂ and ¹⁸F-FDG in a Preclinical Syngeneic Model

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Purpose: Although recent data from the literature suggest that PET imaging with [18]-Fluorodeoxyglucose (¹⁸F-FDG) is a promising technique in multiple myeloma (MM), the development of other radiopharmaceuticals seems relevant. CD138 is currently used as a standard marker in many laboratories for the identification and purification of myeloma cells, and could be used in phenotype tumor imaging. In this study, we evaluated 2 conjugates of an anti-CD138 murine antibody (9E7.4) and compared them to metabolic tracers (⁶⁴CuCl₂ and ¹⁸F-FDG) for PET imaging in a MM syngeneic mouse model. **Subjects and Methods:** 9E7.4 was conjugated to TE2A-benzyl isothiocyanate (TE2A) and desferrioxamine (DFO) chelators for copper-64 (⁶⁴Cu) and zirconium-89 (⁸⁹Zr) labeling. ⁶⁴Cu-TE2A-9E7.4 and ⁸⁹Zr-DFO-9E7.4 antibodies and ⁶⁴CuCl₂ were evaluated via PET imaging and biodistribution studies in C57BL / KaLwRij mice bearing either 5T33-MM subcutaneous tumors or bone lesions. These results were compared to ¹⁸F-FDG-PET imaging. Autoradiography and histology of representative tumors were secondly conducted. **Results:** In biodistribution and PET studies, ⁶⁴Cu-TE2A-9E7.4 and ⁸⁹Zr-DFO-9E7.4 displayed comparable good tumor uptake of subcutaneous tumors. On the opposite, only low-level concentrations of ⁶⁴CuCl₂ were accumulated in MM lesions. PET/CT imaging of the disseminated model with ⁶⁴Cu-TE2A-9E7.4 and ⁸⁹Zr-DFO-9E7.4 showed high uptake of the probes at the site of intra-medullary lesions, greater than that demonstrated with ¹⁸F-FDG-PET and correlating with the bioluminescence imaging of the tumor. Histopathologic analysis of the immuno-PET-positive lesions also confirmed the presence of plasma cell infiltrates within the bone marrow. Comparison of both 9E7.4 conjugates revealed higher non specific bone uptakes of ⁸⁹Zr-DFO-9E7.4 than ⁶⁴Cu-TE2A-9E7.4 (3.1 ± 1.15 vs 1.48 ± 0.29 respectively at 24h PI; $p=0.0061$; non-parametric test) while the opposite was observed for tumor-to-blood ratio (1.42 ± 0.24 vs 4.08 ± 1.09 respectively at 24h PI; $p=0.0391$; non-parametric test). Such observations were consistent with the known in vivo gradual transchelation of ⁸⁹Zr over time which could reduce the efficacy of a ⁸⁹Zr-labeled immuno-PET probe as an effective tool for bone

lesions imaging. **Conclusion:** ^{64}Cu - and ^{89}Zr -labeled anti-CD138 antibody can detect subcutaneous MM tumors and bone marrow lesions with high sensitivity, outperforming ^{18}F -FDG-PET and $^{64}\text{CuCl}_2$ in this preclinical model. ^{64}Cu - anti-CD138 antibody had the most optimal tumor-to-nontarget tissue ratios for translation into humans as a specific and promising new imaging radiopharmaceutical agent in MM.

OP-041

Evaluation of Whole-body MRI vs. ^{68}Ga -PSMA PET/CT for Detection of Biochemical Recurrence in Prostate Cancer Patients

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Purpose: To assess whole-body MRI (wb-MRI) for lesion detection of biochemical relapse in prostate cancer (PCa) patients after curative treatment in comparison to ^{68}Ga -PSMA PET/CT. **Subjects & methods:** This is a prospective IRB-approved trial of 30 patients (age: 65.5 ± 9.6 years) with newly documented biochemical relapse of PCa (mean prostate-specific antigen (PSA) 2.11 ± 1.97 ng/ml) after curative therapy. All patients underwent both wb-MRI including a dedicated pelvic imaging protocol and PET/CT with 167 ± 35 MBq ^{68}Ga -PSMA within a time window of 10.5 ± 9.5 days. PET/CT and MRI datasets were separately evaluated regarding PCa lesion count, lesion type, localization, and diagnostic confidence (3-point scale; 1-3) by two physicians. The reference standard was based on histopathology results, changes of PSA after targeted irradiation, follow-up imaging, and clinical data. Lesion-based and patient-based detection rates were compared using chi2 test. Differences in diagnostic confidence were assessed by Welch test. **Results:** A total of 58 PCa lesions were found in 22/30 patients in the study cohort. ^{68}Ga -PSMA PET/CT detected 57/58 (98.3 %) lesions in 21/30 (70 %) patients, and 15/58 (25.9 %) lesions were detected in 13/30 (43.3 %) patients using wb-MRI. The higher detection rate of ^{68}Ga -PSMA PET/CT was statistically significant both on a per-lesion ($p = 0.001$) and per-patient ($p = 0.039$) basis. In 8/30 patients none of the two modalities actually localized the PCa relapse. Except for one local recurrence in the former prostate fossa that was exclusively detected by wb-MRI, all lesions detected by wb-MRI were also detectable on ^{68}Ga -PSMA PET/CT. ^{68}Ga -PSMA PET/CT offered a superior diagnostic confidence in categorization of PCa lesions compared to wb-MRI (2.7 ± 0.6 vs. 2.3 ± 0.6 , $p = 0.011$). **Conclusion:** ^{68}Ga -PSMA PET/CT significantly outperforms wb-MRI for detection of biochemical relapse in PCa patients after curative treatment.

OP-042

Preliminary results of ^{68}Ga -PSMA PET/CT prospective study in prostate cancer occult recurrence patients: diagnostic performance and impact on therapeutic decision-making

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Introduction: The aim of this prospective study was to investigate the impact of ^{68}Ga -PSMA-11 PET/CT on current management of prostate cancer patients with occult biochemical recurrence (BCR). **Subjects & Methods:** 130 hormone-naïve occult BCR (PSA from 0.05 to 1.6 ng/mL) patients were enrolled in a prospective study (NCT03443609). All patients received a radical treatment (prostatectomy +/- radiotherapy) which allowed to an undetectable PSA level. Before PSMA PET/CT, patients were screened by conventional imaging as mpMRI and bone scan (+ trunk SPECT/CT) and enrolled only if conventional imaging was doubtful or normal. PET images were recorded 1 and 2 hours after injection of 150 MBq of tracer and images interpreted by 2 nuclear physicians. Referring patient physician completed 2 questionnaires to assess PSMA PET imaging influence on therapeutic strategy: one prior and one after PSMA PET/CT indicating treatment plan with-out and with PSMA PET/CT information respectively. Six months after the end of treatment, a PSA assay was requested to evaluate therapeutic efficacy. **Results:** Currently, we have complete data analysis of the first 52 patients. After pre-screening, 7 patients were excluded due to positive MRI (5 pts) or bone scan (2 pts). The median time from radical prostatectomy or radiotherapy to BCR was 4.92y (0.6-15.46). Thirty-eight among the 52 patients (73%) had a positive PSMA PET/CT. Ninety-four lesions were detected, 53/94 in lymph nodes (56.4%) predominantly dispatched on pelvic area (75.5%), 25/94 in bone (26.6%) (mostly on axial skeleton) and 12/94 into prostate bed (12.7%). Detection rates were 56 %, 87 % and 74% for patients with PSA value ranging from 0.05 to 0.3, 0.3 to 0.6 and 0.6 to 1.6 ng/ml respectively. Thanks to PSMA PET/CT, therapeutic management changed in 35/52 patients (67.3%). PSMA-positive patients had undetectable PSA level after stereotaxic radiotherapy or focal surgery based on PSMA results in 30.7% (16/52). In this particular hormone naïve patient population, Rauscher's nomogram (1) was not validate, may be due a too small population. **Conclusion:** Preliminary results of this prospective study showed, in more than half of patients, a major impact of PSMA PET/CT on treatment management allowing them to benefit very early from focal therapy with the great result for 30% of them of PSA complete response. **Reference:** (1) Rauscher I., et al: doi:10.1016/j.eururo.2018.01.006

OP-043

Clinical predictors of PSMA-positive metastases on Ga-68-PSMA PET/CT in treatment-naïve patients with prostate cancer

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Purpose/Introduction: To evaluate the accuracy of established pre-treatment risk stratification systems for prostate cancer (PCa) in predicting PSMA-positive metastases in men undergoing Ga-68-PSMA PET/CT as initial staging examination. **Subjects and methods:** Retrospective analysis in 108 consecutive treatment-naïve patients with histologically proven PCa undergoing Ga-68-PSMA PET/CT (median age, 72 [range, 49–82] a). Prediction of PSMA-positive metastases by serum PSA, clinical T stage (cT), Gleason score (GS), ISUP group, percentage of positive biopsy cores, and derived risk scores (D'Amico score, Roach [RF] and Yale formula [YF], and Briganti nomogram [BN]) was examined with ROC analysis. **Results:** Any PSMA-positive metastases were found in 36 of 108 patients, including LN metastases in 28 patients, extrapelvic LN metastases in 15 patients, and organ metastases in 19 patients (bone, 19; lung, 1). AUC for PSA, cT, GS/ISUP, and percentage of positive biopsy cores regarding PSMA-positive metastases did not differ significantly (range, 0.6–0.8; each $p > 0.05$). D'Amico (AUC, 0.61–0.64) was inferior to RF (0.76–0.83), YF (0.81–0.86) and BN (0.73 to 0.88; each $p < 0.05$). Among the 89 high-risk patients (D'Amico), decision for or against PET imaging based on RF (cutoff, > 18.0), YF (> 10.8) or BN (> 8.0) would have prevented PSMA PET/CT in 4 (5%), 15 (17%) or 18 patients (20%), respectively, while preserving a sensitivity $\geq 95\%$ for PSMA-positive metastases. **Discussion/Conclusion:** Clinical parameters and established pre-treatment risk stratification systems for PCa can predict Ga-68-PSMA PET-positive metastases in treatment-naïve patients. Especially YF and BN may improve identification of patients with the highest probability of metastatic disease detected by Ga-68-PSMA PET/CT.

OP-044

The effect of androgen deprivation therapy on PSMA expression evaluated with ^{68}Ga -PSMA-11 PET/MRI. A prospective, registered clinical trial.

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Purpose: Cell lines and animal models have demonstrated that PSMA expression is altered after initiation of androgen deprivation therapy (ADT). However, the phenomenon is poorly studied in humans. The aim of the study is to evaluate the effect of ADT on PSMA expression by repeated ^{68}Ga -PSMA-11-PET/MRI scans. **Subjects and methods:** In this prospective, registered (NCT03313726), phase 1 trial, newly diagnosed high risk prostate cancer patients (Gleason grade group:5, PSA median:25 ug/L) underwent ^{68}Ga -PSMA-11-PET/MRI immediately before and repeatedly after the initiation of ADT (Degarelix, 240 mg). PET/MRI imaging was repeated either 1,2 and 4 weeks or 2,4 and 8 weeks after ADT administration. Volumes of interest and SUVmax measurements on primary tumour, lymph node and bone metastasis were performed in order to determine the highest time point of PSMA expression. **Results:** Seven men completed the ^{68}Ga -PSMA-11-PET/MRI scans and reached castration

level (s-testo $< 1.7\text{nmol/L}$) after ADT administration and before the second imaging. In total 7 prostate, 15 lymph-node and 14 bone lesions were analyzed. Using pre-treatment SUVmax as a reference, in all primary lesions a mean 16% SUVmax decrease 1 week after ADT was observed. Progressively in 5 patients a descending trend persisted, with a mean SUVmax decrease at 2,4 and 8 weeks of 25%, 37% and 54%, while in 2 patients SUVmax increased at 2 and 4 weeks (mean 5% and 11%). 7 out of 15 lymph node metastasis showed an increase at 2 and 4 weeks (mean 19% and 10%), which was preceded either by a SUVmax decrease (4 cases, mean 14%) or increase (3 cases, mean 18%). In the remaining 8 lymph nodes SUVmax decreased at 1,2,4 and 8 weeks (mean 16%, 31%, 44% and 56%). 7 out of 14 bone metastasis showed a SUVmax increase at 2 and 4 weeks (mean 15% and 22%), after which in 5 lesions SUVmax decreased (mean 23%), in 2 continued rising (mean 33%). 7 remaining lesions had a mean SUVmax reduction at 2,4 and 8 weeks of 24%, 28% and 50%. Overall, no new lesions were detected after ADT compared to baseline ^{68}Ga -PSMA-11-PET/MRI. **Conclusions:** Initial results suggest that PSMA expression evaluated with ^{68}Ga PSMA-11-PET/MRI imaging is affected heterogeneously by ADT. In primary tumour PSMA expression decreased progressively over time with no significant increase. On the other hand, in 50% of lymph node and bone metastasis, SUVmax, after an initial reduction, increased 2–4 weeks after ADT, followed by either a further increase or decrease at 8 weeks.

OP-045

Impact of long-term androgen deprivation therapy on PSMA-ligand PET/CT in patients with castration sensitive prostate cancer

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Purpose: Since the introduction of PSMA-PET/CT with ^{68}Ga Ga-PSMA-11, this modality for imaging prostate cancer (PC) has spread worldwide. Preclinical studies demonstrate that short-term androgen deprivation therapy (ADT) can significantly increase the PSMA-expression on PC cells. Additionally, retrospective clinical data in large patient cohorts suggested a positive association between ongoing ADT and a pathologic PSMA-PET/CT. The present evaluation was conducted in order to further analyze the influence of long-term ADT on PSMA-PET/CT. **Methods:** A retrospective analysis was performed for all patients who were scanned at our institute with ^{68}Ga

Ga-PSMA-11 PET/CT from 2011 until 2017 in order to detect PC (n=1,704). Amongst them, 306 patients were scanned at least twice. Ten of these patients had started and continued ADT with continuous clinical response between two PSMA-PET/CT. These ten patients were included in the current analysis which compared the tracer uptake intensity and volume of PC-lesions in PSMA-PET/CT prior and during ongoing ADT. **Results:** Overall, 31 PC lesions were visible in all ten patients before initiation of ADT. However, under ongoing ADT (duration 42–369 days, median: 230 days), only 14 lesions were visible in eight of the ten patients. The average tracer uptake values decreased in 71% and increased in 12.9% of all PC lesions. 33.3% of all lesions were still visible in six patients with complete PSA response (≤ 0.1 ng/ml). **Conclusions:** Continuous long-term ADT in patients with castration naïve PC demonstrated a significantly negative impact on tumor allocation in PSMA-PET/CT. The majority of PC lesions became invisible under effective ADT. According to this data, in the setting of biochemical relapse PSMA-PET/CT should preferably be conducted prior to commencing ADT, aiming at visualizing the maximum possible extend of disease. PSMA-PET/CT under ADT can potentially be used for a more precise response assessment compared to PSA alone: early detection of isolated hormone-resistant lesions could change the treatment strategies in the future.

OP-046

PET/CT with 68Ga-PSMA for monitoring the treatment of 177Lu-PSMA-617 in Patients with Metastatic Castration-Resistant Prostate Cancer

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Purpose/introduction: In order to determine response of radioligand therapy with (177)Lu-617 PSMA in castrate-resistant prostate cancer usually changes in prostate-specific antigen (PSA)-levels are evaluated. In addition, many centres employ 68Ga-PSMA PET/CT. The aim of our study was to systematically evaluate the use of 68Ga-PSMA PET/CT for monitoring treatment response. **Subjects & methods:** The patients were retrospectively recruited from Universitätsklinik Bonn and Universitätsklinik Aachen. We included 45 patients with metastatic castration-resistant prostate cancer treated with 177Lu-PSMA-617 that had pre- and post-therapeutic imaging before the first and after the third or fourth treatment cycle using 68Ga-PSMA PET/CT. Furthermore, we only considered patients that have been treated with at least one of the new-generation antihormonal drugs (abiraterone or enzalutamide) before the treatment with 177Lu-PSMA-617. PET Scans had to be performed between 5–12 weeks after the respective treatment cycle. The range between the 68Ga-PSMA PET/CT and the PSA measurement had to be within four weeks. We defined a treatment response based on the 68Ga-PSMA PET/CT according to a modified version of the PERCIST criteria. Reduction of minimal 30% in target measurable tumor SUVpeak was considered treatment response, given the absence of new lesions. With regard to PSA we looked at two types of responses. A decline $\geq 50\%$ compared to baseline and

any decline in PSA compared to baseline. Based on these assumptions we calculated sensitivity, specificity, positive predictive value and negative predictive value of the use of 68Ga-PSMA PET/CT for response assessment in radioligand therapy with (177)Lu-617 PSMA. **Results:** 68Ga-PSMA PET/CT predicted a decline of PSA $\geq 50\%$ with a sensitivity of 80%, specificity of 65%, positive predictive value of 74%, and negative predictive value of 72%. Moreover, it predicted any decline of PSA with a sensitivity of 74%, specificity of 82%, positive predictive value of 92% and negative predictive value of 50%. **Discussion/conclusion:** In both scenarios, 68Ga-PSMA PET/CT shows good performance for detection of treatment response. Thus our results indicate that 68Ga-PSMA PET/CT seems to be a useful tool for response evaluation in radioligand therapy with (177)Lu-617 PSMA. The strength of the study is its bicentric character, whereas a limitation is its retrospective character in a small sample.

110 Sunday, October 14, 2018, 08:00 - 09:00, Hall 28

Cardiovascular: From Myocardial Perfusion to Plaque Imaging

OP-047

Diagnostic Value of Transluminal Attenuation Gradient: A proof of concept study with ¹³N-ammonia PET

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Introduction: Transluminal Attenuation Gradient (TAG) refers to the gradient of intraluminal contrast attenuation along a coronary artery. Recently, TAG has been proposed as a parameter to identify hemodynamically significant stenosis. Currently, there are no previous studies comparing TAG to quantitative myocardial perfusion with ¹³N-ammonia Positron Emission Tomography (PET). **Purpose:** To determine the diagnostic value of TAG by Coronary Computed Tomography Angiography (CCTA) for the detection of ischemia with absolute stress myocardial blood flow (MBF) measured with ¹³N-ammonia PET as a reference. **Methods:** We included patients who underwent CCTA and ¹³N-ammonia PET due to suspected or known coronary artery disease (CAD). All patients were studied in a PET/CT scanner (Biograph True Point PET/CT 64-Multislice Scanner, Siemens). Hounsfield Units (HU) were measured at 5 mm intervals from the ostium until the cross-sectional area fell below 2.0 mm² at each main coronary artery (left anterior descending artery, left circumflex artery, and right coronary artery). The TAG was considered the change in HU per 10-mm length of a coronary and calculated as the linear regression coefficient between HU and length from the ostium. Significant CAD was defined as $\geq 50\%$ stenosis on the CCTA. Vessels with inadequate image quality, stent, or with total occlusion were excluded. Stress MBF was analyzed regionally according to the three vascular territories. Ischemia was considered as a

stress MBF < 1.85 ml/gr/min in each vascular territory. **Results:** 56 vessels (22 patients: mean age 63 ± 9 years, 77% male) were assessed, and 10 vessels were excluded. The mean TAG was -12.8 ± -11.1 and mean stress MBF was 2.1 ± 1.9 ml/gr/min. TAG and CCTA had similar accuracy in detecting ischemia (area under the curve 0.75 vs. 0.79, $p=0.75$). Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for TAG were 81%, 69%, 61%, 86%, and 73% respectively, and for CCTA were 71%, 85%, 75%, 83%, and 80% respectively. **Conclusion:** TAG and CCTA showed similar diagnostic value for the detection of ischemia when compared to absolute stress MBF ^{13}N -ammonia PET. Future prospective studies are warranted to fully determine the diagnostic value of the TAG.

OP-048

Relationship between resistant hypertension and coronary vascular function assessed by ^{82}Rb PET/CT in patients with suspected coronary artery disease and normal myocardial perfusion

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Aim: Impaired coronary flow reserve (CFR) represents a significant marker of hypertensive vascular damage and is associated with increased risk of cardiovascular morbidity and mortality. In patients with resistant hypertension (RH) reduction of CFR may occur earlier than coronary atherosclerosis and it may be an early manifestation of developing coronary artery disease (CAD). We assessed the relationship between RH and CFR measured by ^{82}Rb PET/CT in hypertensive patients with suspected CAD and normal myocardial perfusion imaging (MPI). **Materials and Methods:** The overall study population consisted of 87 hypertensive patients with suspected CAD and normal MPI at vasodilator stress ^{82}Rb PET/CT imaging. Patients with diabetes were excluded. RH was defined as blood pressure that remained above goal in spite of the concurrent use of 3 antihypertensive agents of different classes. Coronary artery calcium (CAC) score was measured according to the Agatston method. Resting and hyperemic myocardial blood flow (MBF) and CFR were automatically quantified. A value of $\text{CFR} \leq 2$ was considered reduced. Continuous data were compared using two-sided Student's *t* test. Univariable and multivariable linear regression analyses were used to determine the variables associated with reduced CFR. A *p*-value <0.05 was considered significant. **Results:** In the overall population, 36 patients (38%) had RH. Patients with RH were older (66 ± 13 vs. 58 ± 11 years) and had lower value of hyperemic MBF (1.7 ± 0.77 vs. 2.29 ± 0.95) and CFR (2.14 ± 0.97 vs. 2.89 ± 1.08) compared to those without (all $p < 0.005$). On the contrary, CAC score and baseline MBF were not significantly different between the 2 groups. At univariable analysis, age and RH resulted significant predictors of reduced CFR (both $p < 0.01$), while at multivariable analysis, only RH was independently associated with reduced CFR ($p < 0.05$). **Conclusions:** In patients with suspected CAD and normal MPI the

presence of RH is associated with coronary vascular dysfunction and reduced CFR. The identification of coronary vascular dysfunction could help to identify early structural alterations of the arterial wall in patients with RH.

OP-049

Relationship Between Epicardial Adipose Tissue and Coronary Vascular Function in Patients with Normal Myocardial Perfusion by ^{82}Rb PET/CT

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Background: Epicardial adipose tissue (EAT) is the visceral fat depot of the heart and it directly influences myocardial homeostasis through vasocrine and paracrine mechanism. A reduced coronary flow reserve (CFR) reflects not only the presence of coronary artery stenosis but also coronary vascular dysfunction. There are a few evidences of a direct correlation between increased EAT and impaired CFR in small patients' population with suspected or known coronary artery disease (CAD). However, this association has not been fully investigated. **Purpose:** We assessed the relationship between EAT and CFR in patients with suspected or known CAD and normal myocardial perfusion imaging. **Methods:** The overall study population consisted of 272 subjects referred for the evaluation of suspected or known CAD to stress-rest ^{82}Rb PET/CT and showing normal MPI. CAC score was measured according to the Agatston method. Using unenhanced CT images for CAC, EAT volume was measured (cm^3). The $\ln(\text{CAC}+1)$ score and $\ln\text{EAT}$ transformation were used to reduce heteroscedasticity. Myocardial perfusion was assessed using standardized segmentation of 17 myocardial regions. The summed stress, summed rest and summed difference scores were automatically calculated. Myocardial perfusion was considered normal when the summed stress score was <3. Absolute myocardial blood flow (MBF) was computed (in milliliters per minute per gram) from the dynamic rest and stress imaging series. CFR was defined as the ratio of hyperemic to baseline MBF and $\text{CFR} \leq 2$ was considered reduced. **Results:** In the overall population, 95 (35%) patients showed reduced and 177 (65%) normal CFR. Compared to patients with normal CFR, those with reduced CFR were older (60 ± 11 vs. 67 ± 9 , $P < 0.05$) and showed higher values of $\ln(\text{CAC}+1)$ (3.9 ± 3 vs. 4.7 ± 3 , $P < 0.05$) and $\ln\text{EAT}$ volume (4.5 ± 1 vs. 4.7 ± 1 , $P < 0.05$). At univariable logistic regression analysis age, $\ln(\text{CAC}+1)$ and $\ln\text{EAT}$ resulted significant predictors of reduced CFR. At multivariable analysis, only age and $\ln\text{EAT}$ volume were independently associated with reduced CFR (hazard ratio 1.05 and 1.89 and 95% confidence interval 1.02-1.08 and 1.01-3.54, $P < 0.005$). The addition of $\ln\text{EAT}$ to clinical data significantly increased the global chi-square of the model (from 23.8 to 28.6, $P < 0.05$) in predicting reduced CFR. **Conclusions:** In patients with suspected and known CAD and normal myocardial perfusion, age and EAT are strongly associated with reduced CFR confirming that visceral fat depot may directly in-

fluence coronary vascular function. Thus, EAT evaluation may play a major role in the identification of coronary vascular dysfunction in patients with normal perfusion.

OP-050

Characterization of functionally significant coronary artery disease by a novel coronary computed tomography angiography (CTCA) based index: a comparison with PET perfusion

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Background: Application of computational fluid dynamics (CFD) to three-dimensional CTCA datasets has been shown to provide accurate assessment of the hemodynamic significance of a coronary lesion. Virtual Functional Assessment Index (vFAI) has been recently validated against fractional flow reserve and proposed as a possible surrogate marker of hemodynamic significance of coronary stenoses. **Aims:** To test the hypothesis that vFAI is related with regional flow parameters derived by quantitative PET and can be used to predict perfusion abnormalities downstream stenotic coronary lesions at CTCA. **Methods:** Seventy one patients with mean age 62.2±7.9 years old, stable symptoms and intermediate pre-test likelihood of coronary artery disease (CAD) underwent CTCA and ¹⁵O-water or ¹³N-ammonia PET stress-rest quantitative myocardial perfusion imaging. Three-dimensional reconstruction of CTCA datasets was performed, followed by CFD blood flow simulations using dedicated finite element software. PET studies were considered positive for significant CAD, when more than one contiguous myocardial segments showed stress myocardial blood flow (s-MBF) ≤2.3 ml/g/min for ¹⁵O-water or <1.79 ml/g/min for ¹³N-ammonia. The corresponding myocardial flow reserve (MFR) thresholds were ≤ 2.5 and ≤ 2 respectively. The extent of perfusion defects in ¹³N-ammonia studies was also computed as % of the left ventricle and a reversible perfusion defect involving ≥ 10% of the left ventricle was defined as significant. **Results:** s-MBF and MFR measurements were available in 206 vessels' territories. After exclusion of arteries because of unsatisfactory image quality, vFAI was computed in 196 vessels. vFAI was positively correlated with s-MBF measured either with ¹⁵O-water or ¹³N-ammonia (R=0.47 and R=0.53, p<0.001 for both). A positive correlation was also demonstrated between vFAI and MFR (R=0.40, p<0.001 and R=0.39, p=0.004) for ¹⁵O-water and ¹³N-ammonia measurements respectively. The optimum threshold of vFAI for predicting concordant impairment of both s-MBF and MFR downstream a coronary stenosis ≥30% was 0.8 with sensitivity and specificity values 91% and 82% (AUC: 0.834,

95% CI: 0.730 to 0.937, p<0.001) or 63% and 80% (AUC: 0.788, 95% CI: 0.622 to 0.953, p=0.019) for ¹⁵O-water and ¹³N-ammonia PET studies, respectively. The same threshold had sensitivity and specificity 75%, for predicting a reversible perfusion defect ≥10% of the left ventricle (AUC: 0.813, 95% CI: 0.641 to 0.984, p=0.05). **Conclusion:** vFAI can be readily computed in the majority of coronary vessels from CTCA datasets. It is correlated with PET measured stress MBF and MFR and identifies with reasonable accuracy impaired coronary flow capacity downstream a coronary lesion at CTCA.

OP-051

Value of aortic TBR measured on FDG-PET for the prediction of atherothrombotic events in a cohort of patients with overt coronary and carotid atherosclerotic disease

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Introduction: In patients imaged for oncological indications, high vascular FDG uptake in the ascending aorta on FDG-PET was associated with an increased rate of cardiovascular events during follow-up. Whether the results observed in patients imaged with FDG-PET for oncological indications hold true in patients with overt atherothrombotic disease remains elusive. **Purpose:** The aim of this study was to evaluate the value of aortic tissue to background ratio (TBR) measured on FDG-PET in patients with overt coronary and carotid artery disease to predict atherothrombotic events. **Methods:** A total of 190 patients with non-ST-segment elevation myocardial infarction (NSTEMI, n = 36), stable coronary artery disease (CAD, n = 26) or symptomatic carotid stenosis (n = 128) evaluated with FDG-PET were identified among various clinical studies undertaken at our institution. All patients were imaged with the same PET-CT system 90 minutes after the injection of 4 MBq/kg of FDG. Max SUV of the vascular wall and mean SUV of blood were measured on PET axial slices in 8 regions of interest (ROI) placed on the axial ascending thoracic aorta and 10 ROI in the superior vena cava, respectively. Mean aortic TBR was calculated in each patient as the ratio between the average of vascular max SUV and blood mean SUV. Patients with a follow-up of less than one month were excluded. Clinical events were extracted from medical records. Atherothrombotic events were defined as cardiac death or the occurrence of new myocardial, cerebral or limb ischemia or necrosis. **Results:** Mean age of patients was 67 ± 14.4 years; 70 % were male. Following FDG-PET, patients received anti-platelet and statin therapy. After a mean follow-up of 3.5 years, atherothrombotic events occurred in 27 % of patient. The rate of atherothrombotic events increased with increasing tertiles of TBR: tertile 1 (TBR: 1.22 - 1.57): 20.6 %; tertile 2 (TBR: 1.58 - 1.74): 27 %; tertile 3 (TBR: 1.75 - 2.31): 32.8 %. Aortic TBR was significantly higher in patients who developed a cardiovascular event vs. remained asymptomatic during follow-up (1.77 ± 0.20

vs. 1.65 ± 0.21 ; $p = 0.005$), whereas no difference in aortic TBR was observed in patients who developed neurovascular events vs. asymptomatic patients (1.67 ± 0.18 vs. 1.66 ± 0.21 ; $p = 0.86$).

Conclusions: In patients with overt coronary or carotid artery disease, high aortic TBR was associated with an increased risk of cardiovascular but not cerebrovascular events during follow-up.

OP-052

Role of somatostatin receptor and FDG imaging in capturing plaque inflammation: a PET/CT analysis, corroborated by clinical data

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Several studies demonstrated that atherosclerosis-related vascular inflammation can be measured by means of 18F-FDG-PET. However background (i.e. muscular/myocardial) 18F-FDG signal spillover or interference with patients' comorbidities such as diabetes may hamper signal semiquantification. Up-regulation of somatostatin receptor subtype-2 occurs on the surface of activated macrophages and it has been suggested that PET imaging of somatostatin receptor distribution may also capture vascular inflammation (in absence of relevant interference related to background uptake). **Aim:** to compare regional vascular distribution and biological determinants of visible calcium load, as assessed by computed tomography and plaque inflammations as assessed by both 68Ga-DOTA-TOC and 18F-FDG-PET in the same group of patients. **Methods:** The study included 27 patients with neuroendocrine tumors who underwent 18F-FDG and 68Ga-DOTA-TOC-PET for clinical reasons (12 males, mean age 69.4 ± 8.03 range 56–87). Cardiovascular-risk stratification was performed according to a simplified version of the Framingham model including age, diabetes, smoking, systolic blood pressure and body mass index (BMI). Aortic uptake of both 18F-FDG and 68Ga-DOTA-TOC was measured by drawing regions of interest comprising the entire aorta on each slice of the transaxial PET/CT, then SUVmean for the whole aorta was computed and normalized to blood activity thus obtaining the aortic target-to-background ratio (TBRmean). With the aim of taking into account the presence and degree of aortic hot spots, aortic SUVmax was also recorded and normalized on blood-pool activity (TBRmax). Finally the degree of arterial calcification (AC) was measured using a software program providing Agatston-like scores. Differences in mean values and linear regression analysis were tested for AC, TBRmean and TBRmax and cardiovascular risk-factors. P value of 0.05 was considered statistically significant. **Results:** Aortic TBRmax was significantly higher on 68Ga-DOTA-TOC

than 18F-FDG-PET images ($p < 0.0007$) while no difference were highlighted for TBRmean. Similarly, no correlation was highlighted between TBRmean values and calcium score for both tracers. AC was dependent upon age, while it was not influenced by all the remaining determinants of cardiovascular risk. Framingham risk score correlated with both TBRmean ($p < 0.05$). Finally only TBRmax of 68Ga-DOTA-TOC (and not of 18F-FDG) was higher in diabetics with respect to the remaining patients.

Conclusion: Correlations of both tracers uptake upon ongoing biological determinants of vascular damage/inflammation confirm that PET might provide several different windows on plaque pathophysiology. In this framework 68Ga-DOTA-TOC vascular signal demonstrated to better capture the presence of arterial hot spots and was able to better highlight plaque inflammation in diabetic patients.

201/204 Sunday, October 14, 2018, 10:00 - 11:15, Plenary Hall

Plenary 1: In Vivo Molecular Diagnosis of Cognitive Disorders - A Paradigm Change (incl. Marie Curie Lecture)

OP-053

Alzheimer's Disease Criteria: The Role of Markers of Pathology

B. Dubois; Hôpitaux Universitaires La Pitié salpêtrière - Charles Foix, Paris, FRANCE.

OP-054

AmyPad: A Randomized Clinical Trial to Validate the Impact of Amyloid PET

F. Barkhof; VU University Medical Center, Amsterdam, NETHERLANDS.

OP-055

Marie Curie Lecture: Tau PET Imaging: A History of Challenges and Success

V. Villemagne; Austin Health, Department of Nuclear Medicine and Centre for PET, Heidelberg, AUSTRALIA.

301 Sunday, October 14, 2018, 11:30 - 13:00, Plenary Hall

CME 2 - Thyroid: New Guidelines in Nuclear Thyroidology

OP-056

EANM-SNMMI Joined Guidelines on Thyroid Molecular Imaging

L. Giovanella; Oncology Institute of Southern Switzerland, Nuclear Medicine and PET Centre, Bellinzona, SWITZERLAND.

OP-057

EANM Guidelines on Medullary Thyroid Carcinoma

G. Treglia; Nuclear Medicine and PET/CT Center, Oncology Institute of Southern Switzerland, Bellinzona, SWITZERLAND.

OP-058**EANM Guidelines on Radioiodine Therapy of Benign Thyroid Diseases - Recent Novel Aspects**

F. Verburg; University Hospital Marburg, Department of Nuclear Medicine, Marburg, GERMANY.

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Sunday, October 14, 2018, 11:30 - 13:00, Hall 2

Joint Symposium 3 - Interactive: Paediatrics / SIOPEN: Interactive Session on Neuroblastoma**OP-059****The Role of MIBG in the Evaluation of Children with Neuroblastoma**

L. Biassoni; Great Ormond Street Hospital for Children, NHS Foundation Trust, Department of Nuclear Medicine, London, UNITED KINGDOM.

OP-060**F-18-DOPA in the Evaluation of Neuroblastoma**

A. Piccardo; Ente Ospedaliero "Ospedali Galliera, Genova-I", Genoa, ITALY.

OP-061**Clear Advantages of Ga-68 DOTATATE and I-124 MIBG PET for Managing Neuroblastoma**

M. Hofman; Peter MacCallum Cancer Centre, Cancer Imaging and Theranostics, Melbourne, AUSTRALIA.

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Sunday, October 14, 2018, 11:30 - 13:00, Hall 3

Joint Symposium 4: Cardiovascular / ESMI: New Approaches for Atherosclerosis Imaging**OP-062****Optical and Opto-Acoustic Imaging**

A. Karlas; Institute of Biological and Medical Imaging, Munich, GERMANY.

OP-063**Magnetic Resonance Imaging**

M. Makowski; Charité Hospital, Department of Radiology, Berlin, GERMANY.

OP-064**SPECT and PET**

A. Saraste; Heart Center and PET Centre, University of Turku, Turku, FINLAND.

OP-065**Hybrid Imaging**

J. Bucerius; Maastricht University Medical Center, Department of Nuclear Medicine, Maastricht, NETHERLANDS.

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Sunday, October 14, 2018, 11:30 - 13:00, Hall 5

CTE 2 - Interactive: Technologists: Radionuclide Therapy - A Multidisciplinary Approach**OP-066****Tips and Tricks for Dosimetry Assessment**

M. Konijnenberg; Erasmus MC, Rotterdam, NETHERLANDS.

OP-067**Labelling and Dispensing of Therapeutic Radiopharmaceuticals**

Z. Wimana; Institut Jules Bordet, Nuclear Medicine, Brussels, BELGIUM.

OP-068**Pitfalls During Radionuclide Therapy Administration**

C. Deroose; University Hospitals Leuven, Nuclear Medicine, Leuven, BELGIUM.

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Sunday, October 14, 2018, 11:30 - 12:45, Hall X

M2M: Therapy Effects, Preclinical**OP-069****Therapeutic efficacy of ¹⁷⁷Lu-lilotomab satetraxetan in non-Hodgkin B-cell Lymphoma is controlled by G2/M cell cycle progression**

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We aimed at determining the molecular mechanisms involved in the therapeutic efficacy of ¹⁷⁷Lu-labeled lilotomab satetraxetan (Betalutin®) directed against the CD37 receptor expressed by non-Hodgkin lymphoma (NHL) B-cells. **Materials and methods:** *In vitro*, Ramos, Raji and rituximab resistant Raji (Raji2R, all Burkitt lymphoma), DOHH2 (transformed follicular), Rec-1 (mantle), U2932 and OCILy8 (diffuse large B-cell) lymphoma cell lines were exposed for 18 hours to increasing activities (0–6 MBq/mL) of ¹⁷⁷Lu-lilotomab, of the non-specific ¹⁷⁷Lu-cetuximab or to unlabelled mAbs (0–40 µg/mL). Clonogenic survival, proliferation, expression level of phosphorylated CDK1, cell cycle progression and apoptosis were investigated. *In vivo*, mice bearing subcutaneous Ramos, DOHH2, Raji, Raji2R or OCILy8 tumour xenografts, were treated with ¹⁷⁷Lu-mAbs, with rituximab or lilotomab and tumour growth was monitored. **Results:** We showed in all lymphoma cell lines that unlabelled rituximab was more cytotoxic than lilotomab. When lilotomab was radiolabeled, ¹⁷⁷Lu-lilotomab was more cytotoxic than rituximab in the so determined radiosensitive DOHH2 cells while its cytotoxicity in Ramos cells was less pronounced. The higher response to ¹⁷⁷Lu-lilotomab in DOHH2 cells than in Ramos cells was mainly mediated by lack of G2/M cell cycle arrest in DOHH2 cells followed by strong induction of apoptosis. Inhibition of CDK1 Tyr15 phosphoryla-

tion using MK1775 or PD166285 drugs radiosensitized Ramos cells. These results were supported by *in vivo* data. In Ramos tumour xenograft models, 250 MBq/kg (1.25 mg/kg) ^{177}Lu -lilotomab and 10 mg/kg rituximab could not delay tumor growth compared with untreated mice. ^{177}Lu -lilotomab significantly delayed tumour growth compared with rituximab (used at the same concentration) only if injected activity was increased up to 500 MBq/kg. Conversely, in DOHH2 tumour xenografts, 100 MBq/kg (0.5 mg/kg) ^{177}Lu -lilotomab was more efficient than rituximab. The *in vivo* use of MK1775 was shown to radiosensitize Ramos tumour xenografts to ^{177}Lu -lilotomab. Experiments analysis is ongoing for OCILy8, Raji and Raji2R cell lines. **Conclusion:** These results indicate that ^{177}Lu -lilotomab is an efficient therapeutic tool for NHL, particularly for tumors showing reduced inhibitory CDK1 phosphorylation.

OP-070

Novel targeted radionuclide therapy approach enhances response to immune checkpoint blockade in murine melanoma.

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Purpose: Preclinical studies show that delivering external beam radiation therapy (EBRT) to a single tumor enhances the systemic tumor response to immune checkpoint inhibition (ICI) therapies. We hypothesize that such synergy could be improved upon in the presence of metastatic or multifocal disease by delivering radiation therapy to all disease sites. While this is not feasible with EBRT due to prohibitive toxicities, our novel targeted radionuclide therapy (TRT) approach using systemically administered [^{90}Y]Y-NM600 can deliver tumor-selective radiation to all tumor sites. **Subjects and Methods:** Female C57BL/6 mice were implanted with a single or bilateral syngeneic melanoma (B78) tumors to mimic the single tumor and metastatic scenario. Single-tumor mice (n=3) were administered 9.25 MBq of the positron-emitting [^{86}Y]Y-NM600 and scanned via PET/CT at 3, 24, 48, and 72 h post-injection. ^{86}Y -NM600 uptake in B78 tumors and normal tissues was quantified via a region-of-interest analysis of the images. [^{90}Y]Y-NM600 TRT monotherapy was administered to single-tumor mice at four dose levels: 1.85, 3.7, 5.55, or 9.25 MBq. In combination studies with ICI, single-tumor or two-tumor mice (70–150 mm³; n=6) were administered [^{90}Y]Y-NM600 (1.85/3.7 MBq) followed by three consecutive IP injections of an anti-CTLA-4 mAb (10 mg/kg) at days 4, 7, and 11. The growth of both the primary and secondary tumors was monitored for 30 days, and mice exhibiting complete tumor response (CR) were re-challenged with B78 tumor cells. The hematopoietic toxicity of [^{90}Y]Y-NM600 was monitored biweekly in naïve mice via CBC analysis. **Results:** PET/CT revealed selective accumulation and prolonged retention of [^{86}Y]Y-NM600 in B78 tumors, as well as a rapid clearance from normal tissues. A significant ($P<0.01$), dose-dependent, tumor growth inhibition was observed in mice administered standalone [^{90}Y]Y-NM600 TRT; however, CR was not seen in these cohorts. [^{90}Y]Y-NM600 TRT at 1.85 and 3.7

MBq doses was hematologically safe while 9.25 MBq resulted in transient cytopenia. Both single-tumor and two-tumor mice treated with [^{90}Y]Y-NM600 (1.85 or 3.7 MBq) + ICI experienced significant regression ($P<0.01$) of both the primary and secondary tumors. Contrary to TRT alone or ICI alone treatment arms, CR was achieved in 66% of the single-tumor and 50% of the two-tumor mice treated with TRT+ICI. All complete responders showed immune memory to re-challenge with B78 tumor cells. **Conclusion:** Our results demonstrate that the tumor-selective TRT agent, [^{90}Y]Y-NM600, significantly enhances response to anti-CTLA-4 ICI in a syngeneic murine tumor model, resulting in CR and memory response in most treated mice.

OP-071

Novel targeted radionuclide therapy affords a durable response and tumor immunity in a syngeneic model of T-cell NHL

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Purpose: T-cell non-Hodgkin's lymphomas (NHL) are a class of malignancies that are typically radiosensitive; however, the role of radiation therapy is limited in advanced stage disease by the toxicities associated with large field external beam treatments. Herein, we aimed to test the ability of our novel targeted radionuclide therapy (TRT) agent, [^{90}Y]Y-NM600, to selectively deliver lethal radiation to tumors systemically and achieve tumor remission in a syngeneic mouse model of T-cell NHL. **Subjects and Methods:** NM600 was radiolabeled with ^{86}Y for PET/CT imaging and ^{90}Y for TRT studies. Female C57BL/6 mice were implanted subcutaneously (s.c.) with EL-4 lymphoma cells. Mice bearing syngeneic EL-4 (n=4) tumors were injected IV with 9.25 MBq of [^{86}Y]Y-NM600, and sequential PET/CT scans were acquired at 3, 24, 48, and 72 h post-injection. [^{86}Y]Y-NM600 tumor uptake and normal tissue distribution were determined via region-of-interest analysis of the PET images. To evaluate hematological toxicity, naïve mice were administered 2.2, 4.6, or 9.3 MBq of [^{90}Y]Y-NM600 with CBC and blood chemistry analysis performed bi-weekly. In TRT studies, mice bearing s.c. tumors (700 mm³; n=5) were administered a single 2.2, 4.6, 9.3, or 18.5 MBq dose of [^{90}Y]Y-NM600, or excipient, and tumor growth and overall survival were monitored for 90 days. CBC, blood chemistry, and histological analysis of normal organs was performed in half of the surviving subjects to assess long-term toxicity. The other half were reinoculated with EL-4 cells to test for immune memory. **Results:** PET/CT imaging unveiled selective and persistent tumor uptake of [^{86}Y]Y-NM600 and rapid clearance of the tracer from normal organs and circulation. Starting at 4.6 MBq, a dose-dependent moderate cytopenia was observed in mice injected with [^{90}Y]Y-NM600, which resolved after three weeks. Significant tumor regression ($P<0.001$) was observed in the groups administered 4.6, 9.3, and 18.5 MBq compared to excipient treated controls; however, 18.5 MBq resulted in acute radiotoxicity and death. Compared to controls, median survival was significantly longer ($P<0.0001$) in the 2.2, 4.6, and 9.3 MBq groups, with the

last achieving 80% complete response (CR). Complete responders showed normal CBC, blood chemistry, and organ morphology indicating the absence of long-term toxicities. Re-challenge with EL-4 cells resulted in the rejection of tumors in all subjects.

Conclusions: TRT using [^{90}Y]Y-NM600 can elicit durable responses in mice bearing syngeneic T-cell NHL tumors at doses that result in limited toxicities. TRT may cooperate with the immune system to achieve anti-tumor responses and durable anti-tumor immunity.

OP-072

Efficacy and Toxicity of ^{177}Lu -NeoBOMB1 for prostate cancer treatment - a preclinical study

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Introduction: Overexpression of the gastrin releasing peptide receptor (GRPR) has been reported in multiple tumor types including prostate cancer. GRPR-radioligands are suitable for radionuclide imaging and therapy of GRPR-expressing tumors. NeoBOMB1 is a selective and stable GRPR-antagonist with high receptor affinity. Our previous preclinical studies with radio-labeled NeoBOMB1 demonstrated high radiotracer uptake in the tumor. Furthermore, radiotracer uptake was also observed in the GRPR-expressing pancreas and the kidneys. The latter, due to renal excretion, decreased rapidly over time. The radio-tracer cleared relatively fast from the pancreas as opposed to the much longer retention of the radio-compound in malignant tissue. Furthermore, increasing the peptide mass of NeoBOMB1 favored the tumor-to-pancreas ratio. In this study we aimed to determine the efficacy and safety of ^{177}Lu -NeoBOMB1 therapy using different peptide amounts in a prostate cancer mouse model. **Materials and Methods:** Male balb c nu/nu mice subcutaneously xenografted with the GRPR-expressing human prostate cancer cell line PC-3 received either 3 injections of saline (n=10, naïve), 30 MBq/300 pmol (n=15, group A), 40 MBq/400 pmol (n=15, group B) or 60 MBq/600 pmol (n=15, group C) ^{177}Lu -NeoBOMB1. Injections were administered 1 week apart. To assess toxicity, non-tumor bearing animals received the same treatment (n=4 per group). At 12 and 24 weeks post-therapy, 2 animals of each group were euthanized, the kidneys and the pancreas were removed and analyzed by histopathology. Tumor size and/or animal weight were measured bi-weekly. Study endpoints were: tumor size $\geq 2000 \text{ mm}^3$, $\geq 20\%$ weight loss, any signs of organ (pancreas and kidneys) insufficiency and max age of 230 d. **Results:** The mean tumor size of group A, B and C reached 2000 mm^3 with significant delay as compared to the naïve group: $69 \pm 14 \text{ d}$, $61 \pm 17 \text{ d}$ and $77 \pm 49 \text{ d}$, respectively. In addition, two mice from group A and 1 mouse from group B did not show tumor regrowth after a complete response. Animals treated with ^{177}Lu -NeoBOMB1 also had a significantly longer mean survival time compared to naïve animals ($p < 0.001$). No significant differences in survival were observed among treatment groups. Furthermore, no decrease in animal weight was observed and up to now histopathological anal-

yses showed no clear signs of toxicity related to the therapy.

Conclusions: This preclinical study indicates that treatment with ^{177}Lu -NeoBOMB1 is effective and safe, with no signs of organ toxicity. No significant effect of peptide mass on efficacy and safety was observed.

OP-073

GRPR-targeted radiotherapy using the ^{177}Lu -labeled GRPR-antagonist DOTAGA-PEG₂-RM26

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Aim: Gastrin releasing peptide receptors (GRPRs) are overexpressed in prostate cancer. The ability of GRPR-antagonists to target but not activate GRPRs while displaying fast renal clearance renders them highly attractive for radionuclide therapy. We also hypothesized that anti-HER2 treatment should increase the efficacy of GRPR-targeted radiotherapy. The GRPR-antagonist based ^{177}Lu -DOTAGA-PEG₂-RM26 was chosen from a series of ^{177}Lu -X-PEG₂-RM26 analogues (X=NOTA, NODAGA, DOTA, DOTAGA) owing to highest in vivo stability and favourable biodistribution. The aim of this study was to determine the effect of treatment with ^{177}Lu -DOTAGA-PEG₂-RM26 alone or in combination with the anti-HER2 antibody trastuzumab in a murine model. **Methods:** The peptide-conjugate DOTAGA-PEG₂-RM26 was labeled with lutetium-177. The influence of injected protein dose (50-750 pmol/injection), co-injection of neprilysin inhibitor phosphoramidon and plasma-expander gelofusine, and the biodistribution over time (100 pmol/injection, 0.5-90 h pi) were studied in PC-3 xenografted mice. Dosimetry was evaluated for 100-250 pmol/injection and a pre-clinical therapeutic study was performed in PC-3 xenografted mice. Mice (n=9-10/group) were treated every second day (6 cycles) with intravenous injections of (A) PBS, (B) 200 pmol DOTAGA-PEG₂-RM26, (C) 200 pmol/60 MBq ^{177}Lu -DOTAGA-PEG₂-RM26, (D) trastuzumab (5 mg/kg), or (E) 200 pmol/60 MBq ^{177}Lu -DOTAGA-PEG₂-RM26 and trastuzumab (5 mg/kg). Groups B, C and E were co-injected with phosphoramidon (300 $\mu\text{g}/\text{mouse}$). **Results:** DOTAGA-PEG₂-RM26 was labeled with lutetium-177 with molar activity of 0.3 MBq/pmol. Tumor activity uptake increased from 12 ± 3 to $19 \pm 2 \text{ \%ID/g}$ (1h pi) upon co-administration of phosphoramidon. Co-injection of gelofusine did not improve tumor-to-kidney ratio. Activity uptake in tumors decreased with increasing injected peptide dose from $19 \pm 2 \text{ \%ID/g}$ for 50 pmol to $6 \pm 1 \text{ \%ID/g}$ for 750 pmol. Autoradiography indicated that tumor penetration was insufficient for the 50 pmol injected dose but activity distribution was homogeneous after injection of 100-250 pmol. Tumor-to-organ ratios decreased significantly with increasing peptide dose. Biodistribution of ^{177}Lu -DOTAGA-PEG₂-RM26 over time showed a rapid activity washout from all tested tissues except for kidneys and tumors. Estimated absorbed radiation dose per treatment cycle (200 pmol/60 MBq) was $\sim 11 \text{ Gy}$ to the tumor and $\sim 5 \text{ Gy}$ to the kidneys. Therapy with ^{177}Lu -DOTAGA-PEG₂-RM26 induced a significant inhibition of tumor growth. The median survival

times for control groups (**A** 42 d, **B** 46 d, **D** 44 d) were significantly shorter than for treated (**C** 65 d, **E** 74 d). Trastuzumab together with radiotherapy significantly improved survival. No treatment-related toxicity was observed. **Conclusion:** Radiotherapy using the ^{177}Lu -labeled GRPR-antagonist DOTAGA-PEG₂-RM26 was effective in inhibiting tumor growth in vivo. Anti-HER2 therapy additionally improved survival.

OP-074

First in vivo study of the MDM2/MDMX-p53 antagonist PM2 as potentiator of external radiotherapy in wt p53 cancer

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Background: Radiation treatment amplifies p53 expression in cancer cells with wild-type (wt) p53. Previous *in vitro* studies have demonstrated that amplifying wt p53 expression in combination with external radiotherapy results in increased therapeutic effects in wt 53 cancer cells. Blocking the negative regulators MDM2 and MDMX stabilizes the increased p53 expression and may therefore potentiate radiotherapy outcomes. In this study we explored the efficacy of PM2, a novel stapled peptide, that efficiently blocks the MDM2/MDMX-p53 interaction, as monotherapy and in combination with external gamma radiation therapy in *in vitro* and *in vivo* models. **Methods:** Treatment efficacy of PM2- and radiotherapy was assessed using a panel of wt p53, p53 knock-out (-/-), and mutant p53 cells grown in 2D and 3D systems. Upregulation of p53 and increased apoptotic signaling was evaluated by western blotting, flow cytometry and *ex vivo* immunohistochemistry. Effects of PM2- and/or radiotherapy were evaluated in wt p53 UM-SCC-74B and wt p53 HCT116 xenografts as well as in mutant p53 BON and p53 -/- HCT116 tumor-bearing mice. Finally, biodistribution of the peptide *in vivo* was studied using ^{125}I -labeled PM2. **Results:** PM2 monotherapy and combination-therapy induced effective cytotoxic activity in wt p53 2D and 3D assays, where PM2 in combination with radiotherapy demonstrated synergistic effects on cell survival. This effect that was not observed in p53 (-/-) and mutant p53 cells. In mouse models with HCT116 wt p53 tumors, PM2 and radiation treatment significantly prolonged survival compared to the control and single treatment groups. Biodistribution and autoradiography of ^{125}I -PM2 revealed retained high activity in the tumor. PM2 effects on mutant p53 and p53 -/- tumors were negligible. PM2-dependent p53 stabilization and increased apoptosis was confirmed with *ex vivo* immunohistochemistry. PM2 treatment did not show any indications of acute toxicity. **Conclusion:** This is the first study demonstrating the potential of the stapled peptide PM2 as a radiotherapy potentiator *in vivo*. In the future, a clinical application of PM2 together with radiotherapy in wt p53 cancers may improve tumor control and restore quality of life in cancer patients.

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Do.MoRe: Dosimetry for ^{177}Lu -DOTA-Octreotate Therapie

OP-075

Dosimetry of LUTATHERA in patients with advanced midgut neuroendocrine tumors: results of the Phase III NETTER-1 sub-study

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High levels of somatostatin receptors in NETs are the basis for Peptide Receptor Radionuclide Therapy, a treatment that uses a somatostatin analogue coupled with a beta emitting radionuclide. This report summarizes dosimetry and pharmacokinetic (PK) findings from the Phase III NETTER-1 trial. **Methods:** Dosimetry and PK evaluations were performed in a subgroup of 20 patients (mean age 58 years, range 30-74) in which LUTATHERA treatment (7.4 GBq x4 infusions at 8-week intervals) was administered in association with a commercial amino acid solution for renal protection. PK evaluation of LUTATHERA blood time-activity concentrations was performed using non-compartmental analysis. Whole body planar images were acquired for ≥ 5 time-points for up to 7 days following LUTATHERA administration. Venous blood and urine samples up to day 8 and 48 hours post-administration respectively were also collected. Regions of interest were drawn and used to derive time integrated activity coefficients. Absorbed dose values in target organs were calculated by OLINDA/EXM software. **Results:** PK/biodistribution: blood clearance profiles were biphasic, with serum levels at 8 hours being $\sim 5\%$ Cmax. Systemic clearance was 4.52 ± 1.40 L/h, mean terminal phase volume of distribution was 460 ± 246 L, indicating rapid and broad distribution. This is consistent with whole body image data, showing biodistribution in kidney (main elimination route), spleen, liver and tumor. Dosimetry: estimated mean absorbed doses for cumulative activity of 29.6 GBq were 19 ± 9 Gy for kidneys, 9 ± 7 Gy for liver, 25 ± 24 Gy for spleen, 13 ± 5 Gy for urinary bladder wall, 1.0 ± 0.8 Gy for red marrow and 1.5 ± 0.8 Gy for total body. High tumor absorbed doses in target lesions resulted from the high uptake and long-term retention of LUTATHERA in tumors. Considering the threshold absorbed doses, 23 Gy for kidneys exceeded in 7 patients, 2 Gy for red marrow would have been exceeded in 1 patient who did not complete the 4 cycles. The treatment was well tolerated, with no clinically significant renal toxicity and mild-transient hematological toxicity, not correlated with bone marrow absorbed radiation dose, indicating that laboratory values monitoring during PRRT intervals (WBC, PLT, Hb) to be

the method of choice to assess toxicities rather than absorbed dose. **Conclusions:** These results are in agreement with previous findings of Erasmus MC, demonstrating that renal doses are below commonly accepted thresholds in most cases, and confirm the favorable safety profile of LUTATHERA treatment scheme used in NETTER-1 trial. This dosimetry analysis did not identify predictive factors that would warrant patient-individual dosing.

OP-076

Absorbed doses based on a single measurement point versus three measurement points in 600 patients with neuroendocrine tumours receiving ^{177}Lu -DOTATATE therapy

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Aim: As in all therapies using ionizing radiation, a patient-specific optimization of the delivered radiation should be performed in therapy with ^{177}Lu -DOTA-D-Phe1-Tyr3-octreotate (^{177}Lu -DOTATATE). To simplify the calculation and imaging as much as possible it has been suggested that one imaging session after 96 h could be sufficient [1]. The aim of the present work was to study how well this single-point method correlates with the method used today that is based on three imaging points (24, 96 and 168 h after therapy) with a single exponential fit to determine the absorbed dose. **Materials and Methods:** Six hundred patients (261 female and 339 male) with neuroendocrine tumors with high somatostatin receptor expression were included. SPECT/CT over the abdomen was acquired at 24, 96 and 168 h after start of infusion of ^{177}Lu -DOTATATE (7.4 GBq) and absorbed doses to kidneys and tumours were calculated using the single-point and three-point methods. Differences between the two methods were assessed using Bland-Altman analysis and median, min and max of the difference. To test statistical significance a Wilcoxon matched-pairs signed rank test with a P-value of 0.05 was used. **Results:** In the kidneys and the tumors there was a small but significant difference between single- and three-point methods ($P < 0.0001$). For the kidneys, the single-point method resulted in a bias of -0.16 ± 0.41 Gy (-4%, range -45% to 35%). For tumours, the bias was 1.0 ± 3.0 Gy (-2%, range -48-57 %). In about 10% of the patients, the estimated absorbed dose to the kidneys differed more than 20%. Using a fixed limit of the absorbed dose to the kidneys would, for a four session treatment, have resulted in one less or one additional treatment in these patients when using the single-point method compared to the three-point method. **Conclusions:** Absorbed dose calculations based on only one measurement point may serve as a good approximation for the majority of patients, but would result in sub-optimal treatment in about 10% of the patients. Use of the single-point method at 96 h p.i. at every therapy session would also lead to more complicated logistics when treating patients that travel long distances, compared to our current protocol consisting of a three-point dosimetric evaluation at each fourth treatment session combined with 24 h SPECT scans only during intermittent treatments. 1.Hanscheid H et al. J Nucl Med. 2018;59:75-81.

OP-077

Accuracy and reproducibility of simplified QSPECT dosimetry for personalized ^{177}Lu -octreotate PRRT

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Purpose: To assess the accuracy and inter-observer reproducibility of simplified ^{177}Lu dosimetry protocols based on quantitative single-photon emission computed tomography (QSPECT) with a limited number of scanning time points. **Methods:** Seventy-nine NET patients receiving ^{177}Lu -octreotate therapy (with a total of 279 therapy cycles) were included in our study. Three-time-point (3TP: Day 0, 1 and 3) QSPECT scanning was performed following each therapy administration. Dosimetry was obtained using small volumes of interest activity concentration sampling for the kidney, the bone marrow and the dominant tumour. Accuracy of the simplified dosimetry based on two-time-point (2TP: Day 1 and 3, monoexponential fit) or a single-time-point (1TP_{D3}: Day 3) scanning was assessed, as well as that of hybrid methods based on 2TP for the first cycle and 1TP (Day 1 or 3; 2TP/1TP_{D1} and 2TP/1TP_{D3}, respectively) or no imaging at all (based on IA only; 2TP/NI) for the subsequent induction cycles. The inter-observer agreement was evaluated for the 3TP, 2TP and hybrid 2TP/1TP_{D3} methods using a subset of 60 induction cycles (15 patients). **Results:** The 2TP dosimetry estimates correlated highly with those from 3TP data for all tissues (Spearman $r > 0.99$, $P < 0.0001$) with small relative errors between the methods, particularly for the kidney and the tumour, with median relative errors not exceeding 2% and interdecile ranges spanning over less than 6% and 4%, respectively, for the per-cycle and cumulative estimates. For the bone marrow, the errors were slightly greater (median errors <6%, interdecile ranges <14%). Overall, the strength of correlations between the dose estimates from the simplified methods and those from 3TP method tended to progressively decrease, and the relative errors to increase, in the following order: 2TP, 2TP/1TP_{D3}, 1TP_{D3}, 2TP/1TP_{D1} and 2TP/NI. For the tumour, the 2TP/NI scenario was highly inaccurate due to the interference of the therapeutic response. There was an excellent inter-observer agreement between the three observers, in particular for the renal dose using the two most accurate methods (3TP and 2TP), with mean errors lesser than 1% and standard deviations of 5% or lower. **Conclusion:** A simplified dosimetry protocol based on two-time-point QSPECT scanning on Day 1 and 3 post-PRRT provides reproducible and more accurate dose estimates than the techniques relying on a single time point for non-initial or all cycles, while resulting in limited patient inconvenience as compared to protocols involving scanning at later time points.

OP-078

Evaluation of planar versus hybrid SPECT image methodology for bone marrow dosimetry during ^{177}Lu -DOTATATE treatments reveals the obstacles with bone

marrow metastases and cross-irradiation for the SPECT activity concentration quantification

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Introduction: The aim of this study is to compare the recently developed planar image-based method for bone marrow dosimetry with a hybrid method using SPECT/CT imaging at 24 h.p.i. of ¹⁷⁷Lu-DOTATATE. Predictive ability of the methods is compared by investigating correlations of determined absorbed bone marrow dose, with haematological toxicity during the course of four treatment cycles. The aim is also to investigate the activity distribution in the vertebral column, and how the hybrid methodology can be optimized. **Subjects and Materials:** 45 patients with advanced neuroendocrine tumours treated with ¹⁷⁷Lu-DOTATATE at Sahlgrenska University Hospital in 2011-2016 (ILUMINET-study, EUDRACT nr 2011-etc) were included in this study. Absorbed bone marrow doses were calculated as the sum of the cross-doses from high-uptake organs and the remainder of the body, and the self-dose. Cross-doses were determined by time-activity curves created using planar images and a two-compartment method in the image platform PhONSAi. The self-dose was calculated using the time-activity concentration curve for the remainder of the body adjusted with the activity concentration determined in spheres placed in the vertebral bodies in SPECT-images. To improve recovery and reduce cross-irradiation of false counts in the SPECT-image, we utilized the Monte Carlo based reconstruction code SARec. Three activity concentrations were calculated to represent the activity concentration in the bone marrow; one mean (mean SPECT) and one median (median SPECT) activity concentration based on all visible vertebrae and one where vertebrae enclosing metastases were manually excluded (w/o Mets SPECT). **Results:** The planar method, the hybrid methods mean SPECT, median SPECT, and w/o Mets SPECT, yielded absorbed bone marrow doses after treatment cycle one at 0.19 (0.12-0.32), 0.35 (0.12-1.25), 0.29 (0.11-0.92) and 0.29 (0.15-0.81) Gy/7.4 GBq, respectively. A significant dose-response relationship was established after treatment cycle one between decreased platelet counts and absorbed bone marrow dose using the planar method ($p=0.025$, $r=-0.16$). With hybrid methods, a significant correlation was firstly found after treatment cycle two between absorbed dose and decreased platelet counts using median SPECT ($p=0.018$, $r=-0.35$). **Conclusion:** Early significant dose-response relationships were established. Despite using SARec-reconstructed SPECT-imaging for specific measurement of activity concentration in bone marrow cavities, the hybrid methods were not able to perform better than the planar method. The hybrid methods yielded higher absorbed bone marrow doses compared to the planar method as both bone metastases and cross-irradiation will influence the activity quantification. Further studies on minimizing influence of bone metastases and cross-irradiation are on-going.

OP-079

Imaging of ¹⁷⁷Lu with a handheld gamma camera - quantification of the activity in superficial lesions

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Aim: Small field-of-view handheld gamma cameras have mainly been used for ^{99m}Tc sentinel-node imaging, but may offer possibilities for radionuclide therapy when small superficial structures need to be imaged as function of time after administration. The capability of activity quantification from the acquired planar images is yet little investigated. Our aim is to develop an activity quantification method for ¹⁷⁷Lu, based on a multiple-photopeak method. **Materials and methods:** The CdZnTe-based Crystal-Cam handheld gamma camera (Crystal Photonics GmbH, Berlin, Germany), with a 4x4cm² field-of-view and 16x16 detector elements, was used. Measurements were performed for phantoms and patients, with energy windows over 55keV, 113keV, and 208keV, and with MEGP and LEHR parallel-hole collimators. Prior to measurements, homogeneity corrections for ¹⁷⁷Lu and each collimator were developed, based on flat-field acquisitions. Sensitivity measurements of a disk source were made in air, for different source-collimator distances. Activity quantification was accomplished by defining a model of the count rate in each of the energy windows, as a function of the source depth and activity. Either gross, or net count rates after a triple energy window scatter correction, were modeled. The model incorporated distant-dependent detector sensitivity, photon attenuation, and scatter/buildup, where the latter was based on calibration measurements and corrected for differences between the narrow-beam and the effective attenuation. The depth and activity of a source was determined by minimizing the differences between the modeled and measured count rates in the three energy windows. **Results:** For a disk source placed behind Lucite of different thicknesses, relative activity deviations (mean±SD) of 3.1%±5.6% and 12.5%±8.1% were obtained for MEGP and LEHR, respectively. The corresponding results for measurements of spherical sources in water at different depths were -7.4%±1.7% (MEGP) and -1.5%±9.3% (LEHR). The ¹⁷⁷Lu-DOTATATE uptake in superficial lesions of two patients 24h, 92h and 168h after infusion were compared between the handheld camera and conjugate-view images from a SPECT/CT camera. The average relative activity difference between the handheld and conventional camera was -2% (range -14% to 18%) when using the MEGP collimator and -10% (range -28% to 41%) when using the LEHR collimator. The accuracies were dependent on the strategy used for region of interest (ROI) drawing, use of background ROIs, and use of scatter correction. Generally, better results were obtained with the MEGP collimator. **Conclusion:** Activity quantification of ¹⁷⁷Lu in superficial structures can be performed using the handheld gamma camera and the developed quantification method.

OP-080

Cellular dosimetry of ¹⁷⁷Lu-DOTATATE: parameter analysis and correlation with In Vitro Cytotoxicity

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Purpose: Targeted radionuclide therapy is very effective for treatment of metastatic tumors. Correlating dosimetry to biological responses at cellular level can help unveiling underlying physical processes. Only simplified in vitro (micro)dosimetry models are available and the absorbed dose to cellular targets is approximated with a generalized dosimetry model using S-values. Therefore, we performed parameter analysis of absorbed doses to cellular targets/decay and modelled cellular dosimetry of ¹⁷⁷Lu-DOTA-Tyr3,octreotate (¹⁷⁷Lu-DOTATATE) for correlation with experimental survival fractions. **Subjects and Methods:** Monte Carlo N-Particle (MCNP6.1) was used to simulate transport of ¹⁷⁷Lu electrons emitted from cell surface (CS), cytoplasm (CY), or Golgi (G). Absorbed energy fractions to nucleus, CS, CY, G and entire cell/decay (F6 tally) were calculated for monolayer cells, taking human osteosarcoma cells (U2OS+SSTR2) as reference, and including various shapes, dimensions, nucleus positions and cell proximities. ¹⁷⁷Lu-DOTATATE uptake was measured during 4h tracer incubation and afterwards during 6 days in medium, membrane-bound and internalized fractions of U2OS+SSTR2 cells. Time-integrated activities were determined for source regions over the 6-day period. Clonogenic survival assays were performed for 0.1–2.5 MBq. The dose to the nucleus was calculated applying the MIRD scheme to geometrically-shaped realistic cells and to voxelised cells, derived from actual cells in microscopic images, assuming an infinite medium and including dynamic changes in proliferation, proximity variations and cell death. The absorbed dose to the source cell (selfdose) and neighbouring target cells (crossdose) were determined. **Results:** S-values differ from -60% for selfdose and -90% for crossdose, comparing spheres to ellipsoids. Reducing the reference cell volume (CY:2450 μm³, N:1050 μm³) by 46% leads to +58% in absorbed dose, whereas increasing it by 57% leads to -25%. The cross dose (5–8% of selfdose for touching cells) decreased 99% at a distance of 5 cell diameters. $S_{N<G}$ was approximately half $S_{N<CY}$ for all dimensions, whereas the smaller the cell the higher the dose contribution by CY versus CS. Therefore, these data suggest the source would be most effective if located in CY. The absorbed doses to the nucleus for 0.1 MBq–2.5 MBq were 1.7 Gy–3.1 Gy, 38% lower than MIRDcell (2.7 Gy–5.0 Gy). The corresponding measured survival fractions were 60%–40%, leading to the following linear dose-response curve: $SF = \exp(-(0.32 \pm 0.07)D)$ ($\alpha/\beta > 100$ Gy). **Conclusion:** We propose a more refined dosimetry model for *in vitro* radiobiological experiments, offering correlation of biological endpoints to main dosimetry parameters, guiding the choice of targeting agents or the alleged translocation of molecular carriers to the Golgi, which could be usefully linked to clinical practice.

OP-081

Patient-Specific Dosimetry of ¹⁷⁷Lu-DOTATATE Peptide Receptor Radionuclide Therapy with High Activities

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Objectives: The aim of the study is to analyze post-therapeutically the dosimetry of three patients with neuroendocrine tumors treated with high activities of ¹⁷⁷Lu-DOTATATE and to compare the results of three different computer codes used for calculating the absorbed dose to the kidneys. In addition, the blood-based and image-based techniques applied to estimate bone marrow absorbed doses were analyzed. **Methods:** Multiple blood samples (up to 96h), 24h SPECT/CT data and a series of WB planar images (up to 95h) were acquired after an administered therapy activity of 14.4–19.3 GBq. The administered activities were chosen based on pre-dosimetry kidney absorbed dose coefficients obtained without kidney protection with the aim not to exceed a kidney absorbed dose of 23 Gy after a single administration of ¹⁷⁷Lu-DOTATATE (170–237 MBq). Time-activity curves (TAC) and the corresponding time-integrated activity coefficients (TIACs) for kidneys, blood, whole-body and lumbar vertebrae 2–4 (representing bone marrow) were calculated. Based on these data, patient-specific kidney absorbed dose coefficients were obtained with NUKDOS, OLINDA 1.1 and IDAC-Dose 2.1. Absorbed doses to the blood were calculated as described by Eberlein et al. (1). Image-based and blood-based bone marrow absorbed doses were analyzed and compared. **Results:** In blood we observed lower than 8% of the injected activity 2h after injection (assuming a blood volume of 5.3 liter). Compared to the standard therapy (7.4 GBq) the absorbed dose to the blood after 48 h is higher (mean: 186 ± 54 mGy vs. 79 ± 16 mGy (1)). Image-based (NUKDOS) and blood-based bone marrow absorbed doses ranged from 0.3–0.8 Gy (LV2–4-based) and 0.1–0.3 Gy (blood-based), respectively. Patient-specific kidney absorbed dose coefficients and doses were identical for NUKDOS, OLINDA 1.1 and IDAC-Dose 2.1 and well below 23 Gy (Pat 1: 0.7 Gy/GBq, 9.6 Gy; Pat 2: 0.3 Gy/GBq, 4.8 Gy; Pat 3: 0.4 Gy/GBq, 7.0 Gy). **Conclusions:** This study provides the first post-therapeutic dosimetry data of ¹⁷⁷Lu-DOTATATE patients receiving patient-specific higher activities compared to the standard ¹⁷⁷Lu-DOTATATE treatment. The results of this study show that high ¹⁷⁷Lu-DOTATATE activities can be administered safely based on pre-therapeutic kidney dosimetry. In addition, blood-based bone marrow absorbed doses are by a factor of three lower than image-based bone marrow absorbed doses advocating the use of image-based dosimetry. When patient-specific kidney masses are used, OLINDA 1.1 and IDAC-Dose 2.1 results were similar to NUKDOS which uses patient-specific voxel-based S-values. **References:** 1. Eberlein et al. EJNMMI. 2015

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Pitfalls & Artefacts 2 - Interactive Clinical Cases:
Oncology / Physics: Artefacts in Hybrid Imaging

OP-082

Basic Artefacts in Oncology CT

G. Antoch; University Hospital Düsseldorf, Department of Diagnostic and Interventional Radiology, Düsseldorf, GERMANY.

OP-083**Artefacts in SPECT/CT**

R. Hustinx; University Hospital Center of Liege, Department of Nuclear Medicine and Oncology Imaging, Department of Medical Physics, Liège, BELGIUM.

OP-084**Artefacts in PET/CT**

B. Sattler; University Hospital Leipzig, Department for Nuclear Medicine, Leipzig, GERMANY.

OP-085**Is it Artefact or Physiological Uptake?**

W. L. Wong; Mount Vernon hospital, Nuclear Medicine, Middlesex, UNITED KINGDOM.

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Sunday, October 14, 2018, 11:30 - 13:00, Hall 4

Clinical Oncology - Rapid Fire Session: Mix it up, Please!

OP-087**Voxel-based analysis of dynamic ^{18}F -FET PET enables molecular genetic and histologic glioma characterisation**

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Purpose: The assessment of glioma grade with dynamic ^{18}F -FET PET is typically performed by analysing the mean time-activity curve of the entire tumour, or a suspicious area within a heterogeneous tumour. This work aimed to ensure a comprehensive, automated and reader-independent glioma characterisation and identification of aggressive sub-volumes by performing a voxel-based analysis with diagnostically relevant semi-quantitative parameters. **Subjects and methods:** 123 dynamic ^{18}F -FET PET scans of patients with a newly diagnosed glioma classified according to molecular-genetic and histologic properties (Table1) were evaluated. A voxel-wise generation of parametric maps of time-to-peak (TTP), late slope (Slope_{15-40}), and tumour-to-background ratios obtained from 5-15 (TBR_{5-15}), and 20-40 min p.i. (TBR_{20-40}) summation data was performed. The established TBR_{20-40} -threshold of 1.6 was applied for biological tumour volume (BTV) definition. Within the BTV, volume fractions consisting of voxels with a specific parameter value were calculated, yielding the percentage volume histogram (PVH), e.g. the percentage portion of voxels with negative Slope_{15-40} within the BTV. The correlation with molecular-genetic (IDH-mutant, IDH-wildtype) and histologic classification (WHO grades II, III, IV) was assessed (Spearman's ρ) and compared to VOI-based parameters. **Results:** We found most significant differences between histologic and

molecular-genetic groups for PVH data with $\text{TTP} < 20$ min p.i., $\text{Slope}_{15-40} < 0$ SUV/h, and TBR_{5-15} and $\text{TBR}_{20-40} > 2$. Both, correlation with WHO grade and IDH mutation status, were higher for PVH data (Table2) compared to the corresponding VOI-based parameters. Similarly, ROC analysis revealed a higher sensitivity and specificity for the identification of high-grade or IDH-wild-type gliomas with PVH data compared to VOI-based parameters. All PVH data yielded an area under the curve (AUC) of 0.8, except $\text{PVH}_{\text{TBR}_{20-40} > 2}$ which showed a significant correlation with WHO grade ($p < 0.001$, $\text{AUC} = 0.7$), and a less significant correlation with IDH status ($p = 0.045$, $\text{AUC} = 0.6$). Aggressive sub-volumes defined by $\text{TTP} < 20$ min p.i. and negative Slope_{15-40} showed a high overlap with each other (dice coefficient 0.7), and a lower overlap with $\text{PVH}_{5-15} > 2$ and $\text{PVH}_{20-40} > 2$ defined hot-spots (dice 0.5 and 0.4), indicating complementarity of kinetic and static parameters. **Conclusion:** Partitioning of the entire tumour according to voxel-wise properties provides valuable information for a comprehensive and automatic glioma characterisation. Moreover, the 3D information enables a fast visual screening supporting the identification of aggressive sub-volumes, thus guiding individual therapy instrumentation.

OP-088**[^{11}C]-Methionine-PET/MRI is superior to MRI alone for detecting residual tumour burden in glioblastoma multiforme undergoing radiochemotherapy - analysis of a prospective trial**

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Introduction: Recently our group presented first results of a prospective study investigating the overall prognostic relevance of the integration of [^{11}C]-Methionine (^{11}C -MET)-positron emission tomography /magnet resonance imaging (PET/MRI) into treatment planning and follow-up of patients with glioblastoma multiforme treated with combined radiotherapy and temozolomide (RCTx) (Krause M, abstract OC-0594, Annual Congress of the European Society of Radiation Oncology 04/2018). The abstract presented here

focusses on the qualitative and quantitative evaluation of C11-MET-PET with respect to detection rate of residual tumour burden compared to contrast enhanced MRI alone.

Subjects and methods: This analysis included patients with histologically confirmed glioblastoma multiforme, macroscopic total tumour resection, indication for combined radiochemotherapy with temozolomide, start of radiochemotherapy latest 7 weeks after surgery. 11C-MET-PET/MRI was performed on a sequential PET/MRI (Philips Ingenuity PET/MRI) before and 3 months after end of radiotherapy, and every 3 months during follow-up. The uptake pattern of 11C-MET was rated qualitatively and quantitatively (tumour to reference ratio (TTR)). Uptake of MRI-contrast media (MRI-CM) was rated as indication of glioblastoma residue respective recurrence. **Results:** From 102 recruited patients, 83 pts met the above stated criteria. Before start of RCTx, 11C-MET identified tumour suspicious lesions in 54 patients compared to lesions in 35 patients with MRI ($p < 0,005$). 4 groups were distinguished according to PET/MRI uptake pattern. Group I ($n=25$): no pathologic 11C-Met-uptake, no MRI contrast enhancement. Group II ($n=31$): 11C-MET- and MRI-CM-uptake suspicious for tumour. Group III ($n=23$): 11C-MET-uptake suspicious for tumour without MRI-CM-uptake. Group IV ($n=4$): MRI-CM suspicious for tumour tissue without 11C-MET-uptake. In group I, 7 patients showed suspicious 11C-MET uptake 3 months after RCTx (TTR (mean $\pm$ SD): $1,73 \pm 0,38$), which increased to TTR: $1,99 \pm 0,42$ after 3 months. In group II, the mean TTR before RCTx was $2,76 \pm 1,20$, decreased after RCTx to $2,08 \pm 0,58$, raised again 3 months later to TTR $2,56 \pm 1,70$. In group III, the TTR before RCTx was $2,13 \pm 0,78$, decreased after RCTx to TTR $1,94 \pm 0,89$ and TTR $1,93 \pm 0,74$ three months later. **Conclusion:** Combined 11C-MET-PET/MRI before RCTx yielded significantly more information concerning remaining tumour burden than MRI alone. Qualitative and quantitative analysis was found to be well correlated. Integrative analysis of individual TTR-ratios before radiotherapy and during follow-up with respect to prognostic value for site and risk of recurrence is currently under way.

OP-089

Fibroblast Activating Protein specific ^{68}Ga -PET/CT in Gliomas

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Purpose/Introduction: Targeting Fibroblast Activating Protein (FAP) - positive tumors is a new diagnostic approach allowing the visualization of tumor stroma in addition to morphological and metabolic imaging. Here we evaluated FAP-specific imaging as a potential new diagnostic tool for gliomas. Preclinically, we analyzed the target affinity and specificity of two FAP ligands (FAP-02 and FAP-04) in vitro and the pharmacokinetics and biodistribution of both ligands in a subcutaneous glioblastoma mouse model. Clinically, we used ^{68}Ga -labelled FAP-02

and FAP-04 for PET-Imaging in 14 glioma Patients (3 IDH mutant gliomas grade II, 11 IDH wildtype glioblastomas). **Subjects and Methods:** Radioligand binding studies with ^{177}Lu - and ^{68}Ga - radiolabeled FAP-02 and -04 were performed using the human glioblastoma cell line U87MG, FAP-transfected human fibrosarcoma cells and CD26-transfected human embryonic kidney cells. For preclinical pharmacokinetic and biodistribution studies, U87MG xenografted nude mice were injected with ^{68}Ga -labeled compounds and underwent small-animal PET imaging. For biodistribution studies ^{177}Lu -labeled compounds were used. Clinical PET/CT Scans were performed 30 minutes post intravenous application of ^{68}Ga -FAP-02 / 04 (80 nmol/GBq). Standardized uptake values (SUV) were analyzed and corrected for healthy background (BG). PET Scans were correlated with corresponding MRI scans. **Results:** In vitro, both FAP-02 and FAP-04 showed a high binding specificity to their target structure FAP. In pharmacokinetic and biodistribution animal studies FAP-04 showed higher tumor accumulation, delayed elimination and better tumor -to-organ ratios than FAP-02. Clinically, Glioblastomas showed marked tracer uptake (average SUVmax $4,24 \pm 2,37$) and excellent SUVmax/BG values (average $24,34 \pm 12,11$) due to very low tracer uptake in healthy brain parenchyma (average SUVmax $0,18 \pm 0,08$). IDH mutant gliomas showed only slightly elevated tracer uptake (average SUVmax $0,35 \pm 0,10$). In Correlation with MRI scans, we observed spots with markedly increased uptake next to areas with low or missing uptake in projection on the contrast enhancing areas of glioblastomas. **Discussion/Conclusion:** FAP-specific imaging is a promising new diagnostic approach for gliomas. Markedly increased tracer uptake in Glioblastoma, but not in IDH mutant glioma may allow non-invasive grading. The heterogenous uptake pattern of FAP-specific tracers within glioblastomas may be helpful for biopsy planning. Further studies with greater number of patients, intraindividual comparison with MRI and Amino-acid-based-PET imaging and correlation with histology are necessary to further evaluate the diagnostic value of FAP-specific imaging in gliomas.

OP-090

Stress lymphoscintigraphy for early detection and management of cancer related lymphoedema

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Aim: Axillary or pelvic lymph nodes dissection place patients with melanoma, breast, urological or gynaecological cancer at life-long risk for the development of secondary lymphedema. Our aim was to evaluate the role of Stress-Lymphoscintigraphy for early detection and management of cancer-related-lymphedema. **Material and Methods:** We imaged 81 consecutive patients, which received a lymph node dissection: 13 melanoma, 45 breast cancer (3 bilateral), and 23 with uro-gynaecological

cancer, ages 52 $\pm$ 9. Test was performed at least 1 year after surgery and after completion of chemo and radiation treatments. A dose of the ^{99m}Tc -HSA-nanocolloidal, 50 MBq, 0.4 mL, was injected intradermally. The patients were imaged upright for upper limbs, or supine for lower limbs, minimizing the distance from the collimator face to the limbs. Two planar static scans at rest were acquired immediately after tracer injection (180°–300°, 128x128, LEGP collimator). Stress scans were acquired after weight-lifting (or stepping) for 2 mins. After that the patients performed a prolonged muscular exercise limited by symptoms, and delayed scans were acquired at 60 min after tracer injection. According to International Society of Lymphology the Clinical Stage (CS) and Transport Index (TI) were evaluated. **Results:** A total of 107 limbs (53 upper limbs, and 54 lower limbs) have been studied. Five patterns of lymphoscintigraphy were observed as a result of exercising: I) Normal visualization of lymphatic collectors, after exercising, in 23 limbs (22%), CS 0-1, TI <10. II) presence of collateral lymphatic vessels (<3) in 25 limbs (23%), CS 0-1, mean TI <12. III) an unusual uptake of antecubital or popliteal lymph nodes in 19 limbs (18%), CS 1-2, TI = 15. IV) a lymphangiectasia or lymph stagnation points at delayed scan (1h) in 25 limbs (23%) at CS 2-3, TI <20 V) dermal backflow in 15 limbs (14%), CS 2-3, TI <25. **Conclusion:** The scans at rest and after a quick exercise allow to better visualize lymphatic pathways. The delayed scans, after symptom-limited exercising, might visualize the residual lymph nodes draining lymph and better evaluate the effect of muscular exercise on lymph flow. In our experience, Patients with patterns I-III might benefit from an exercise program (under supervision of physiotherapist) as a first-line treatment. The patterns IV-V appear to be predictive of swelling of limb. This test might allow an earlier and personalized lymphoedema treatment, requiring an interdisciplinary approach with Complex Physical Therapy and Microsurgery (Supermicrosurgical Lymphatico-venular anastomosis and/or Autologous Lymph Node Transfer).

OP-091

Robot-assisted radioguided surgery using a novel DROP-IN gamma probe, a first-in-human translation

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Aim: Robot-assisted laparoscopic surgery has become an established technique for the management of prostate cancer and is increasingly gaining popularity for other types of cancer. During sentinel node (SN) procedures, radioguidance is provided using a traditional laparoscopic gamma probe, where the probe maneuverability restricts nodal identification. This restriction is especially limiting when low activity lesions are

located nearby a high activity background. Another key limitation is that the surgeon sits behind a surgical console and needs to verbally guide the probe positioning by the bedside assistant. To increase maneuverability and regain control on laparoscopic gamma tracing, a tethered DROP-IN gamma probe was designed which can be maneuvered using the Prograsp® robotic surgical tool. Here we present the first-in-human feasibility study of this technology. **Materials and methods:** Ten prostate cancer patients scheduled for a prostatectomy with a SN procedure received intraprostatic injections with (indocyanine green-) ^{99m}Tc Technetium-nanocolloid and underwent preoperative SN identification (lymphoscintigraphy and SPECT/CT). Surgical excision was guided by a combination of DROP-IN radioguidance and Firefly fluorescence guidance. The usability of the DROP-IN probe technology was evaluated with the operating surgeons. Anatomical regions where traditional gamma tracing is often difficult were indicated (i.e. the right obturator region, right iliaca interna and externa regions and left presacral region). **Results:** During surgery, the DROP-IN probe, when inserted via the assistant port, left space for the insertion of additional tools (e.g. for tissue retrieval). 20 SNs were resected under guidance from DROP-IN gamma tracing (with a median of 675 counts measured per node *in vivo*), 95% of these SNs was also identified using *in vivo* fluorescence imaging. During gamma tracing, the surgeon was able to independently maneuver the DROP-IN probe using the Prograsp® forceps. Even in the pre-defined difficult to scan regions (50% of excised SNs), the rotational freedom with which the probe could be positioned made it possible to distinguish SNs from background signal. Clinical implementation of the DROP-IN probe was rated positive. **Conclusion:** The successful first in-human application of the DROP-IN gamma probe indicates the technology has the potential to improve the integration of radioguided surgery concepts in the (robot-assisted) laparoscopic surgery workflow. Next to the studies on SN procedures, the DROP-IN technology is currently under evaluation in receptor targeted ^{99m}Tc -PSMA I&S radioguidance procedures.

OP-092

Quantification of an Adnectin PD-L1 PET tracer, [^{18}F]BMS-986192, in humans

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Aim: To quantify [^{18}F]BMS-986192 ([^{18}F]anti-PD-L1 tracer) uptake in patients with non-small-cell lung cancer (NSCLC). To this end, kinetic modeling of dynamic uptake data was performed and used to validate the use of simplified uptake metrics, such as SUV. **Materials and methods:** Twelve patients with advanced NSCLC eligible for Nivolumab treatment participated in this study. Simultaneously with injection of 3 MBq/kg [^{18}F]BMS-986192 a 60-min dynamic PET-CT scan was started, followed by a 30-min whole body PET-CT scan. Continuous arterial and venous blood sampling was performed in order to determine a metabolite corrected plasma input function. Visual assess-

ment of tumor uptake was performed by a nuclear medicine physician and determined as focal uptake exceeding the local background. Tumor volumes of interest were semi-automatically derived and time activity curves were fitted by several plasma input functions, including reversible and irreversible two tissue compartment models. Simplified uptake parameters included Patlak and multiple SUV parameters. **Results:** Fifteen tumors from 7 patients showed tumor uptake. The time activity curves showed a reversible component and best fits were obtained with a reversible two-tissue compartment model with k_4 fixed to 0.02 min^{-1} . The parameter best describing the uptake was the net influx rate, K_i , with values ranging from 7.6×10^{-3} to $3.1 \times 10^{-2} \text{ min}^{-1}$. From the simplified measures $\text{SUV}_{70-90 \text{ min}}$ correlated best with K_i , with an R^2 value of 0.85. Analysis of whole blood instead of parent in plasma input did not improve the correlation. **Conclusion:** A two tissue reversible model with k_4 fixed to 0.02 min^{-1} seems the most robust model for quantification of the PD-L1 PET tracer [^{18}F]BMS-986192. SUV measured at 80 minutes post injection, normalized for body weight, is the best simplified parameter for uptake assessment. This allows for clinical implementation of this tracer and to assess its predictive value for response evaluation during PD-(L)1 immune checkpoint inhibition.

OP-093

Immunotherapy Response Assessment with F-18 FDG PET/CT in Metastatic Melanoma: First Results

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Immune checkpoint inhibitors PD-1 (e.g., nivolumab, pembrolizumab) have demonstrated objective tumor responses in patients with advanced melanoma. These novel agents have distinct mechanisms of action compared to traditional cytotoxic chemotherapy. Making an assessment of therapy benefits in a given patient is challenging, especially soon after the initiation of therapy. **Aim:** to explore the utility of the ^{18}F -FDG-PET/CT for treatment monitoring in patients with metastatic melanoma receiving pembrolizumab. **Patients and methods:** 36 subjects were enrolled in this prospective trial; mean age was 59 y (range: 37–86 y), 8 women, 18 men, all patients had an ECOG performance status 0. Fifteen patients had previously received BRAF+MEK inhibitors. All 36 enrolled subjects with metastatic melanoma were evaluable for their response to therapy with pembrolizumab. A baseline scan of the whole body of each patient with ^{18}F -FDG PET/CT was performed before the planned treatment initiation (PET-0). The patients were examined again with PET/CT three months later to evaluate the therapy response (PET-1). In order to confirm or exclude a progression of melanoma metastatic disease, PET/CT was once again performed six months after the initial PET/CT study (PET-2). The therapy response was assessed at PET-1 and PET-2 according to the PET response criteria for solid tumors (PERCIST) and the Im-

mune RECIST (iRECIST). The therapy response was categorized as a partial or complete metabolic response, stable metabolic disease, a pseudo-progression and progressive metabolic disease. **Results:** Four patterns of response to pembrolizumab were observed: 11 patients had a response in baseline lesions, among them 7 had a complete response. Stable disease or steady decline in total tumor volume was recorded in 5 patients. Responses after an initial increase in total tumor burden (pseudo-progression) were notified in 4 patients. Finally, a reduction in total tumor burden during or after the appearance of new lesions in one patient was observed. Fifteen patients had progressive metabolic disease, and ten patients among them died. Out of 7 (33%) patients with negative FDG PET scans no one progressed within the 6–12 months follow-up period. **Conclusion:** A new response system, the iRECIST, was used in our study in patients treated with pembrolizumab. A pseudo-progression was found in 5 (23.8%) subjects. This analysis confirmed that the use of successive PET/CT studies were needed to discriminate a pseudo-progression from a real progression. In order to avoid a misinterpretation and premature termination of effective immunotherapy treatment, immune related response criteria for PET should be created.

OP-094

Imiomics Using Whole-body FDG PET/MR in Staging and Treatment Response Evaluation of Non-Hodgkin Lymphoma Patients Treated With CAR-T Cells

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Introduction: *Imiomics* is a new imaging analysis concept for automated detection of tumor lesions and anomalies using whole body PET/MRI. In non-Hodgkin lymphoma (NHL), PET/CT with fluorodeoxyglucose (FDG) is now a gold standard in staging and treatment response assessment; FDG PET/MR has demonstrated to be equivalent to FDG PET/CT in assessment of these malignancies, reducing the radiation burden significantly. CAR-T cells have shown promising effects in therapy refractory NHL patients. We aim to assess whether staging and response evaluation of NHL patients treated with CAR-T cells can be reliable using *Imiomics* on FDG PET/MR images compared to visual analysis. **Subjects&Methods:** Whole body FDG PET/MR scans were acquired, according to standardized protocols, in pre- and post-treatment assessments of NHL patients. Using *Imiomics*, the PET/MR images were registered to a reference coordinate system. The PET data was then statistically compared (voxel-wise t-test, $p < 0.001$, minimum cluster size of 50 voxels) with an atlas containing a voxel-wise representation of FDG uptake in healthy individuals. This approach generated so called probability-maps (p-maps), showing the extent of statistically significant abnormal regions for each PET scan. For comparison visual assessment was performed by two experienced observers, with manual VOIs outlined on the fat and water MR images for each lesion with pathologic FDG uptake. Manual VOIs were then compared slice-by-slice to the p-maps generated by *Imiomics*. **Results:** Initial results, based on 4 patients and 10

scans, showed concordance for pathologic lesions between observers and Imiomics in 70% of the total lesions (56/81) both at staging and at response evaluation, which rises to 100% for lesions ≥ 10 mm (56/56). The discordant cases, not detected by Imiomics, were lymph nodes ≤ 10 mm, a small bone marrow lesion (8mm) and one hepatic lesion (9mm). All these lesions were judged as irrelevant to the disease. Conversely, Imiomics could point out anomalies not considered as pathologic lesions in lung-liver interface, renal pelvis, bladder, brain and bowels. **Conclusion:** Imiomics has demonstrated to be a promising tool in the detection of lesions and in the evaluation of therapy response in whole-body PET/MR images, even though this method needs to be applied in larger cohort of patients to be fully validated. Improvements to this technique must be addressed in optimising the co-registration, especially in anatomic regions with large inter- and intraindividual variability (e.g. bowels, secretory urinary system).

OP-095

Potential application of 18F-FDG PET /CT scan in multisystem and single system Langerhans cell histiocytosis- a tertiary care center experience from 2011 to 2017

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Objective: In this retrospective study, we evaluated the role of FDG PET /CT in patients with multisystem or single system Langerhans cell histiocytosis (LCH) for disease extent, restaging and response to therapy. **Methods:** The population for this retrospective study was pooled database of 40 PET/CT scan in 26 patients (18males, 8 females; 15 children and 11 adults) aged 22.07 ± 19.97 years (range 1- 69 years) with pathological confirmed cases of LCH and referred to nuclear medicine department for assessment of disease status from January 2011 to December 2017. All the patients underwent 18F-FDG PET/CT imaging. PET/CT data were interpreted by two experienced nuclear medicine physicians and were used to assess metabolic and morphological tumor status and response after chemotherapy. Of these 15 scans were for staging and 24 scans for restaging/follow-up purposes. PET/CT findings were compared with conventional imaging (CT/MR) wherever available. **Results:** Out of 26 patients, 13 patients had multisystem disease (low risk - 8, high risk -5) and 13 single system disease (multifocal -6, unifocal-7). F18 FDG PET/CT was positive in 22/26 and detected skeletal (n=20), lymph nodal (n=13), liver (n=2), lung (n=4), pituitary (n=3), thyroid (n=2) and ano cutaneous lesion (n=2). FDG PET/CT identified more lesions than conventional imaging in 16 patients involving bones, lymph nodes and ano-cutaneous lesions in both the disease groups. In 4 patients with lung involvement, no significant FDG uptake was noted in the lung lesions. PET/CT upstaged the disease from single system to multisystem involvement in 2/3 patients with primary pituitary involvement and 2/2 patients with primary thyroid involvement. In PET-positive lesion SUV max was 7.9 ± 3.5 (range 3.9- 16.8). At follow-up for response evaluation, the complete metabolic response was

noted in patients with a single system or multisystem with low-risk group (n=5) as compared to multisystem with high-risk group (n=2) in whom disease progression was noted. **Conclusion:** In this retrospective study we conclude that except for lung involvement FDG PET/CT is better than conventional imaging both for the single system and multisystem LCH for initial staging as well as restaging and response evaluation.

OP-096

¹⁸F-FDG PET/MR including DWI in initial N-Staging in patients with malignant melanoma: Is it a possible replacement for sentinel lymph node biopsy?

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Purpose: To analyze the performance of 18F-fluorodesoxyglucose positron emission tomography / computed tomography (18F-FDG PET/CT), 18F-FDG PET / magnetic resonance imaging (18F-FDG PET/MRI) as well as 18F-FDG PET/MRI and diffusion weighted imaging (DWI) in comparison to sentinel lymph node biopsy (SLNB) in initial N-staging in patients suffering from malignant melanoma. **Subjects & Methods:** Fifty-two patients suffering from histopathologically proven malignant melanoma (female: n=30, male: n=22, mean age: 50.5y) were included in this retrospective study. 18F-FDG PET/CT and consecutive PET/MRI including DWI was performed in all patients prior to lymphoscintigraphy with SPECT/CT and consecutive SLNB. The sentinel lymph nodes detected by SPECT/CT were characterized as benign or malignant by two readers in 18F-FDG PET/CT, 18F-FDG PET/MRI as well as in 18F-FDG PET/MRI including DWI images. Focal tracer uptake was considered as a sign of malignancy in all hybrid imaging modalities. In PET/MRI, these additional morphological criteria were considered as indicators for malignancy: necrosis, absence of a fatty hilus, loss of oval shape, irregular cortical thickness and extracapsular spread. In 18F-FDG PET/MRI including DWI, all of the aforementioned criteria as well as and diffusion restriction were considered as indicators of malignancy. By using histopathologic results after SLNB as a reference standard, sensitivity, specificity as well as positive (PPV) and negative predictive values (NPV) were calculated. **Results:** In the analyzed cohort, 87 lymph nodes were considered as sentinel lymph nodes by lymphoscintigraphy and SPECT/CT. Seventeen lymph nodes were metastatic according to the reference standard after SLNB. For 18F-FDG PET/CT, a sensitivity, specificity, PPV and NPV of 17.7%, 95.6%, 50.0% and 82.3% was calculated. For PET/MRI, we found a sensitivity, specificity, PPV and NPV of 23.5%, 96.9%, 66.7% and 82.3%. In 56 lymph nodes, DWI was available for analysis. The additional information of DWI led to two additional false positive findings in PET/MRI. **Conclusion:** Due to its low sensitivity and specificity, even advanced hybrid imaging techniques such as 18F-FDG PET/MRI including DWI are unable to improve the sensitivity and specificity in initial N-Staging in patients with malignant melanoma and will therefore not be able to replace SLNB in the near future.

401 Sunday, October 14, 2018, 14:30 - 16:00, Plenary Hall
CME 3 - Cardiovascular: SPECT or PET?

OP-097

Detection of CAD

F. Bengel; Hannover Medical School, Department of Nuclear Medicine, Hannover, GERMANY.

OP-098

Myocardial Blood Flow Quantification

A. Manrique; Caen University Hospital, Department of Nuclear Medicine, Caen, FRANCE.

OP-099

Infection

F. Hyafil; Bichat Hospital, Department of Nuclear Medicine, Paris, FRANCE.

OP-100

Innervation

H. Verberne; Academic Medical Center, Department of Nuclear Medicine, Amsterdam, NETHERLANDS.

402 Sunday, October 14, 2018, 14:30 - 16:00, Hall 2

Joint Symposium 5 - Inflammation & Infection / Cardiovascular / EULAR: Guidelines on Vasculitis

OP-101

Clinical Aspects of Vasculitis

M. Cimmino; University of Genoa, Rheumatology, Genoa, ITALY.

OP-102

Clinical Implementation of Imaging in Vasculitis

C. van der Laken; Free University of Amsterdam, Rheumatology, Amsterdam, NETHERLANDS.

OP-103

Radiological Aspects of Vasculitis

T. Bley; University Hospital Würzburg, Radiology, Würzburg, GERMANY.

OP-104

Nuclear Medicine Aspects of Vasculitis

R. Slart; Department of Nuclear Medicine and Molecular Imaging, University of Groningen, University Medical Center Groningen, Groningen, NETHERLANDS.

403 Sunday, October 14, 2018, 14:30 - 16:00, Hall 3

Joint Symposium 6 - Oncology / ISNS / EHNS: What is Changing in the Sentinel Node Procedure?

OP-106

MSLT-II and the Implications for Sentinel Node Biopsy in Melanoma

J. Klode; University Hospital Essen, Clinic for Dermatology, Essen, GERMANY.

OP-107

Sentinel Node Biopsy in Breast Cancer - New Insights and Indications

J. van der Hage; Leiden University Medical Centre, Department of Surgery, Leiden, NETHERLANDS.

OP-108

Changing Management in Head and Neck Cancer - Results of the Consensus Conference on Sentinel Lymph Node Biopsy

M. McGurk; University College Hospital London, H/N Oncology Department, London, UNITED KINGDOM.

OP-109

New Insights and Indications in Sentinel Node Biopsy - What Changes for Nuclear Medicine?

S. Vidal-Sicart; Hospital Clínic, Department of Nuclear Medicine, Barcelona, SPAIN.

404a

Sunday, October 14, 2018, 14:30 - 15:30, Hall 5

Mini Course 1: Non-Imaging Nuclear Medicine Diagnostic

OP-111

Isolated Limb Perfusion – Experimental Innovation

P. Fragoso Costa; University Hospital Essen, Clinic for Nuclear Medicine, Essen, GERMANY.

OP-112

State of the art of GFR and Platelet studies in Nuclear Medicine

M. Burniston; Barts Health NHS Trust, Nuclear Medicine, London, UNITED KINGDOM.

405

Sunday, October 14, 2018, 14:30 - 16:00, Hall X

M2M: PSMA Targeting

OP-113

Development and Characterization of a PSMA-targeting Antibody for SPECT/CT, Fluorescence Imaging and Targeted Photodynamic Therapy of PSMA-expressing Tumors

A. Kip¹, S. Heskamp¹, G. M. Franssen¹, C. Frielink¹, G. Fracasso², K. Herrmann³, M. Gotthardt¹, M. Rijpkema¹, S. Lutje¹; ¹Radboud university medical center, Nijmegen, NETHERLANDS, ²University of Verona, Verona, ITALY, ³University Hospital Essen, Essen, GERMANY.

Introduction: Prostate cancer (PCa) recurrences after surgery frequently occur, amongst others as a result of incomplete tumor resection, resulting in positive tumor margins. To improve PCa management, the multi-modal PSMA-targeting agent [111-In]In-DTPA-D2B-IRDye700DX was developed and characterized in vitro and in vivo. This agent can be used for both pre- and intra-operative tumor localization, fluorescence image-guided surgery, and eradication of (residual) tumor tissue by PSMA-targeted photodynamic therapy (tPDT), which is a highly selective cancer treatment based on targeting molecules conjugated to photosensitizers that can induce cell destruction upon exposure to near-infrared (NIR) light. **Methods:** The anti-PSMA monoclonal antibody D2B was conjugated with IRDye700DX and DTPA and subsequently radiolabeled with [111-In]In. tPDT functionality was first tested in vitro, on PSMA positive and negative cell lines, at different conjugate doses and NIR light exposures. In vivo, the optimal time point and dose for tPDT were determined in BALB/c nude mice with PSMA⁺ s.c. LS174T-PSMA xenografts after intravenous injection of [111-In]In-DTPA-D2B-IRDye700DX followed by μ SPECT/CT, near-infrared fluorescence imaging, and biodistribution at 24, 48, 72, and 168 hours p.i. To assess the therapeutic potential of tPDT, growth of LS174T-PSMA xenografts and overall survival of mice treated with the conjugate followed by 1–3 times of NIR light irradiation (100 or 150 J/cm²) at 24 hours p.i. was compared to mice that received either NIR light or PBS alone. **Results:** In vitro, tPDT was PSMA-specific for PSMA⁺ tumor cells. Efficiency increased with light exposure and conjugate dose, cell viability decreasing up to 15.3 $\pm$ 1.5 % after treatment with 150 J/cm². Biodistribution revealed no significant differences in tumor uptake in mice at 24, 48, 72, and 168 hours p.i.. PSMA⁺ tumors were clearly visualized with both μ SPECT/CT and NIR fluorescence imaging. Median survival of mice treated with DTPA-D2B-IRDye700DX and 3x150 J/cm², 1x150 J/cm², 3x100 J/cm² of NIR light was significantly improved compared to both control groups (70, 61, and 36 days vs. 16 days for both controls, respectively, p=0.0009). Treatment with 3x150 J/cm² resulted in significantly prolonged survival compared to treatment with 3x100 J/cm² (p=0.0224). No significant difference was observed between mice that received 3x150 J/cm² or 1x150 J/cm² (p=0.6714). **Conclusion:** Proof-of-principle was provided that [111-In]In-DTPA-D2B-IRDye700DX can be used for detection of PSMA⁺ xenografts with radionuclide and fluorescence imaging and for PSMA-targeted PDT. PSMA-tPDT (80 μ g/mouse, irradiation at 24 h p.i.) resulted in significant prolongation of median survival. In the future, multi-modal PSMA-targeting agents may be used to improve outcome after PCa surgery.

OP-114

Synthesis and Biological Evaluation of 1,2,3-Triazole-linked ¹⁸F-Labeled PET Tracers for Imaging of PSMA

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Aim: In the development of PSMA-PET tracer, there has been a significant inverse relationship between binding affinity to PSMA and pharmacokinetic properties. The aim of this study is to find compounds having rapid clearance property while retaining good binding affinity to PSMA. **Materials and methods:** Nine ¹⁸F-labeled compounds, a combination of R₁ and R₂ substituents, were synthesized in good radiochemical yields using a Cu(I)-catalyzed click chemistry between ¹⁸F-labeled azides (R₁) and *N*-propargyl substituted Lysine-urea-Glutamates (R₂). 22RV1 and PC-3 PIP/flu cell lines were used to evaluate compounds in vitro and in vivo, and ¹⁸F-DCFPyL was used for comparison. **Results:** In vitro binding assay using 22RV1 cell line revealed that the compound (FC313) having pyridine moiety has the best binding affinity (IC₅₀=7.06 nM) to PSMA. MicroPET imaging of 22RV1-xenografted mouse was performed for different R₂ substituted compounds (FC303, FC313, and FC323). All compounds exhibited intense uptake in 22RV1 tumors and rapid renal clearance, among which FC303 resulted in the best pharmacokinetic properties with no significant nonspecific organ uptake. Additional microPET imaging with PC-3 PIP/flu tumor bearing mouse was performed for FC303 and FC313, which showed more intense tumor uptake and better tumor-to-background ratio than 22RV1 tumor. In the biodistribution study with PC-3 PIP/flu tumor bearing mouse, PSMA+ PC-3 PIP tumor uptake of ¹⁸F-FC303 reached the maximum at 0.5 h postinjection (%ID/g, 13.80 $\pm$ 3.35, n=4), and maintained for 4 h with no significant decline. The PC-3 PIP/flu and PC-3 PIP/muscle ratios were 58 and 31 at 0.5 h, 118 and 76 at 1 h, 192 and 265 at 2 h, and 313 and 582 at 4 h, respectively. **Conclusion:** Based on in vitro and in vivo studies on new compounds, FC303 was confirmed to have promising characteristics for PET imaging of prostate cancer. Further preclinical studies are currently underway to enter clinical development.

OP-115

A Complete Response following A Single Treatment with ²²⁵Ac-RPS-074 in LNCaP Xenografts

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Aim: Targeted alpha radiotherapy (TAT) using Actinium-225 is a highly promising strategy for the treatment of PSMA-expressing prostate cancer, but side effects such as dry mouth and dry eye are currently severe and irreversible. New ligands with improved normal tissue kinetics are required to deliver maximum therapeutic effect without unacceptable side effects. We evaluated the therapeutic dose response of ²²⁵Ac-RPS-074, a trifunctional ligand that targets PSMA and binds serum albumin, in a preclinical LNCaP xenograft model. **Materials and Methods:** RPS-074 was synthesized from a 3-ethynylphenylurea-Glu-urea-Lys derivative, *N*-(4-(4-iodophenyl)butanoyl)lysine and macropa-NCS.

RPS-074 was radiolabeled with Ac-225 in 15 min at 25°C and pH 5–6. Male BALB/C nu/nu mice bearing LNCaP xenograft tumors (4 mice/time point) were injected with 105 kBq ²²⁵Ac-RPS-074 and sacrificed at 4h, 24h, 7d, 14d and 21d post injection (p.i.). For the therapy study, LNCaP bearing mice (7/group) were randomly assigned to one of four groups: 148 kBq, 74 kBq, 37 kBq ²²⁵Ac-RPS-074 or vehicle. Tumor volumes were measured 3x weekly for 75d, and mice were sacrificed when tumor volume exceeded 2000 mm³. **Results:** ²²⁵Ac-RPS-074 labeling was quantitative. Tumor uptake peaked at 24h p.i. (12.7±1.5 %ID/g) in concert with clearance from the blood, and was sustained beyond 14d p.i. (11.9±1.5 %ID/g). Kidney uptake was highest at 4h p.i. (6.7±0.4 %ID/g) and rapidly decreased such that tumor-to-kidney ratios exceeded 5 by 24h p.i. Activity levels in normal tissues decreased with blood activity. All mice treated with 148 kBq ²²⁵Ac-RPS-074 survived to 75d without loss of body weight and revealed decreasing tumor volumes by 10d p.i. At 30d p.i. 86% (6/7) of tumors were undetectable. At 75d, absence of tumors was confirmed by µPET/CT imaging and dissection. Mice in the 74 kBq group also exhibited decreasing tumor volumes by 10d p.i., but after 42d p.i. tumor re-growth was observed in 86% of mice, and 14% of mice did not survive to the study's endpoint. Although tumor volumes increased following treatment with 37 kBq ²²⁵Ac-RPS-074, survival was significantly prolonged relative to the control (vehicle) group. **Conclusion:** ²²⁵Ac-RPS-074 shows a promising biodistribution profile and a well-defined dose response. A single cycle of 148 kBq ²²⁵Ac-RPS-074 induced a complete response in 86% of mice and a partial response in 14% of mice. With a promising side effect profile and demonstrable efficacy in large tumors (initial volume >800 mm³), ²²⁵Ac-RPS-074 merits clinical translation for TAT of prostate cancer.

OP-116

Fully Convolutional Neural Network to Assess Skeleton Tumor Burden in Prostate Cancer Using ⁶⁸Ga-PSMA-11 PET/CT: Preliminary Results

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Aim: Treatment of bone metastases plays an important role for patients with metastatic prostate cancer (mPC). PSMA-based PET imaging is increasingly used to delineate bone tumor burden before therapy. Bone scan Index (BSI) and Bone- PET-Index (BPI) are promising in assessing treatment outcome in patients with mPC. However, the semiautomatic segmentation using conventional methods in skeleton tumor burden assessment can be time-consuming and lengthy. The emerging of deep learning methods have provided great potential to extend the limit of conventional methods. We aimed to assess the feasibility of deep learning network in bone lesion delineation and tumor burden quantification. **Methods and Materials:** A fully convo-

lutional neural network (FCNN) concept was proposed to automatically detect bone lesions and characterize osseous tumor burden from ⁶⁸Ga-PSMA-11 PET/CT imaging. A pipeline of two FCNNs was employed in a cascaded form. The first part of the cascaded network generates bone mask from CT images as anatomical regions of interest (ROI), while the second part detects and segments bone lesions based on PET imaging restricted to the anatomical regions within the generated bone mask. For proof-of-concept test, 50 ⁶⁸Ga-PSMA-11 PET/CT from patients with mPC were included. SUV of PET images were calculated and the bone lesions were semi-automatically annotated using an in-house developed software. Forty ⁶⁸Ga-PSMA-11 PET/CT scans were used as training data set for the FCNN and the remaining 10 scans were used as test dataset for performance assessment. The performance of the developed method was evaluated by considering the overall segmentation result in the form of a slice-wise lesion detection accuracy and Dice score, including the Recall and Precision scores. **Results:** The developed deep learning method has achieved a slice-wise detection accuracy of 91% with a positive predictive value (PPV) of 78%. The average segmentation Dice score was 76%, with a Recall and Precision scores of 86% and 66%, respectively. **Conclusion:** Our results highlight that even in a small size training dataset, deep learning can successfully detect bone lesions in a ⁶⁸Ga-PSMA-11 PET/CT setting. A higher accuracy for lesion segmentation should be obtained by increasing the number of training dataset and providing physiological lesion contouring to guide the training process. Accurate bone lesions detection and segmentation could be further implemented in the treatment setting.

OP-117

Multimodal anti-PSMA ligands for intra operative tumor detection and targeted photodynamic therapy of PSMA-expressing tumors

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Introduction: Incomplete resection of prostate cancer (PCa) and its metastases may lead to disease recurrence and consequently poor patient outcome. To obtain complete resection of tumor tissue, prostate specific membrane antigen (PSMA) targeting multimodal ligands containing both a radiolabel and a photosensitizer are developed. These ligands may be used for intra-operative tumor detection, accurate tumor delineation, and tumor-targeted photodynamic therapy (tPDT); a selective cancer treatment that induces cell destruction upon exposure to near-infrared (NIR) light. The aim of our study was to develop and evaluate multimodal [¹¹¹In]In-DOTAGA-IRDye700DX-PSMA targeting agents for intra-operative detection and treatment of PSMA-positive tumor lesions. **Methods:** Different variants of glutamate-urea-lysine based DOTAGA-PSMA-targeting ligands, varying in their linker moieties, were synthesized using solid phase chemistry, coupled to IRDye700DX and labeled with ¹¹¹In. PSMA-mediated binding and internalization was determined *in vitro* using PSMA-expressing LNCaP cells. Furthermore,

LS174T-PSMA positive and negative cells were exposed to 300 J/cm² NIR irradiation and cell viability was determined with the CellTiter-Glo® assay. **In vivo** tumor targeting properties were evaluated in BALB/c nude mice with subcutaneous LS174T-PSMA positive and negative LS174T tumors using microSPECT/CT, NIR fluorescence imaging, and ex vivo biodistribution studies (2 hours p.i. of ¹¹¹In-labeled multimodal ligands, 0.3 nmol, 10 MBq/mouse). **Results:** Multimodal ligands showed specific binding to PSMA-expressing LNCaP cells. **In vitro** PDT resulted in a specific kill of PSMA expressing cells (LS174T-PSMA: 87.6% ± 5.8% compared to LS174T: 2.8% ± 2.7%). **In vivo**, accumulation in LS174T-PSMA tumors of [¹¹¹In]In-DOTAGA-IRDye700DX-PSMA ligands (11.1 ± 0.8 and 14.1 ± 1.4 %ID/g) was significantly higher than that of [¹¹¹In]In-DOTAGA-PSMA ligands without the fluorophore (5.7 ± 0.3 and 6.5 ± 1.9, P<0.05). In PSMA-negative tumors, uptake was <0.85 %ID/g for all ligands. Moreover, prolonged blood circulation was observed for ligands with the IRDye700DX fluorophore (0.68 ± 0.01 and 1.00 ± 0.15 %ID/g) compared to the ones without IRDye700DX (0.08 ± 0.04 and 0.07 ± 0.02 %ID/g, 2 hrs p.i.). Subcutaneous LS174T-PSMA tumors could be clearly visualized using microSPECT/CT and NIR fluorescence imaging. **Conclusions:** Here we demonstrate highly specific and efficient uptake of newly developed [¹¹¹In]In-DOTAGA-IRDye700DX-PSMA-targeting ligands in PSMA-positive tumors. Furthermore, the feasibility of [¹¹¹In]In-DOTAGA-IRDye700DX-PSMA ligand-mediated tPDT on PSMA-positive cells was demonstrated **in vitro**. In the future, these ligands can be used for intra-operative tumor detection to improve the surgical outcome of PCa patients.

OP-118

Discovery of 2-MeO-[¹⁸F]DCFPyL ([¹⁸F]PSMA-7) as PET-probe suitable for imaging of small PSMA positive lesions

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Aim: Prostate specific membrane antigen (PSMA) expressed by the vast majority of prostate cancers (PCa) is a particularly promising target for PCa staging and imaging. PSMA specific PET ligands are already widely used in PCa diagnostics. Especially, [¹⁸F]DCFPyL enables the detection of PCa lesions with sensitivity higher than that of the widely used [⁶⁸Ga]Ga-PSMA-HBED-CC. However, [¹⁸F]DCFPyL has some limitations with respect to the detection of very tiny lesions and pharmacokinetics. The aim of this study was the development of ¹⁸F-labeled PSMA specific probes with improved PSMA sensitivity and imaging properties. **Methods:** Nine potential PSMA ligands, with general structure HO-X(Y)-CO-Glu-OH {where, X = Glu[NH(CH₂)₂NH], Lys, 4-ThiaLys, 4-[NH(CH₂)₂NH-(CO)-O]Nva, 5-triazolo-Nle; Y = 2-[¹⁸F]FPh, 6-[¹⁸F]F-Py, 6-[¹⁸F]F-2-and -4-MeO-Py, 6-[¹⁸F]F-Pz and 6-[¹⁸F]F-Pdz} were prepared. The cellular uptake of the radiotracers in PSMA⁺ LNCaP C4-2 and PSMA⁺ PC-3 cells was determined after 2 h and 4 h incubation time and compared to that of [¹⁸F]DCFPyL. Tracers were evaluated by μPET in normal rats employing PSMA⁺ peripheral ganglia as target structures mimicking small

PCa lesions. For the best candidate the resulting PET images were assessed in comparison to [¹⁸F]DCFPyL and [¹⁸F]PSMA-1007 scans with respect to key image quality parameters, like signal-to-noise ratio, sharpness and resolution. **Results:** Radio-fluorinated probes were produced in 20–40% RCYs and excellent radiochemical purities. HO-Glu{NH(CH₂)₂NH-6-[¹⁸F]F-Py}-CO-Glu-OH, [¹⁸F]Thia-DCFPyL and [¹⁸F]PSMA-7 demonstrated PSMA specific cellular uptake comparable or higher than that of [¹⁸F]DCFPyL (%ID/10⁵ cells: 1.13±0.03 and 3.20±0.02; 1.21±0.03 and 3.07±0.02; and 2.03±0.03 and 3.31±0.01 vs. 1.55±0.05 and 3.1±0.03 after 2 and 4 h, respectively). While the signal-to-noise ratio of the [¹⁸F]Thia-DCFPyL, [¹⁸F]DCFPyL and [¹⁸F]PSMA-1007 was comparable (4.04, 6.4±1.9 and 6.2±1.9), it was higher for [¹⁸F]PSMA-7 scans (8.2±1.7). The image sharpness measured for the superior cervical ganglion was significantly higher for [¹⁸F]PSMA-7 and [¹⁸F]PSMA-1007 compared to [¹⁸F]DCFPyL (0.075±0.027 and 0.097±0.025 vs. 0.019±0.008). The resolution determined for the apical pair of spinal ganglia was comparable for all three tracers (1.09±0.04 and 0.92±0.07 vs. 1.00±0.14). [¹⁸F]PSMA-1007 demonstrated higher blood protein binding (%ID: 62.6±10.7 vs. 12.9±3.0 and 16.3±4.2) and bone uptake (%ID: 33.2±9.5 vs. 12.4±4.3 and 9.9±1.9) than [¹⁸F]DCFPyL and [¹⁸F]PSMA-7. Noteworthy, the MeO substituent in 4th instead of 2nd position and 4-ThiaLys instead of the Lys residue in [¹⁸F]PSMA-7 resulted in the diminished PSMA specific uptake and significantly worse image quality. **Conclusion:** [¹⁸F]PSMA-7 is a promising candidate for the high quality visualization of small PSMA-positive lesions which deserves careful preclinical and clinical evaluation.

OP-119

¹⁸F-Labeled dual AmBF₃-Glu conjugated Lys-ureido-Glu derivative for imaging PSMA expression in prostate cancer with positron emission tomography

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Introduction: Expressed in most prostate cancers (PCa), the membrane-bound glycoprotein prostate-specific membrane antigen (PSMA) is an attractive diagnostic imaging biomarker. Previously, we reported the synthesis and evaluation of ¹⁸F-labeled HTK01157, a PSMA-617 derivative containing an ammoniomethyl-trifluoroborate (AmBF₃) motif for radio-labeling using the facile ¹⁸F-¹⁹F isotope exchange reaction. Despite its excellent LNCaP tumor uptake (12.1±2.93%ID/g) and tumor-to-background contrast ratios (tumor-to-blood= 17.3±6.01; tumor-to-muscle= 47.6±31.3) at 1-h post-injection, ¹⁸F-HTK01157 showed significant hepatobiliary excretion (12.8±5.12%ID/g in intestines). In this study, we designed and evaluated a novel PSMA-617 derivative, ¹⁸F-HTK01174, containing two AmBF₃-Glu motifs to minimize hepatobiliary excretion. **Methods:** After assembling the PSMA-617 pharmacophore (tranexamic acid-2-Nal-Lys-ureido-Glu) on solid phase, Lys was coupled to the C-terminus, followed by Glu to both the α- and ε-amino groups of Lys. After coupling azidoacetic acid to Glu,

peptides were cleaved off the solid support and clicked with *N*-propargyl-*N,N*-dimethyl-ammoniomethyl-trifluoroborate to obtain the desired dual AmBF₃-Glu conjugated standard. Affinity to PSMA was measured via competition binding assays using LNCaP cells and ¹⁸F-DCFPyL as the radioligand. Radiofluorination was conducted via ¹⁸F-¹⁹F isotope exchange reaction. PET imaging and biodistribution studies were performed in mice bearing PSMA-expressing LNCaP PCa xenografts at 1-h post-injection, and results were compared with those obtained from ¹⁸F-DCFPyL, the most popular ¹⁸F-PSMA-targeted tracer in the clinic. For blocking studies, mice were co-injected with 0.5 mg of nonradioactive DCFPyL. **Results:** HTK01174 had high binding affinity to PSMA with K_i = 0.22±0.01 nM. ¹⁸F-HTK01174 was obtained in 7±6% (n=3) decay-corrected radiochemical yield with >99% radiochemical purity and 211±48 GBq/μmol specific activity. Both ¹⁸F-HTK01174 and ¹⁸F-DCFPyL successfully delineated PSMA-expressing LNCaP tumors in PET images with excellent tumour-to-background contrast and minimal hepatobiliary excretion (<0.4%ID/g average intestinal uptake for both tracers). Compared with ¹⁸F-DCFPyL, ¹⁸F-HTK01174 exhibited higher uptake in LNCaP tumors (7.95±1.64 vs 16.8±2.23%ID/g) and superior tumor-to-blood (26.1±3.33 vs 32.0±7.82), tumor-to-muscle (46.8±18.3 vs 78.0±33.3) and tumor-to-liver (3.64±0.57 vs 84.5±18.7) contrast ratios. Co-injection with nonradioactive DCFPyL reduced the uptake of ¹⁸F-HTK01174 in LNCaP tumors by >95%, demonstrating its specific PSMA targeting. **Conclusion:** We successfully solved the high intestinal uptake problem of ¹⁸F-HTK01157 with the conjugation of two AmBF₃-Glu motifs to the PSMA-617 pharmacophore. The resulting ¹⁸F-HTK01174 showed not only minimal hepatobiliary excretion, but also superior tumor uptake and tumor-to-background contrast ratios when compared with ¹⁸F-DCFPyL. With excellent tumor uptake, tumor-to-background contrast and ease of synthesis, ¹⁸F-HTK01157 warrants further investigation as a PSMA PET imaging agent.

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Sunday, October 14, 2018, 14:30 - 16:00, Hall Y

Do.MoRe: Image Processing / Analysis

OP-120

Multi-Task Deep Learning for the Detection of Lesions on ⁶⁸Ga-PSMA PET/CT Imaging

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Purpose: The emerging PSMA targeted radionuclide therapy provides an effective method for the treatment of advanced metastatic prostate cancer. To optimize diagnostics, therapy monitoring and ultimately the theranostic benefit, it is urgently needed to characterize all the lesions to target before the treatment. However, this is extremely challenging considering the factor that dozens of lesions of heterogenous size and uptake may distribute in a variety of anatomical context with different background. Until now, there is no successful computer-aided

lesion detection methods for PSMA imaging. **Methods:** A cohort of 71 patients with advanced metastatic prostate cancer were scanned with ⁶⁸Ga-PSMA-11 PET/CT. For proof-of-concept, we focus on the detection and segmentation of bone & lymph node lesions in the pelvic area. To train the network, the bone and lymph node lesions were manually labelled by a nuclear medicine expert. A multi-task deep learning architecture (MulTi-Net) based on fully convolutional neural networks was developed to detect the lesions. It aimed to first extract salient features from PET and CT, the combined features would then be adopted to automatically detect all the lesions in a 3D manner. The framework contains five fully connected convolutional layers and two sigmoid classification layers. In contrast to conventional V-Net, it deleted pooling layer to avoid possible losing of fine texture information. A cross-hair filter was integrated to extensively reduce hyperparameters and speed up the training procedure. An additional regularization was added to deal with class imbalanced tumor-to-background ratio. For comparison, the detection accuracy of conventional W-Net (cascaded V-Nets) were calculated. **Results:** Compared with conventional W-Net, the multi-task deep learning has improved the detection precision from 72.8% to 90.2%, recall from 59.9% to 76.3% for bone lesion. For the lymph node lesion (n=63), it improved the detection precision from 57.8% to 81.4% and recall from 44.1% to 62.6%. **Conclusion:** We proposed the first deep learning method for automatic detection of lesions on ⁶⁸Ga-PSMA-11 PET/CT images. A multi-task deep learning method was developed to improve the detection accuracy compared with conventional W-Net. The preliminary test on pelvic area confirmed the potential of deep learning methods. At the moment, more data is being processed, since increasing the amount of training data will further enhance the performance of the developed deep learning methods.

OP-121

Feature Extraction Optimization by Measuring Radiomics Feature Noise in ¹⁸F-FDG PET Images: A multi-center study

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Aim: Radiomics evaluation based on in vivo Positron Emission Tomography (PET) has been widely performed for disease characterization. Nevertheless, several textural features have been reported to be sensitive to acquisition variations, reconstruction protocols, region-of-interest delineation and differences in PET value discretization. Our goal was to (a) measure the variance of several textural radiomic features in a multi-center study and (b) to establish a feature rank of radiomic features based on optimal feature extraction parameters. Our hypothesis built on the assumption that variations across multi-center evaluations with the same physical phantom with homogeneous spheres can help to characterize the radiomic noise of individual features. **Materials and Methods:** Reconstructed NEMA IQ PET images acquired with site-specific clinical routine protocols at 13 PET/CT systems were collected [1]. Semi-automated delineation of the four largest spheres was done using iso-count region grow-

ing applying maximum volume constraints in the Hermes Hybrid 3D software. For each image data set, voxel values in the spheres were normalized to the mean of a cuboid background region to calculate tumour-to-background (TBR) values. Thirty four textural features were extracted from the TBR-normalized spheres including Grey level co-occurrence matrix (GLCM), Grey level zone size matrix (GLZSM) and Neighborhood grey tone difference matrix (NGTDM) features. This was done for four different bin sizes (0.01, 0.025, 0.05, 0.1) and 3 Kriging resampling (1, 2 and 4 mm) combinations (12 overall). Relative standard deviations (RSD) across the 13 imaging systems were calculated for each of the 12 configurations and the 4 spheres (48 overall). Feature extraction configurations minimizing the mean RSD across spheres were selected to establish a feature rank.

Results: Most stable features with their optimal values (RSD, resolution, bin size) were GLCM Information correlation (0.00%, 4mm, 0.01), GLZSM Small zone size emphasis (2%, 4mm, 0.01), GLCM Entropy (2.07%, 4mm, 0.01) and GLZSM Zone size percentage (3.55%, 4mm, 0.01). Least stable features were NGTDM Complexity (55%, 4, 0.01), Contrast (56%, 4mm, 0.01), Cluster shade (76%, 1mm, 0.01) and Cluster prominence (84%, 4mm, 0.01). **Conclusions:** As a result of our investigation, we identified textural features and their optimized parameters that minimize their multi-center variations. **References:** 1: Rausch I, et al; *Variation of system performance, quality control standards and adherence to international FDG-PET/CT imaging guidelines. A national survey of PET/CT operations in Austria.* Nuklearmedizin 2014;53(6):242-248

OP-122

PET segmentation of bulky tumors: inter-observer variability of four segmentation approaches

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Purpose: PET-based tumor delineation is an error prone part of image analysis and feature extraction. Due to partial-volume-effects, image noise and varying intrinsic contrast, tumour segmentations are challenging, especially for patients with large, heterogeneous and bulky tumour FDG-load (MATV>300mL). In order to facilitate this process, automatic segmentation algorithms have been developed, each of them with their specific limitations. Therefore, nowadays, most delineations are performed manually, which is time-consuming and subjective. Hence, there is a need for other approaches leading to less variability without being fully automatic. This study compares the inter-observer variability and the segmentation quality of four (manual and semi-automatic) segmentation approaches with different levels of user-interaction. **Methods:** Twenty datasets of FDG PET-CT images with bulky tumours were independently segmented by six observers using four approaches: (I) A manual segmentation; (II) an interactive threshold-based segmentation; (III) an interactive threshold-based segmentation with the additional presentation of a PET-gradient image; (IV) and the selection of the most reasonable result from four established

predefined automatic segmentation algorithms ('Select-the-best'). The performed segmentations were compared by their Jaccard coefficients (JC) and percentage volume differences (PVD). In order to obtain a reference segmentation, a majority vote (MV) segmentation was calculated for each tumour including all performed segmentations. All segmentations were compared with the MV segmentation regarding their positive predictive value (PPV), sensitivity (SE) and PVD. **Results:** In general, less user-interaction resulted in a decrease in inter-observer variability. The JC and PVD values of the Select-the-best and the gradient approach were significantly better than the JC and PVD values of the other two approaches (p-value<0.01). The manual segmentation led to the lowest JC (median: 0.74, Interquartile range (IQR): 0.17) and to the highest PVD (median: 11.5%, IQR: 40.5%) values. The pure threshold-based and the manual segmentations also resulted in significant lower and more variable PPV+SE values when compared with the MV segmentation. None of the four presented automatic segmentations by itself led to reliable results, while 'select-the-best approach' resulted in the overall best inter-observer agreement across all approaches tested (JC: median: 0.87, IQR: 0.13; and PVD: median: 0%, IQR: 29%). **Conclusion:** FDG PET segmentations of bulky tumours with less user-interaction showed less inter-observer variability. However, none of the methods led to good results in all cases, but use of either the gradient or the 'select-the-best' method outperformed the other approaches.

OP-123

Automated pixelwise statistical analysis in the routine assessment of bone scintigraphy

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Purpose/introduction: Bone scintigraphies are widely used to depict and map bone metabolism, in particular osteoblastic bone lesions. However, there is a lack of automated solutions for pixelwise statistical analysis. Thus, the aim of this work is to fill this need. **Subjects & methods:** A dataset of 62 bone scintigraphies (35 females and 27 males) obtained with ^{99m}Tc-Oxidronate and without visible abnormalities was chosen to build a normal database. A second dataset of 30 scans (15 females and 15 males) containing patients with bone disease was randomly chosen from our database for testing. The automated methodology comprises three main steps: a) spatial normalization of the body/skeleton, b) intensity normalization and c) comparison of the patient's scan with the normal database. Three different types of intensity normalization were tested: normalization by the injected activity and body weight (NIABW); normalization by the median intensity in the bones (skull, spine, pelvis, femurs, humerus) (NMIB); normalization by the median intensity in the soft tissue of the thighs (NMIST). To decide on the best normalization we used two criteria: i) lesser variability in the dataset of normal scans and ii) higher z-scores on areas with bone disease, relative to the normal scans. **Results:** In the normal dataset, con-

sidering a region containing relevant parts of the body (skeleton and thorax), the mean inter-subjects pixelwise coefficients of variation for the three normalizations, NIABW, NMIB and NMIST, were respectively: 0.30, 0.24 and 0.37 in the anterior projection; 0.30, 0.23 and 0.33 in the posterior projection; and 0.28, 0.22 and 0.26 in the geometric mean of both projections. Best results, i.e., low inter-subject variation in the dataset of normal scans, were obtained by the NMIB. Considering the test dataset, overall the NMIB was the best intensity normalization, i.e., it detected more abnormalities (higher z-scores), followed by the NIABW. In two superscans, the NIABW was able to detect more abnormal foci than the other two normalization methods. The NMIST detected more abnormalities in the soft tissues. **Discussion/conclusion:** The herein proposed automated statistical analysis tool can help physicians during daily routine practice visual/qualitative analysis by giving additional useful pixelwise statistical information. Furthermore, it will improve longitudinal follow-up evaluations, in particular the assessment of response to therapy. Finally it is a useful research tool for statistical group comparisons and may be used in automated computer-aided classifications or diagnosis. **Financial support:** This work is supported by the project LISBOA/NORTE-01-0247-FEDER-017685, from PORTUGAL2020.

OP-124

An Automatic Lung Segmentation Method for the Extraction of PET Radiomic Features to Predict High Degree Radiation Pneumonitis

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Aim: Patient treatment with radiotherapy may develop symptomatic lung toxicity, known as radiation pneumonitis (RP). Some studies have found a connection between the presence of interstitial pneumonitis on pre-treatment FDG PET/CT images and an increased risk of RP. One of the drawbacks for a clinical application of the method is the difficulty to perform manual lung segmentations. The aim of this study is to develop a fully automatic method to segment the lung, and extract standardized uptake value (SUV) related parameters and texture features, for the identification RP risk. We verified our method comparing it to a manual segmentation and applied to of high risk subgroup of patients. **Materials and Methods:** Data from 55 lung cancer patients (RP with ROTC Grade ≥ 1) of pre-therapy PET/CT scan were retrospectively compiled. Image analysis and data processing was performed with an in-house algorithm developed in Python (v3.4.6). The segmentation method starts with a thresholding segmentation of the lungs followed by a morphological post-processing to split the lungs between right and left and, to extract non desired structures (trachea and bronchi).

The resulting mask is used as the basis for the PET segmentation. To minimize the activity spill-in from surrounding structures (as heart or liver) to the lungs, any region with a SUV >1.5 which overlaps the mask and the rest of the body was removed. From the segmented PET lungs, 8 SUV-related and 21 texture parameters were extracted. The segmentation was validated, comparing 9 random patients SUV-based parameters (SUV_{max} , SUV_{95} , SUV_{50} , SUV_{25} and SUV_{mean}) to a manually segmentation realized by a physician. After the validation phase, the algorithm was applied to and exploratory identification of low vs. high pneumonitis grade. **Results:** Comparison of the fully-automated method with the manual lung segmentation, showed a good linear fit regression in all of parameters analyzed ($R^2 \geq 0.96$). Analysis of SUV and texture parameters suggests a relationship among an increase of this values and the degree of RP. The SUV_{95} ($p < 0.05$), SUV_{mean} ($p < 0.03$) and texture features from Hmean ($p = 0.02$), Skewness ($p = 0.05$), decrease for skewness, Autocorrelation ($p = 0.01$) and the GLRM matrix HGZE ($p < 0.05$); were the most prominent. **Conclusion:** The proposed algorithm resulted to be a reliable method for lung segmentation. The increase in some parameters was related with the evolution of higher degrees RP, suggesting to be potential candidate to develop a radiomics model.

OP-125

Anthropometer3D: Automatic Multi-slice Segmentation Software for the Measurement of Anthropometric Parameters from CT of PET/CT

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Introduction: Muscle Body Mass (MBM), Fat Body Mass (FBM), Lean Body Mass (LBM), Visceral Fat Mass (VFM) and Subcutaneous Fat Mass (SCFM) are body composition parameters used in oncology. Our aim was to develop and evaluate a software, called Anthropometer3D, allowing the measurement of these parameters from a automatic multi-slice segmentation of CT from PET/CT data. **Subjects & methods:** Anthropometer3D is based on an automatic multi-atlas segmentation of CT over the usual acquisition field of a PET/CT (from the ischia to the eyes) with extrapolation coefficients to take into account body parts beyond the limited acquisition field. The multi-atlas database is composed of 30 truncated CTs manually segmented to isolate 3 types of voxels belonging to muscle, fat and visceral fat. This database is used to segment new patients according to a multi-atlas process. To evaluate Anthropometer3D, a leave-one-out cross-validation method was performed. Anthropometer3D measurements were performed on each of the truncated CTs to measure $MBM_{Anthro3D}$, $FBM_{Anthro3D}$, $LBM_{Anthro3D}$, $VFM_{Anthro3D}$ and $SCFM_{Anthro3D}$. The gold standard was based on the manual segmentation of the corresponding whole-body examinations leading to the measurement of $MBM_{ManualWB}$, $FBM_{ManualWB}$, $LBM_{ManualWB}$, $VFM_{ManualWB}$ and $SCFM_{ManualWB}$. A manual segmentation of one CT slice at level L3 was also used to estimate $MBM_{ManualL3}$, $FBM_{ManualL3}$, $LBM_{ManualL3}$, $VFM_{ManualL3}$ and $SCFM_{ManualL3}$. The correlation between Anthropometer3D, the reference standard, and the

segmentation at level L3 was analyzed using Dice coefficient, Intra-Class Correlation (ICC) and Bland-Altman plot. **Results:** The population was heterogeneous with 15 females and 15 males, mean age 57 years-old (min 27; max 74) and a mean body mass index of 27 kg/m² (min 18; max 40). Dice coefficients between the reference standard and Anthropometer3D were excellent (mean $\pm$ SD): muscle voxels 0.95 $\pm$ 0.02, fat voxels 1.00 $\pm$ 0.01 and visceral fat voxels 0.97 $\pm$ 0.02. The ICC were almost perfect (minimal value of 95% Confidence Interval (CI) of 0.97). All Bland-Altman plot values (mean difference, 95% CI and slopes) were better for Anthropometer3D than for estimates using manual segmentation at level L3, for example the mean difference was +1.5% [CI -12%;+15%] between FBM_{Anthro3D} and FBM_{ManualWB} and -7%[CI -39%;+25%] between FBM_{ManualL3} and FBM_{ManualL3}. **Conclusion:** Anthropometer3D allows an automatic measurement of MBM, FBM, LBM, VFM, and SCFM based on a multi-slice segmentation. It is more precise than estimates generally made using segmentation at L3 level.

OP-126

Comparison of machine learning algorithms, and pre-processing, for building prognostic models in non-small cell lung cancer using clinical and radiomics features from ¹⁸F-FDG PET/CT images.

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Regarding the radiomics workflow, only primary tumor volumes were characterized after (semi)automated segmentation in both PET and low-dose CT components of PET/CT. Three different grey-level discretization methods (histogram equalization, linear re-sampling, fixed bin-width interval) were considered for 2nd- and higher-order textural features. All available clinical variables and radiomics features were entered in the two ML pipelines (features selection and classifier) under comparison, namely the Support Vector Machines (SVM) with Recursive Feature Elimination and Random Forests (RF) with 100 to 500 trees (steps of 50) with Embedded Wrapper method. These two pipelines were compared for the classification problem of identifying patients with overall survival less than 6 months in a cohort of 101 non-small cell lung cancer stage 2 and 3 patients. The cohort was split into a learning set (67%) for training the models with cross-validation and a testing set (33%) for performance evaluation (accuracy, specificity, sensitivity). We also compared the results if we pre-process the images, by segmenting the tumor or not. In the training set, the best model built by RF with a small number of features (10) reached an accuracy of 82% (sensitivity-specificity 88%-76%). In the testing set, this model obtained 62% accuracy (sensitivity-specificity 71%-53%). Improved accuracy was obtained by including a higher number of features (22), with accuracy of 71% (sensitivity-specificity 71%-71%) in the testing set. With SVM, the best model built with a small number of features (11) obtained an accuracy of 84% (sensitivity-specificity 86%-82%). In the testing set, this model obtained 53% accuracy (sensitivity-specificity 53%-53%). Similarly as with RF, higher accuracy could be ob-

tained by including additional features (25), with accuracy of 91% (sensitivity-specificity 94%-88%) in the training, and in the testing set, with accuracy of 59% (sensitivity 64%, specificity 53%). For the comparison of non segmented and segmented images, we had better performance with segmentation. For instance, for the SVM method, only with PET features, we can arrive the balanced accuracy of 1 (91 features) but we can never achieve more than 70% of accuracy, for the non-segmented case. Our results show that although Support Vector Machines has better results for the training, for the validation it does not perform well enough. RF, on the other hand, shows an acceptable performance, on both sets, since RF can better predict such real life problems, while SVM is easier to train. We can also deduce that the segmentation increases the performance of the process.

OP-127

Feasibility of a phantom with 3D printed inserts with realistic uptake patterns to study the performance of radiomics features

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Background: Before radiomic features can safely be implemented in a clinical setting, their reproducibility across PET/CT systems and other confounding factors have to be determined. In this study, we designed three phantom-inserts with realistic tumor shapes and activity uptake patterns in order to study the performance of PET radiomic features under various conditions.

Methods: Three tumors were segmented from typical FDG-PET images of patients with non-small cell lung cancer, transformed in a 3D-object, scaled, and printed with a SLA 3D-printer. Every 3D-printed tumor-insert reflects a specific heterogeneity uptake pattern and irregular shape, the first insert simulates a tumor with homogeneous uptake, while the second simulates uptake heterogeneity in the sagittal view and the third a necrotic core. The latter two are achieved by two separated compartments that can be filled with different activity solutions. The inserts are placed at equal distances in the NEMA image quality phantom. First experiments were performed on a Siemens Biograph mCT40 (acquisition of thirty minutes in list-mode). The data were reconstructed using various reconstruction algorithms, scan durations (noise), and post-reconstruction smoothing factors with five replicates for each setting. For every tumor, CT- and PET-based segmentations were generated and 430 radiomic features were extracted. The coefficient of variation (COV) of the features was calculated across reconstruction algorithm with post-reconstruction smoothing of 2 and 5mm full-width-at-half-maximum (FWHM) for both delineation methods and 60sec scan duration, as well as across the five replicates for each reconstruction algorithm and scan duration. **Results:** The inserts varied in size and uptake heterogeneity (e.g. the three tumors resulted in a volume of 56, 34, and 77 ml and an energy value of 1.5e6, 3.8e5 and 2.0e6). The COV varied across tumor types, smoothing factors, reconstruction methods, scan durations, and delineation methods. For example, for 5 mm FWHM

Gaussian smoothing, the COVs of the SUV_{mean} for the three tumors were 1.5%, 9.0% and 3.1% and 1.7%, 2.2%, and 2.3% for PET- and CT-based segmentation, respectively. With increasing scan duration, i.e. decreasing noise, the COV decreased. E.g. the COVs of the SUV_{mean} decreased from 1.6% over 0.7% to 0.5% for 30, 60 and 300sec scan duration for one of the tumors. **Conclusions:** 3D-printed inserts of three tumors were constructed yielding three irregular shapes and three realistic uptake patterns, which can be used for a (multi-center) study to assess the variability of radiomics features at different PET/CT systems and with various acquisition and/or reconstruction settings.

407 Sunday, October 14, 2018, 14:30 - 16:00, Hall 1

Teaching Session 1 - Interactive Clinical Cases:
Neuroimaging: Basics of Neuroimaging

OP-128

Neuroanatomy Recall (CT and MRI)

E. Van de Giessen; University of Amsterdam, Academic Medical Center, Nuclear Medicine, Amsterdam, NETHERLANDS.

OP-129

Bases of Molecular Neuroimaging

I. Peñuelas; Clinica Universidad de Navarra, Radiopharmacy Unit, Nuclear Medicine Department, Madrid, SPAIN.

OP-130

Reading a Clinical PET of the Brain with Cases

S. Morbelli; IRCCS Azienda Ospedaliera Universitaria San Martino, Department of Nuclear Medicine, Genoa, ITALY.

408 Sunday, October 14, 2018, 14:30 - 16:00, Hall 4

Special Symposium: 20 Years of PET/CT in Clinical Practice

OP-131

45 Years of PET

M. Phelps; UCLA, Nuclear Medicine/Molecular and Medical Pharmacology, Los Angeles, UNITED STATES OF AMERICA.

OP-132

PET/CT - A Fun Idea or Dire Need?

D. Townsend; Singapore, SINGAPORE.

OP-133

Bringing PET/CT into Clinical Reality

G. Antoch; University Hospital Düsseldorf, Department of Diagnostic and Interventional Radiology, Düsseldorf, GERMANY.

OP-134

Bringing PET/CT into Clinical Reality

A. Bockisch; Universitätsklinikum Essen, Universität Duisburg Essen, Klinik für Nuklearmedizin, Essen, GERMANY.

OP-135

Making PET/CT Great Again

I. Carrio; Hospital de la Santa Creu i Sant Pau, Department of Nuclear Medicine, Barcelona, SPAIN.

OP-136

Looking into the Future: Digital Revolution?

M. Forsting; UK Essen, Institut für Diagnostische und Interventionelle Radiologie und Neuroradiologie, Essen, GERMANY.

409 Sunday, October 14, 2018, 14:30 PM - 16:00, Hall 6

Thyroid: Targeted Imaging of Malignant Thyroid Tumours

OP-138

Evaluation of the CCK-2 receptor agonist ^{177}Lu -PP-F11N for PRRT of medullary thyroid carcinoma - Results of a phase 0 "Lumed" Study.

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Purpose/Introduction: Despite the introduction of new molecular targeted therapies, there is still an unmet need for an effective systemic therapy for advanced medullary thyroid carcinoma (MTC). As MTC expresses cholecystokinin-2 (CCK-2) receptors at a high incidence and density, targeting the CCK-2 receptor with radiolabelled gastrin analogues is a potential approach for radionuclide therapy. Unfortunately, kidney and bone marrow toxicity precluded therapeutic applications of CCK-2 receptor specific radiotracers until now. The aim of this prospective study is the feasibility testing of targeting CCK-2 receptors with the novel gastrin analogue [^{177}Lu -DOTA-(DGLu)6-Ala-Tyr-Gly-Trp-Nleu-Asp-PheNH₂] (^{177}Lu -PP-F11N) in six patients with advanced MTC (ClinicalTrials.gov: NCT02088645). **Subjects and Methods:** Six patients received two injections of 1 GBq ^{177}Lu -PP-F11N, one injection with and the other without Physiogel (Gelofusin = plasma expander for nephroprotection) infusion. Planar scintigraphy and SPECT/CT scans were performed at several time points for up to 72 h post injection in order to calculate tumour- and organ doses using 3D voxel- and MIRD based dosimetry (Dosimetry Research Tool v5.2, Siemens Medical Solutions, USA). Blood samples were taken for bone marrow dose calculations. ECG, blood count and blood chemistry were measured up to 12 weeks after the second administration of ^{177}Lu -PP-F11N in order to evaluate adverse events. **Results:** Adverse reactions (mainly hypotension, flushing and hypokalemia) were self-limiting and not higher than grade 1, according to CTCAE version 4.03. In all patients, ^{177}Lu -PP-F11N accumulation was visible in tumor tissue, in the kidneys, stomach and the colon.

Altogether, 14 tumours were eligible for dosimetry. The median (range) radiation dose for tumours, kidneys and bone marrow was 0.88 Gy/GBq (0.69–2.85), 0.090 (0.045–0.115) and 0.010 (0.008–0.016). These resulted in median tumour-to-kidney dose ratios of 12.8 (6.0–52.4) (without Physiogel) and 12.4 (6.4–29.8) (with Physiogel), which was not significantly different ($p=0.85$). The median tumour-to-bone marrow dose ratio was 87.9 (52.8–316.4). **Discussion/Conclusion:** The administration of the novel CCK-2 receptor ligand ^{177}Lu -PP-F11N was safe in all six examined patients. Visualization of metastasized/recurrent disease in all patients provides evidence that CCK-2 receptor targeting with ^{177}Lu -PP-F11N is feasible in patients with MTC. The dosimetry results indicate tumour doses that could enable radionuclide therapy. Dosimetry results for kidneys and bone marrow revealed low organ doses, as well as excellent tumour-to-kidney and tumour-to-bone marrow ratios. Further studies will be necessary to evaluate the theranostic potential of ^{177}Lu -PP-F11N in patients with CCK-2 receptor expressing tumours.

OP-139

^{18}F -Dopa PET/CT in the Localization of Persistent Medullary Thyroid Carcinoma (MTC)

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Introduction: In patients diagnosed with medullary thyroid carcinoma (MTC), suspicion of relapse is defined by increased calcitonin (CT) values, specific marker of this type of tumor. Although recurrence accounts for 34–44% in these patients and is mostly locoregional, accurate localization is not always feasible by conventional imaging methods. For half of the patients showing elevated calcitonin values, different imaging studies do not enable visualization of sites of recurrent disease. Therefore, a molecular / functional imaging method for early localization of biochemical relapse is required. ^{18}F -DOPA PET/CT, based on increased activity of amino acid transporter in neuroendocrine tumors, is a promising method. **PURPOSE:** To assess performance of ^{18}F -DOPA PET/CT as a localizing tool in patients with recurrent MTC. **Materials and Method:** 22 patients were analyzed (9 male, 13 female) age 25–85 years with histopathological MTC diagnosis and increased calcitonin values over 200 pg/ml post surgery. Patients were administered 150mg Carbidopa VO one hour before receiving 0.05 a 0.07 mCi/kg de ^{18}F DOPA EV. Whole-body was scanned on PET/CT GEMINI 64 TOF at 60 minutes post injection, as well as acquisition of early and delayed images of the neck and superior mediastinum. Studies showing at least one region with abnormal ^{18}F DOPA uptake were considered positive. A correlation was established between calcitonin and SUVmax values by compromised region. **Results:** - Recurrent disease was localized in 20 (91%) from 22 patients analyzed. ^{18}F DOPA PET CT was not conclusive in one patient and negative in another. Average SUVmax was 9.09. Only locoregional disease was localized in 7 (35%) from the 20 patients with positive ^{18}F DOPA PET CT, locoregional jointly with distant disease in 45% of the patients, and presence of distant metastases was determined in the remain-

ing 20%. - In patients with negative ^{18}F DOPA PET-CT, calcitonin level was quite close to the minimum level required for study eligibility (251pg/ml) and CEA level was also low. - All the cases with distant metastases showed calcitonin level over 800 pg/ml. - From the total, 5 patients (22,7%) had familial MTC (4 with MEN2A and one with MEN2B), of which 4 (80%) showed calcitonin values over 9000 pg/ml. From the 4 cases with MEN2A, 3 were distant metastases and 1 locoregional. Distant metastases were detected in the patient with MEN2B. **Conclusion:** ^{18}F DOPA PET-CT seems to be a useful tool for the localization of locoregional and distant recurrent disease in MTC patients.

OP-140

Diagnostic Value of ^{18}F -Fluorocholine PET/CT for the Detection of Medullary Thyroid Carcinoma

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Aim: Disease recurrence in patients operated for medullary thyroid carcinoma (MTC) is over 30%. Conventional imaging fails to accurately evaluate disease extent; currently, nuclear medicine imaging has a limited role in MTC staging. The aim of the study was to assess the diagnostic accuracy and potential role of ^{18}F -Fluorocholine (^{18}F -FCH) PET/CT in MTC patients - preliminary results for preoperative primary staging are presented. **Materials, methods:** Fifty-nine patients with newly diagnosed MTC on fine-needle aspiration cytology (FNAC), referred for oncological treatment between January 2014 and December 2017 were enrolled. Fifteen patients performed a preoperative three phase ^{18}F -FCH PET/CT of the head and neck (0 min, 45 min and 90 min pi.) and whole-body ^{18}F -FCH PET/CT (60 min post application). Preoperative serum calcitonin and CEA levels were measured. All surgically removed lesions were histologically analysed. Suspicious lesions not surgically removed were estimated using conventional imaging methods (US, CT, MRI or bone scan). Statistical analysis was performed in R version 3.4.4, results with $p < 0.05$ were considered statistically significant. **Results:** Twelve of fifteen patients (80%) were surgically treated and histology samples were correlated with PET/CT imaging; data from three patients (20%) with metastatic disease was correlated with conventional imaging and FNAC results. Eleven patients had histologically confirmed MTC, one patient had histologically confirmed papillary thyroid carcinoma (PTC). Patient-based sensitivity for detection of MTC was 100%, positive predictive value was 93,3%. All primary MTCs, and the PTC lesion, were detected. Point estimates (95% CI) for compartment-based analysis of histologically or radiologically confirmed neck lymph nodes metastases (central [VI], left/right lateral [II-V], retropharyngeal and superior mediastinal compartments [VII]) in 13/15 patients were as follows: sensitivity 100% (77%-100%), specificity 85% (72%-94%), positive predictive value 67% (43%-85%), negative predictive value 100% (91%-100%). Distant metastases were detected in three patients and confirmed with conventional imaging. Metastases were detected in distant lymph nodes (3 patients), bones (2 patients) and lungs (1 patient). Patients with distant metastases on ^{18}F -FCH had higher calcitonin (median of 5060

vs 422.25 ng/l, $p = 0.07$) and CEA levels (median of 95.8 vs 21.9 $\mu\text{g/l}$, $p = 0.54$) compared to patients with locoregional disease.

Conclusion: Based on preliminary results, ^{18}F -FCH PET/CT could be a promising radiotracer for primary staging of MTC. Further analysis of our trial data and correlation with other prospective studies are needed to define the exact role of ^{18}F -FCH in MTC management.

OP-141

German prospective multicenter study to compare different Thyroid Imaging Reporting and Data Systems (TIRADS) for the assessment of thyroid nodules

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Background: Thyroid nodules are common finding in iodine-deficiency countries such as Germany; most of these nodules are benign. Thyroid ultrasound (US) is a widespread method, which may be used to detect suspicious features of nodules and to perform risk stratification for malignancy. A standardization of ultrasound reporting may be achieved by using TIRADS. Currently various TIRADS variants exist, but none has been incorporated into an international guideline. Aim of this study was to compare three variants of TIRADS in terms of risk stratification of thyroid nodules for malignancy. **Methods:** We prospectively classified thyroid nodules according to ultrasound criteria in four Nuclear Medicine centers from 2015 to 2017. Thyroid nodules were classified according to ACR-TIRADS, EU-TIRADS and TIRADS introduced by Kwak et al. A thyroid scan using Tc-99m-pertechnetate or I-123 was performed, if the nodule had a diameter of 1 cm or above. We assessed a subgroup of patients with hypofunctional and isofunctional nodules, in which the nodules were resected and compared the results of histology the TIRADS variants. **Results:** A total of 504 nodules were classified so far, histology was available in 285 patients (205 female, median 46.5 years, 80 male, median 54 years) with 292 nodules (110 malignant (38%) and 182 benign). Malignant nodules were found to be significantly smaller as compared to benign nodules (12.9 mm vs. 23.1 mm, $p < 0.0001$). The prevalence of malignancy was found to be in ACR-TIRADS class TR1-TR5 0%, 0%, 12.5%, 34.9% and 58.5% respectively. In EU-TIRADS for classes 2-5 malignancy rate was 0%, 5.2%, 20% and 52.9%. 0%, 3%, 9.5%, 20.4%, 53% and 77.4% malignancy rate was found for Kwak-TIRADS classes 2-5. **Conclusion:** All three variants TIRADS yield fairly comparable malignancy rates. The highest rate for malignancy was found in nodules which were classified as Kwak-TIRADS class 5.

OP-142

Papillary thyroid microcarcinoma: Do we need postoperative DxWBS to reveal hidden metastatic lesion?

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Purpose: Thyroid microcarcinoma (PTMC) has an excellent prognosis unless aggressive pathology or metastasis. This study aims to evaluate the initial risk stratification of PTMC by using pathological evidence and clinical value of postoperative I-131 diagnostic WBS (DxWBS) to classify risk stratification and to consider further I-131 treatment in PTMC patients. **Material and method:** Sixty patients, who performed postoperative DxWBS during January 2014 to May 2017 were enrolled in this study. Risk stratification, according to ATA 2009 of each patient was recorded by using pathological report alone (p-initial risk stratification) and comparison with additional stimulated serum Tg, Tg antibody and postoperative DxWBS. Changing of risk stratification and DxWBS findings were recorded and analyzed. **Results:** There are 49 female and 11 male PTMC patients with age range 13-72 years old. Of the 60 PTMC patients, 30/60 (50%) were classified as p-initial low risk. Of these, 13/30 (43.3%) had changed to higher risk when using additional information from serum markers and postoperative DxWBS, which 10/13 (76.9%) had changed to intermediate risk stratification, due to regional lymph node metastases on DxWBS and all of them had low stimulated serum Tg ($< 10 \text{ ng/ml}$). Three out of 13 patients (23.1%) had changed to high risk stratification due to presence of lung and bone metastases on DxWBS along with very high stimulated serum Tg. The remaining 30 patients (50%) were p-initial intermediate risk. Of these, 1/30 (3.3%) had changed to high risk stratification by presence of lung metastasis on postoperative DxWBS as well as high serum Tg level. There is significantly higher risk stratification in p-initial low risk group, compared to p-initial intermediate risk group (43.3% vs 3.3%, $p\text{-value} < 0.001$) by additional findings from postoperative DxWBS and stimulated serum Tg. **Conclusion:** PTMC is not always low risk. Stimulated serum Tg is not helpful to predict regional lymph node metastasis, but it is of value in prediction of distant metastasis. Postoperative DxWBS is recommended in pathological low risk PTMC patients to identify hidden metastatic lesion, accurate risk stratification and consider further I-131 treatment.

OP-143

Volumetric Assessment Based On Baseline FDG PET Can Predict Survival In Medullary Thyroid Cancer Patients Scheduled For Vandetanib Treatment

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Introduction: The metabolically most active lesion of pre-therapeutic ^{18}F -FDG PET/CT can predict Progression-Free-Survival (PFS) in patients with medullary thyroid carcinoma (MTC) scheduled for treatment with the tyrosine kinase inhibitor (TKI) vandetanib. However, this conventional approach for response assessment failed in Overall Survival (OS) prediction. In a more

sophisticated approach, we aimed to explore the prognostic value of intratumoral textural features (TF) as well as volumetric parameters (Tumor Lesion Glycolysis, TLG) derived by ^{18}F -FDG PET. **Methods:** Eighteen patients with progressive MTC envisaged for vandetanib underwent baseline ^{18}F -FDG PET/CT prior to and 3 months after TKI initiation. CT scans were performed every 3 months and analyzed according to Response Evaluation Criteria in Solid Tumors. By manual segmentation of 109 metastases in a baseline PET (median, 5 volume of interests (VOI) per patient) and 56 metastases in a follow-up PET (median, 2 VOI per patient), intratumoral TF and TLG were computed. The impact of $\text{SUV}_{\text{max/mean}}$, TLG, imaging-based TF as well as clinical parameters {tumor marker doubling times (calcitonin, carcinoembryonic antigen, CEA), prior therapies, RET (rearranged during transfection) mutational status, and disease type} for prediction of both PFS and OS was evaluated. **Results:** Within follow-up (median, 6.4 years), 12 patients suffered from progressive disease (median, 2.6y), whereas 9 patients died (median, 4.1y). In a ROC analysis, the pretherapeutic TF Complexity demonstrated predictive capability for OS (cutoff=59, $\text{AUC}=0.78$, $P=0.03$). Of note, increasing Complexity predicted shorter survival (>59 , $\text{OS}=3.3\text{y}$, 10/18), whereas less complex tumor shape portended superior outcome (<59 , $\text{OS}=5.3\text{y}$, 8/18). Additionally, the volumetric parameter TLG derived at baseline demonstrated a similar tendency for OS prognostication (cutoff=2694, $\text{AUC}=0.83$, $P=0.005$): Increasing TLG was also associated with reduced OS (>2694 , $\text{OS}=3.5\text{y}$, 11/18 vs. <2694 , $\text{OS}=5\text{y}$, 7/18). Subsequent Kaplan-Meier analysis differentiated between high- and low-risk groups ($p<0.009$, respectively). The hazard ratio for cancer-related death after TKI initiation was 6.1 for Complexity and 9.5 for TLG. Among investigated clinical parameters, the age at initiation of TKI treatment demonstrated significance for PFS prediction ($P=0.02$; OS, n.s.). **Conclusions:** The TF Complexity and the volumetric parameter TLG hold potential for OS prognostication. Hence, beyond conventional SUV measurements, other metrics for analysis of FDG uptake and tumor texture can provide superior prognostic information in MTC patients scheduled for TKI treatment.

OP-144

^{18}F -DOPA and ^{18}F -FDG PET/CT in Sporadic Medullary Thyroid Cancer: washout rate of ^{18}F -DOPA, between early and late scans, correlated with Calcitonin and CEA doubling time and positive FDG PET/CT

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Aim: our purpose was to investigate a possible correlation between serum calcitonin or carcinoembryonic antigen doubling-times (CTdt, CEAdt) with wash out rate of ^{18}F -DOPA, by comparing early and late scans in patients with Medullary Thyroid Cancer (MTC). Our other aim was to find association of wash-out rate of ^{18}F -Dopa with positive ^{18}F -FDG PET/CT. **Material and Methods:** 30 patients were scanned with ^{18}F -DOPA

in our medical center, in staging and after biochemical relapse of MTC. Among these 30 patients, we have retrospectively enrolled 14 patients with the following inclusion criteria: 1) Sporadic MTC diagnosis 2) Persistent or biochemical relapse of CT after primary or secondary surgery for MTC; 3) ^{18}F -DOPA PET/CT performed with early acquisition images (8-12 minutes) and late images (50-70 min). 4) ^{18}F -FDG PET/CT performed within 1 month after ^{18}F -DOPA. ^{18}F -fluoride was produced by means of $^{18}\text{O}(\text{p},\text{n})$ ^{18}F nuclear reaction on PETtrace 16.5 MeV cyclotron (GE Healthcare). ^{18}F -DOPA was synthesized by nucleophilic fluorination pathway on FASTLab synthesizer (GE Healthcare) in our Radiopharmacy. SUV_{max} , SUV_{mean} , were measured in both early (SUV_{maxE} , $\text{SUV}_{\text{meanE}}$) and late (SUV_{maxL} , $\text{SUV}_{\text{meanL}}$) ^{18}F -DOPA PET-acquisitions. Wash-out rate of ^{18}F -DOPA was calculated from $\text{deltaSUV}_{\text{max}}$ and $\text{deltaSUV}_{\text{mean}}$, between late and early acquisitions as $\text{deltaSUV}_{\text{max}}=[(\text{SUV}_{\text{maxL}}-\text{SUV}_{\text{maxE}})/\text{SUV}_{\text{maxE}}]$ and $\text{deltaSUV}_{\text{mean}}=[(\text{SUV}_{\text{meanL}}-\text{SUV}_{\text{meanE}})/\text{SUV}_{\text{meanE}}]$. PET/CT results were validated with clinical and radiological or cytological follow up. **Results:** Higher $\text{deltaSUV}_{\text{max}}$ (wash out rate) was associated with positive ^{18}F -FDG-PET (-0.49 ± 0.18 vs -0.24 ± 0.22 $P=0.039$). We found a very strong correlation between CTdt with $\text{deltaSUV}_{\text{max}}$ ($P=0.0001$), $\text{deltaSUV}_{\text{mean}}$ ($P=0.003$), SUV_{maxL} ($P=0.006$), $\text{SUV}_{\text{meanL}}$ ($P=0.007$), and a mild correlation with $\text{SUV}_{\text{meanE}}$ ($P=0.047$). No association was found between CTdt, SUV_{maxE} , SUV_{maxL} , $\text{SUV}_{\text{meanE}}$ and $\text{SUV}_{\text{meanL}}$ and $\text{deltaSUV}_{\text{mean}}$ with positive FDG-PET. No association was found between CEAdt and $\text{deltaSUV}_{\text{max}}$. Mean SUV_{maxE} and $\text{SUV}_{\text{meanE}}$ were respectively 5.7 (range 2.6-11.7) and 3.5 (range 1.3-7.3). Mean SUV_{maxL} and $\text{SUV}_{\text{meanL}}$ were respectively 3.6 (range 1.1-9.3) and 2.7 (range 0.6-6.1). Mean $\text{deltaSUV}_{\text{max}}$, patient based, was 40% (48% in the metastatic lesions as lung or liver and 33% in lymph nodal lesions). **Conclusion:** Our preliminary results suggest that higher wash-out rates ($\text{deltaSUV}_{\text{max}}$ and $\text{deltaSUV}_{\text{mean}}$) of ^{18}F -DOPA between early and late acquisitions is correlated with lower CTdt (less than two years) and may represent a negative prognostic factor. In this clinical setting ^{18}F -FDG PET/CT positivity is associated with higher wash-out rate, indicating a more aggressive pattern of disease.

OP-145

Focal thyroid incidentaloma on FDG-PET/CT: SUV and EU-TIRADS classification predict malignancy

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Aim: To evaluate the performance of SUV-ratio and the new classification EU-TIRADS by ultrasonography in the risk stratification of malignancy of focal thyroid incidentaloma discovered on FDG-PET/CT. **Materials and methods:** Were prospectively included 165 patients with focal thyroid incidentaloma discovered on FDG-PET/CT between July 2015 and 2017. Ultrasonography was performed in 109 patients with EU-TIRADS score; and allowed characterization of nodules in 102 patients. The score and the ratio of focal thyroid incidentaloma SUV_{max} to liver SUV_{max} (rSUV_{max}) were compared to fine needle aspiration cytology

± needle core biopsy (n=16) and/or surgical resection (n=16) that was considered as the gold standard. **Results:** Incidence of focal thyroid incidentaloma discovered on FDG-PET/CT was 2.2%. According to the gold standard, the rate of malignant nodules was 20% (20/102), that was 73% (75/102) for benign nodules while 7% (7/102) remained undetermined. Neither size nor SUV_{max} were predictive of malignancy ($p=0.25$ and 0.26 respectively). A $rSUV_{max} > 1.7$ was predictive of malignancy with a sensitivity of 92% and a specificity of 59% ($p=0.02$). The EU-TIRADS score remained also predictive of malignancy in this population ($p<0.0001$). No nodule below 20 mm EU-TIRADS 3 with a $rSUV_{max} < 1.7$ was malignant. **Conclusions:** The rate of malignancy in focal thyroid incidentaloma discovered on FDG-PET/CT is high. The new classification EU-TIRADS by ultrasonography and the $rSUV_{max}$ allowed risk stratification concerning malignancy that could avoid futile fine needle aspiration cytology and surgery.

404b Sunday, October 14, 2018, 15:45 - 16:45, Hall 5

Mini Course 2: Lymphoscintigraphy and Sentinel Node

OP-146

Lymphoscintigraphy in Lymphedema

N. Giroto; Hospital/Institute, Clinical Hospital Center, Department of Nuclear Medicine, Rijeka, CROATIA.

OP-147

A Technologist's Guide to Sentinel Lymph Node Scintigraphy

J. Jamsek; University Medical Centre Ljubljana, Department for Nuclear Medicine, Ljubljana, SLOVENIA.

501 Sunday, October 14, 2018, 16:30 - 18:00, Plenary Hall

CME 4 - Paediatrics: PET/MR in Paediatrics - Sharing Experiences

OP-148

PET/MR in Paediatrics - Brain Tumours

L. Borgwardt; Copenhagen University Hospital, Rigshospitalet, Clinic for Clinical Physiology, Nuclear Medicine & PET, Copenhagen, DENMARK.

OP-149

PET/MR in Paediatrics - Extra-Cranic Solid Tumours

R. Kluge; Universität Leipzig, Klinik und Poliklinik für Nuklearmedizin, Leipzig, GERMANY.

OP-150

PET/MR in Paediatrics - Non-Oncologic Applications and Future Developments

P. Zucchetta; University Hospital, Nuclear medicine, Padua, ITALY.

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Sunday, October 14, 2018, 16:30 - 18:00, Hall 2

Joint Symposium 7 - Neuroimaging / EAN / SNMMI: Clinical Trials in Dementia - Expectations on Molecular Imaging

OP-151

INTRODUCTION

OP-152

Update on Clinical Trials in Dementia

J. Hort; Department of Neurology, 2nd Medical Faculty, Charles University and Motol University Hospital, Prague, CZECH REPUBLIC.

OP-153

Amyloid PET in Anti-Amyloid Clinical Trials

V. Garibotto; Department of Medical Imaging, Geneva University and Geneva University Hospitals, Geneva, SWITZERLAND.

OP-154

PET in Clinical Trials Beyond Amyloid PET

S. Minoshima; Health University of Utah, Department of Radiology and Imaging Sciences, Salt Lake City, UNITED STATES OF AMERICA.

OP-155

PET Methodology for Longitudinal Measurements

A. Lammertsma; VU University Medical Center, Amsterdam, NETHERLANDS.

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Sunday, October 14, 2018, 16:30 - 18:00, Hall 3

Joint Symposium 8 - Oncology / IASLC: New Techniques for Diagnosis and Prognostication of Lung Cancer Patients

OP-157

Lung Cancer Screening: State of the Art and Future Implementation in Europe

G. Veronesi; Humanitas Cancer Center, Milan, ITALY.

OP-158

Predictive Risk Models in Cancer: How to Improve Differential Diagnosis in Indeterminate Lung Nodules

M. C. Tammemagi; Brock University | Department of Health Sciences, St. Catharines, CANADA.

OP-159

Clinical Implications of Highly Sensitive Isolation and Molecular Characterization of Circulating Tumour Cells in Lung Cancer

P. Paterlini Brechot; Université Paris Descartes, Unité INSERM U1151, Paris, FRANCE.

OP-160

Radiomics - The Future of Advanced Feature Analysis in Lung Cancer Imaging

P. Lambin; Department of Radiation Oncology (MAASTRO), GROW - School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, NETHERLANDS.

505

Sunday, October 14, 2018, 16:30 - 18:00, Hall X

M2M : PSMA - Expanding Effects

OP-161

Impact of Modulating Albumin Affinity on Tumor and Normal Tissue Kinetics of PSMA-Targeting Ligands for Radioligand Therapy

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Aim: Recently, ^{177}Lu -labeled small molecules such as ^{177}Lu RPS-063, ^{177}Lu PSMA-Alb02 and ^{177}Lu CTT1403, have used albumin binding to increase uptake in PSMA-expressing tumors. However, these ligands also show high uptake in the kidneys, an indication that in vivo pharmacokinetics may not be suitable for use in radioligand therapy (RLT). We aimed to develop a next generation trifunctional ligand with significantly decreased kidney uptake without loss of tumor uptake. **Materials and Methods:** Ligands were synthesized from ((1-carboxy-5-(3-(3-ethynylphenyl)ureido)pentyl)carbamoyl)glutamic acid, DOTA and either N^6 -(2-(4-iodophenyl)butanoyl)lysine (RPS-063, RPS-071) or N^6 -(4-(4-iodophenyl)butanoyl)lysine (RPS-072, RPS-077). The three moieties were conjugated via various configurations of PEG linker. PSMA affinity was determined by competitive binding assay using LNCaP cells and albumin affinity was determined by high performance affinity chromatography of the radiolabeled constructs. The ligands were labeled with $^{68}\text{Ga}/^{177}\text{Lu}$ in 15 min at 95°C and pH 4-5 (HCl/NaOAc buffer). Male BALB/C nu/nu mice bearing LNCaP xenograft tumors (4/time point) were injected intravenously with 0.36-1.3 MBq (13-23 pmol) of ^{177}Lu -labeled ligand and sacrificed at 4, 24 and 96 h post injection (p.i.). **Results:** The IC_{50} of RPS-063 (MW=1761.7 Da) and RPS-077 (MW=1789.8 Da), structurally identical with exception of the albumin-binding group (ABG), was 1.5 ± 0.3 nM and 1.7 ± 0.3 nM, respectively. RPS-071 (MW=2185.2 Da) and RPS-072 (MW=2213.2 Da) also differed only by the ABG and IC_{50} was 10.8 ± 1.5 nM and 6.6 ± 3.7 nM, respectively. Affinity for albumin was determined to be 20.1 ± 0.8 μM (^{68}Ga RPS-071), 1.8 ± 0.2 μM (^{68}Ga RPS-063), 0.41 ± 0.0 μM (^{68}Ga RPS-072) and <0.40 μM (^{68}Ga RPS-077). Clearance from the blood corresponded to albumin affinity, with ^{177}Lu RPS-072 and ^{177}Lu RPS-077 showing substantial activity (>5 %ID/g) at 24 h p.i. The kinetics of tumor uptake also reflected blood clearance, with ^{177}Lu RPS-072 (34.9 ± 2.4 %ID/g) and ^{177}Lu RPS-077 (27.4 ± 0.6 %ID/g) peaking at 24 h p.i. and persisting through 96 h. In contrast, ^{177}Lu RPS-063 (30.0 ± 3.1 %ID/g) and ^{177}Lu RPS-071 (12.4 ± 0.9 %ID/g) peaked at 4 h p.i. and cleared significantly ($p < 0.0001$) by 96 h. Kidney uptake correlated more strongly with molecular weight than with PSMA affinity, as ^{177}Lu RPS-063 and ^{177}Lu RPS-077 showed significantly higher uptake ($p < 0.011$) than ^{177}Lu RPS-072 at all time points, and ^{177}Lu RPS-071 after 24

h ($p < 0.0001$). **Conclusions:** Linker length and/or configuration was found to modulate albumin binding and in vivo pharmacokinetics. ^{177}Lu RPS-072 displays optimal pharmacokinetics for RLT, including a high area under the curve (AUC) for the tumor and low AUC for kidneys. These characteristics are particularly appealing for an α -particle emitting radioligand, and warrant the investigation of ^{225}Ac RPS-072 in targeted alpha radiotherapy.

OP-162

Dosimetry of ^{177}Lu -PSMA 617 after Mannitol infusion and Glutamate candies administration: a strategy to reduce adsorbed dose to kidneys and parotid glands

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Purpose: Radio ligand treatment (RLT) with ^{177}Lu -PSMA (prostate-specific membrane-antigen) is a promising option for prostate cancer patients with castration resistant metastatic disease (mCRPC). Since April 2017, at IRST-IRCCS Meldola-Italy, a prospective phase II study is ongoing and patient's dosimetry to kidneys (KDs), parotid glands (PGs) and red marrow (RM) is part of the study. **Methods:** According to our protocol (EUDRACT / RSO 2016-002732-32) 500 ml of a 10 % solution of mannitol is administered before ^{177}Lu PSMA-617 infusion to reduce KDs uptake as described [1]. Moreover, 2 candies containing iron mineral glutamate are administered orally during RLT infusion to reduce PGs uptake. So far, 30 patients have been enrolled and 6 consented to perform dosimetric study. Whole body (WB) planar scans and blood samples were acquired at different times post injection (1h, 16-24h, 36-48h, 120h) and a SPECT/CT image of abdominal region was acquired at 16-24 h post injection. The conjugate view approach was used for determination of the counts after definition of region of interest (ROI). In order to generate the time-activity curves, for each scan KDs and PGs counts were normalized to the whole body counts at the first acquisition, that corresponds to the injected activity. Blood samples activity measured with a High-Purity Germanium detector were used for RM time-activity curve estimation. The dose calculation was performed by using the MIRD formalism (OLINDA/EXM software). For PDs the unite sphere model density doses available in OLINDA/EXM software was used assuming a morphology similar to a sphere. **Results:** The dosimetric results were compared to the published ones [2,3] with unpaired T-test. No statistically significant difference was found for whole body (median[range]: 0.04[0.02-0.05] vs 0.05[0.01-0.10] mGy/MBq, p-val-

ue=0.37) or RM (0.04[0.001–0.08] vs 0.03[0.01–0.06], p-value=0.85) absorbed dose (Figure 1). Absorbed dose to KDs was lower for our patient cohort (0.20[0.11–0.31]) compared to data [2,3] (0.86[0.20–1.90]), with statistically significance (p-value=0.001). Median PGs absorbed dose was reduced but not significantly different (0.79[0.33–1.24] vs 1.73[0.30–9.50], p-value=0.24). **Conclusions:** These results indicate the possibility to reduce KDs and PGs absorbed during ^{177}Lu -PMSA RLT with the co-administration of 10% mannitol and iron glutamate candies. Likely, this approach might be more relevant for RLT with alpha emitters. **References:** [1] Matteucci et al Eur J Nucl Med Mol Imaging. 2017 Dec;44(13):2189–2194. [2] Baum R et al. JNM 2016;57(7):1006–1013. [3] Kabasakal L et al EJNMMI 2015;42:1976–1983.

OP-163

Enhancing treatment efficacy of ^{177}Lu -PSMA-617 with the conjugation of an albumin-binding motif: preclinical dosimetry and endoradiotherapy studies

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Introduction: The PSMA (prostate-specific membrane antigen)-targeted ^{177}Lu -PSMA-617 is currently the most popular radiotherapeutic agent for treating metastatic prostate cancer (PCa). Clinical data showed that ^{177}Lu -PSMA-617 can be effective in treating metastatic PCa and reducing patients' PSA levels. However, the complete response rate was low, and many patients still progress after treatment. To improve treatment efficacy, we designed and synthesized a novel albumin-binding-conjugated ^{177}Lu -PSMA-617 derivative, ^{177}Lu -HTK01169, with extended blood retention time to maximize tumor uptake.

Methods: PSMA-617 and HTK01169 that contained *N*-[4-(*p*-iodophenyl)butanoyl]-Glu as an albumin-binding motif were synthesized using the solid phase approach. Binding affinity to PSMA was determined by in vitro competition assays using LNCaP PCa cells and ^{18}F -DCFPyL as the radioligand. ^{177}Lu labeling was performed in acetate buffer (pH 4.5) at 90°C for 30 min. SPECT/CT imaging, biodistribution and endoradiotherapy studies were conducted in mice bearing PSMA-expressing LNCaP PCa xenografts. Radiation dosimetry was calculated using OLINDA software. **Results:** Lu-PSMA-617 and Lu-HTK01169 bound PSMA with high affinity (K_d values = 0.24 and 0.04 nM, respectively). SPECT imaging and biodistribution studies showed that ^{177}Lu -PSMA-617 and ^{177}Lu -HTK01169 were excreted mainly via the renal pathway. With fast blood clearance (0.68 %ID/g at 1 h post-injection), the tumor uptake of ^{177}Lu -PSMA-617 peaked at 1 h post-injection (15.1%ID/g), and gradually decreased to 7.91%ID/g at 120 h post-injection. With extended blood retention (16.6 and 2.10%ID/g at 1 and 24 h, respectively), the tumor uptake of ^{177}Lu -HTK01169 peaked at 24 h post-injection (55.9%ID/g), and remained at the same level by the end of the study (120 h). Based on dosimetry calculations, ^{177}Lu -HTK01169 delivered 8.3-fold higher radiation dose than ^{177}Lu -PSMA-617 to LNCaP tumor xenografts. For the endoradiotherapy study, the mice (n=8) injected with ^{177}Lu -PSMA-617 (18.5 MBq) all reached

humane endpoint (tumor volume >1000 mm³) by Day 62 with a median survival of 47 days. Mice injected with 18.5 MBq (n=7), 9.3 MBq (n=8), 4.6 MBq (n=8) or 2.3 MBq (n=8) of ^{177}Lu -HTK01169 had a median survival of 152, 102, >47 (ongoing) and 32 days, respectively. **Conclusion:** The novel albumin-binding motif *N*-[4-(*p*-iodophenyl)butanoyl]-Glu significantly extended the blood retention time of ^{177}Lu -HTK01169, and dramatically improved its uptake into PSMA-expressing LNCaP tumor xenografts. Compared with mice injected with ^{177}Lu -PSMA-617, improved overall survival was achieved in mice injected with the same, one-half or even one-quarter dose of ^{177}Lu -HTK01169. Conjugation of an albumin-binder to endoradiotherapeutic agents currently used in the clinic is a promising strategy to enhance their treatment efficacy.

OP-164

Terbium-161 for PSMA-Targeted Radionuclide Therapy of Prostate Cancer

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Introduction: Prostate-specific membrane antigen (PSMA)-targeting radioligands have been developed for diagnostic imaging and radionuclide therapy of prostate cancer. ^{177}Lu -PSMA-617 has been employed for targeted radioligand therapy of metastasized disease. ^{161}Tb -PSMA-617 is believed to be a valid alternative due to the emission of beta particles and short-range (Auger/conversion) electrons which are particularly suited for the treatment of small lesions and single cancer cells. The aim of this study was to perform a proof-of-concept therapy study using ^{161}Tb -PSMA-617 in PSMA-positive PC-3 PIP tumor-bearing mice.

Methods: ^{161}Tb -PSMA-617 and ^{177}Lu -PSMA-617 were obtained at high radiochemical purity (>98%). The therapy experiment was performed with nude mice 6 days after PC-3 PIP tumor cells inoculation (average tumor volume: ~85 mm³). Endpoint criteria were defined as body weight loss of >15% or tumor size of >800 mm³. Groups of six mice received saline (Group A; control), ^{177}Lu -PSMA-617 (5 MBq, 1 nmol, Group B as a reference), ^{161}Tb -PSMA-617 (5 MBq, 1 nmol, Group C) and ^{161}Tb -PSMA-617 (10 MBq, 1 nmol, Group D), respectively. The mice were monitored over 12 weeks by measuring of the tumor size and body weight every second day. Blood plasma parameters were determined when an endpoint criterion was reached. **Results:** The fast tumor growth in control mice required euthanasia between days 18–24 resulting in a median survival time of 19 days. The tumor growth was delayed in mice of Groups B and C where the endpoint was reached between days 30–40 and days 30–66, respectively, with median survival times of 37 and 36 days. Tumor growth inhibition was most effective in mice of Group D in which the first endpoint was reached at day 40. The median survival time in this group was 65 days while two mice were still alive at day 84 when the study was terminated. Body weight

loss was observed as a consequence of the fast tumor growth in the control group. Blood plasma parameters (creatinine, blood urea nitrogen, alkaline phosphatase) were in the same range for treated mice and untreated controls indicating the absence of early side effects. **Conclusion:** ^{161}Tb -PSMA-617 application resulted in an effective and dose-dependent tumor growth inhibition without causing undesired side effects. To investigate the anticipated advantage of ^{161}Tb over ^{177}Lu , respective radioligands should be tested in more detail and at various activities on a preclinical level followed by translation of this promising concept to clinical trials.

OP-165

Optimizing the treatment regimen for targeted alpha therapy of mCRPC with ^{225}Ac -PSMA-617

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Aim: PSMA-targeting alpha-therapy (PSMA-TAT) of mCRPC with ^{225}Ac -PSMA-617 (8 MBq, 3 cycles, 8 week intervals) already demonstrated promising anti-tumor activity, but also induced severe and often irreversible xerostomia (1,2). Our objective was to optimize the treatment protocol to improve tolerability.

Methods: Patients with PSMA-positive mCRPC that were resistant against or ineligible for approved options and presented with progressive disease were treated with ^{225}Ac -PSMA-617 under the conditions of the updated declaration of Helsinki, § 37 (Unproven interventions in clinical practice) and in accordance to the German Pharmaceuticals Law §13(2b) as a salvage therapy. In n=20 patients (concept A) only the first cycle was performed with a fixed dose of 8 MBq and in case of a >50% PSA-response at week-8, the treatment activity was reduced by 2 MBq for the next cycle, respectively. In n=20 patients (concept B), already at cycle-1 the treatment activity was reduced from 8 MBq to 6 MBq. Depending on PSA-response at week-8, treatment activity was escalated, de-escalated or kept constant. In n=5 patients (concept C, ongoing) 4 MBq ^{225}Ac -PSMA-617 and 4 GBq ^{177}Lu -PSMA-617, i.e. 50% of the respective single dose, were administered as a cocktail-regimen. **Results:** For concept A treatments were conducted with 8/8/6 MBq in 4 patients, 8/6/6 MBq in 13 patients, 8/6/4 MBq in 3 patients. PSA response rate was comparable to the already published (2) protocol because only favorable responders de-escalated dose; de-escalated patients did not discontinue due to dry mouth but this might include some psychological bias in awareness of the favorable response. For concept B 10 patients completed with 6/6/6 or further de-escalation, 5 had to escalate and 5 left therapy due to non-response. Tolerability of non-escalating patients was improved, but counteracted by the decreased anti-tumor activity. For concept C no patient discontinued due to dry mouth, yet. Until now 60% (3/5) demonstrated positive PSA-response. The observations for this group are currently ongoing. **Conclusion:** Dose de-escalation protocols or radionuclide combinations of low-dose ^{225}Ac amended by beta-therapy, seem promising approaches to improve the tolerability of PSMA-TAT without losing

too much anti-tumor activity. **References:** 1.Targeted α -Therapy of Metastatic Castration-Resistant Prostate Cancer with ^{225}Ac -PSMA-617: Dosimetry Estimate and Empiric Dose Finding. J Nucl Med. 2017 Oct;58(10):1624-1631. 2. Targeted Alpha Therapy of mCRPC with ^{225}Ac -PSMA-617: Swimmer-Plot analysis suggests efficacy regarding duration of tumor-control. J Nucl Med. 2018 Jan 11. [Epub ahead of print]

OP-166

Molecular Imaging of Prostate Cancer: A direct comparison of the preclinical characteristics of [^{18}F] DCFPyL and [^{18}F]PSMA-1007 and the impact of glutamic acids on [^{18}F]PSMA-1007

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Aim: For the imaging of PSMA-positive prostate cancer, several fluorine-18 (^{18}F)-labelled compounds have been developed and translated into the clinics. Next to a clinical study comparing the tracer-specific characteristics of [^{18}F]DCFPyL and [^{18}F]PSMA-1007 intra-individually⁽¹⁾, a direct comparison of their preclinical characteristics has only recently been published⁽²⁾. In this work, the importance of glutamic acids in the structure of [^{18}F]PSMA-1007 is further elucidated using derivatives with none to three glutamic acids (Glu), respectively. Furthermore, [^{18}F]DCFPyL and [^{18}F]PSMA-1007 are evaluated regarding their preclinical characteristics using the in vitro and in vivo methods established at DKFZ Heidelberg, Germany. **Materials and Methods:** The precursors for radiofluorination containing different amino acid linkers (0-3 Glu) were synthesized by means of solid phase chemistry. The radiolabeling of [^{18}F]PSMA-1007, its derivatives, and [^{18}F]DCFPyL were performed prior to each experiment as described^(3,4). The binding affinities of non-radioactive reference compounds were determined by competitive binding assays against [^{68}Ga]Ga-PSMA-10 in LNCaP cells. The internalization of the respective radioligands in LNCaP cells was compared. Biodistribution and pharmacokinetics were evaluated in vivo in LNCaP-tumor bearing BALB/c Nude mice using μPET . **Results:** The Glu variation in the linker structure resulted in similar binding affinities (K_i 3-14 nM) whereby the insertion of three Glu showed the highest K_i values. Internalization assays revealed that the insertion of Glu influences the internalization rate, whereby the insertion of two Glu ([^{18}F]PSMA-1007) leads to the highest internalization rate ($54.04 \pm 13.7\%$) in a total range between $27.3 \pm 3\%$ to $54 \pm 13.7\%$. In comparison to [^{18}F]PSMA-1007, a higher proportion of [^{18}F]DCFPyL remains cell surface bound; only $27.83 \pm 4.31\%$ of the radiotracer is internalized. [^{18}F]DCFPyL also has a slightly lower binding affinity (18.02 ± 9.63 nM). μPET imaging showed outstanding imaging properties, especially of [^{18}F]DCFPyL and [^{18}F]PSMA-1007. In mice, the liver uptake is reduced by introduction of Glu linkers. The data will be analysed more detailed soon. **Conclusion:** Comparative cell experiments revealed a high binding affinity for all tracers and the highest internalization rate for [^{18}F]

PSMA-1007. The insertion of Glu in the linker structure plays an important role in pharmacokinetics due to the decreased lipophilicity of the respective radiotracer. Especially [^{18}F]DCFPyL and [^{18}F]PSMA-1007 are of excellent imaging quality. Their apparent non-inferiority is currently under further assessment in clinical trials. **References:** (1) Giesel F et al (2017): JNM, doi: 10.2967/jnumed.117.204669. (2) Robu S et al (2018): EJNMMI Res., 8(1):30. (3) Cardinale J et al. (2017): JNM, 58(3):425–431. (4) Chen Y et al. (2011): Clin Cancer Res., 17(24):7645–53.

OP-167

Evaluation of the effect of monosodium glutamate on ^{68}Ga -PSMA-11 uptake in salivary glands, kidneys, and LNCaP tumour in immunodeficient mice

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Aim: Prostate specific membrane antigen (PSMA) ligands labeled with therapeutic radioisotopes (^{177}Lu , ^{225}Ac) have demonstrated effectiveness in treating prostate cancer, albeit with significant potential salivary and renal toxicity. We evaluated the potential of monosodium glutamate (MSG) to reduce salivary and kidney uptake of a PSMA radioligand without affecting tumour uptake. **Materials and methods:** Male immunodeficient mice were inoculated subcutaneously with LNCaP cells. The precursor for ^{68}Ga -PSMA-11 was purchased and labeling was performed in HEPES buffer with microwave-assisted heating. Under isoflurane anesthesia, MSG in PBS (657 mg/kg, n=10; 329 mg/kg, n=5; 164 mg/kg, n=5) or PBS (n=17) was injected intraperitoneally. Fifteen minutes later, ^{68}Ga -PSMA-11 (1.86±0.71 MBq) was administered intravenously. Sixty minutes afterwards, the mice were sacrificed, organs were harvested and assayed on a gamma counter. An in vitro competition assay in LNCaP cells with increasing concentrations of MSG against a PSMA ligand (^{18}F -DCFPyL) was performed. Analysis was performed with R 3.4.0. Outliers were identified by Grubb's test. Welch's t-test was used to compare normally distributed data or Wilcoxon's rank sum test otherwise. A significance level of $p < 0.05$ was used. **Results:** ^{68}Ga -PSMA-11 was obtained in 66.3±9.6% decay-corrected radiochemical yields with > 99% radiochemical purity and 82.6±44.3 GBq/μmol specific activity. Tumour uptake was not statistically different between groups: 657 mg/kg (8.42±1.40), 329 mg/kg (7.19±0.86), 164 mg/kg (8.20±2.44), PBS (8.67±1.97). Kidney uptake was significantly lower in the 657 mg/kg group (85.79±24.20 %ID/g) compared with 329 mg/kg (158.61±26.16), 164 mg/kg (211.45±27.42), and PBS groups (182.57±33.52); $p < 0.001$. Difference between 329 mg/kg and 164 mg/kg groups was significant ($p < 0.05$), but not when they were respectively compared with PBS. Salivary gland uptake was lower in 657 mg/kg (3.72±2.12) and 329 mg/kg (5.74±0.62) groups compared with the PBS group (10.04±2.52); $p < 0.01$. There was no significant difference between 164 mg/kg (14.17±4.27) and PBS groups or between 657 mg/kg and 329 mg/kg groups. Muscle uptake was also generally lower in MSG treated groups. Competition of MSG against ^{18}F -DCFPyL in LNCaP cells yielded a K_i value of 58.12 μM. **Conclusion:** MSG decreased salivary gland

and kidney uptake of ^{68}Ga -PSMA-11 in a dose-dependent manner. Tumour uptake was not significantly affected in vivo, but in vitro assays showed MSG can compete with a PSMA radioligand at micromolar concentrations. Future work is needed to assess if decreased organ uptake is only secondary to MSG competition with the PSMA protein or if another undetermined pathway is being blocked.

OP-168

Impact of [^{18}F]PSMA1007 uptake in PET-imaging in prostate cancer using different peptide concentration: preclinical PET/CT study in mice.

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Objectives: Prostate-specific membrane antigen (PSMA) is playing a key role in the theranostics of prostate cancer. However, effect of the PSMA peptide concentration on tumor uptakes on PET has not been investigated until now. The purpose of this study was to evaluate whether different peptide concentration might influence [^{18}F]PSMA-1007 uptake in the tumor using the xenograft model. **Methods:** Tumor xenograft models were established using LNCaP (PSMA-positive prostate cancer cell line) which was subcutaneously inoculated bilaterally into male SCID mice (n=9). Mice were divided into three groups (each n=3) so that the tumor sizes were comparable in each group. Three kinds of [^{18}F]PSMA-1007 solutions with different molar activity (MA) were prepared for each group (high MA: 1,173 GBq/μmol, medium MA: 117.3 GBq/μmol, and low MA: 11.7 GBq/μmol, respectively). Mice (body weight 18.5 ± 1.83 g) were investigated using a small animal PET scanner (Siemens Inveon PET/CT) at 60 min post injection of each [^{18}F]PSMA-1007 solution under isoflurane anesthesia. Tumor uptakes on PET were compared among the three groups by the Tukey HSD test. Immunohistochemical staining and western blot analyses were performed to confirm the upregulation of PSMA in LNCaP tumor using anti-PSMA antibody (ab140348, Abcam). **Results:** [^{18}F]PSMA-1007 PET showed significantly lower tumor uptakes (SUVmax= 2.0 ± 0.7) in the low MA group compared to medium MA group (SUVmax= 7.3 ± 1.5) and high MA group (SUVmax= 7.3 ± 2.6) ($p < 0.01$ and $p < 0.01$, respectively). Immunohistochemical staining and western blot analyses revealed the significant upregulation of PSMA in the LNCaP tumors. It was indicated that high peptide concentration of PSMA (resulting in low MA of radiolabeled PSMA-1007) showed inhibitory effect on the tumor uptakes on [^{18}F]PSMA-1007 PET due to the competitive binding to the target. **Conclusions:** We suggest that MAs of PSMA radioligands should be maintained at a higher level to prevent underestimation of the tumor uptake. It is also important to consider the necessary MA of corresponding PSMA radioligand for therapy in comparison to that of diagnostic PSMA radioligand to justify their tandem use in the precision medicine of prostate cancer.

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Sunday, October 14, 2018, 16:30 - 18:00, Hall Y

Do.MoRe: Standardization & Calibration

OP-169**Intercomparison exercises: Why is it important to calibrate Radionuclide Calibrators for different radionuclides**

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Aim: Radionuclide calibrators are commonly used in hospitals to measure the activity before administration. For each radionuclide, the radionuclide calibrator has a calibration setting which is determined for a specific well defined geometry in a standard position. A variety of radionuclides are clinically used in Nuclear Medicine such as pure beta emitters and gamma emitters. Since 1996, NPL ran 10 intercomparison exercises to assess the measurement capability for radionuclides with different characteristics. **Materials and Methods:** The intercomparison exercises covered the following radionuclides: ⁶⁷Ga (1996), ¹²³I (1996, 2000, 2015), ¹¹¹In (1997), ²⁰¹Tl (2001), ⁸⁹Sr (2003), ^{99m}Tc (2006), ⁹⁰Y (2009) and ¹⁷⁷Lu (2012). The sources for the intercomparison exercises were prepared and supplied by different manufactures depending on the radionuclide. The solutions were prepared from a bulk solution from which nominal activities were dispensed into 10 ml P6 vials (1996–2009) and 10R Schott vials (2012, 2015). A randomly chosen subset was sent to NPL for standardisation of the solution using the NPL secondary ionisation chambers previously calibrated for the various radionuclides and to check homogeneity of the solution. The presence of gamma-ray emitting contaminants was checked using high-resolution gamma spectrometry. The participants were asked to submit their results to NPL to be compared to the NPL certified value. **Results and conclusions:** For ^{99m}Tc, 96 % of the participants that took part in the exercise reported results within 5 %. Results of the same order were found for ⁶⁷Ga. The ²⁰¹Tl and ¹⁷⁷Lu intercomparison exercises highlighted the issues of measuring radionuclides in the presence of impurities, with 70 % and 82 % respectively of the participants measuring within 5 %. The results highlighted the difficulties of measuring pure beta emitters such as ⁸⁹Sr and ⁹⁰Y with only 58 % and 40 % respectively measuring within 5 % of the certified value. The ¹²³I intercomparison exercises showed the difficulties of measuring radionuclides with characteristic x-rays with energies lower than 30 keV. For the intercomparison exercises in 1996 and 2000 only 28 % and 29 % respectively of the participants would measure within the 5 %. In the last ¹²³I intercomparison exercise 85 % of the participants reported results within 5 %. The intercomparison exercises are an important way to identify possible measurement problems within the nuclear medicine community and provide support to the community in how to resolve the issues arising from using the same equipment to measure a variety of radionuclides.

OP-170**Validation of an EARL Protocol using Digital PET**

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Introduction: Recently, a time-of-flight PET system with digital photon-counting technology (Philips Healthcare) was introduced. This system potentially provides an improved image quality compared to conventional systems. It was recently showed in a phantom study that this digital PET system can fulfil EANM-research-LtD (EARL) accreditation specifications for tumour imaging with FDG-PET/CT (*Koopman et al., EJNMMI physics* 2017). We aimed to validate whether conventional PET and digital PET provide similar standardized uptake values (SUVs) when using an EARL-compatible protocol. **Subjects and methods:** We performed a prospective side-by-side PET comparison study in 20 patients referred for FDG-PET/CT. For each patient, data were acquired using a conventional scanner (cPET, Ingenium TF PET/CT, Philips Healthcare) and a digital scanner (dPET, Vereos PET/CT, Philips Healthcare). Both PET/CT scanners were EARL-accredited. The PET scanning order was randomized per patient and for each system an EARL-compatible reconstruction was applied. Per patient, FDG-positive lesions were included up to a maximum of 5. For each lesion, we measured SUVmean and SUVmax on both cPET and dPET images. Lesion axial diameters were measured on CT. Δ SUV was calculated by $(\text{SUV}_{\text{dPET}} - \text{SUV}_{\text{cPET}}) / \text{SUV}_{\text{cPET}}$. Based on EARL contrast recovery coefficient (CRC) limits, we considered a limit of 20% for Δ SUVmean and 25% for Δ SUVmax as acceptable. **Results:** Average lesion size in 72 included lesions was 15 ± 7 mm (range 5–41 mm). On cPET, the average $\pm$ standard deviation of SUVmean and SUVmax were 3.9 ± 2.0 and 5.7 ± 3.4 , respectively. On dPET, SUVmean increased with 18% to 4.5 ± 2.1 ($p < 0.001$), while SUVmax increased with 19% to 6.5 ± 3.4 ($p < 0.001$). For 41 out of 72 lesions (57%), Δ SUVmean was considered acceptable, while for 44 lesions (61%), Δ SUVmax was considered acceptable. **Conclusion:** Using EARL-compatible reconstructions, dPET provided higher SUVs than cPET. This increase in SUV was moderately within acceptable limits. In 40% of the lesions those limits were exceeded, probably because EARL CRC specifications imply larger limits for small lesions and SUVs generally increase with prolonged FDG-uptake.

OP-171**Evaluating the stability of PET radiomic features using specially designed imaging phantoms simulating heterogeneous radiotracer uptake in PET**

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Aim: Accurate quantification of intratumoral uptake heterogeneity using radiomic features is important for precise characteri-

zation of cancer lesions using PET. However, these features have varying stability due to different noise levels and image contrast. This study investigated the effect of different scanners (analogue and digital PET/CT), noise levels and image reconstruction protocols on several radiomic features using phantom experiments.

Materials and methods: A specially designed insert was placed in the casing of the NEMA-NU2 image quality phantom, simulating different patterns of radiotracer uptake. The insert consisted of several compartments in which separately fillable shapes, created using laser-based stereolithography 3D printing, could be placed. These compartments had different configurations of shapes (wall thicknesses 0.4 mm) including spheres, a torus, pixelated rectangular shapes and an organic shape resembling a tumour. The background compartment was filled with an activity concentration of 2.4 kBq·mL⁻¹ (according to the EARL recommendations), whereas other compartments were filled with 2, 4, and 8 times the background concentration. Data were acquired in list-mode for 15 min per bed position using an analogue (Biograph Horizon; Siemens Healthcare) and digital PET/CT (Vereos; Philips Healthcare). The list-mode files were histogrammed into frames with different lengths (single frame of 15 min, and five frames of 1, 2 and 3 min per bed positions for the Vereos). Data were reconstructed according to EANM guidelines, with point-spread function modelling, and varying matrix sizes. Images were analysed using LIFEx¹, calculating 47 features.

Results: Heterogeneous uptake could be accurately simulated using the phantom. Radiomic features were considerably affected by scanner performance, with a median difference of 38% (0.10–8.7·10²%) between the EANM reconstructed images of the two scanners. For images with different voxel sizes, the median difference was 29% (2.1–1.6·10⁴%) and 13% (0.9–4.5·10²%) for Vereos and Horizon, respectively. For the PSF reconstructions, the number of iterations influenced quantification of radiomic features, with a median of difference of 2.3% (0.23–7.4%) and 9.5% (0.40–41%) for Vereos and Horizon, respectively. With varying count statistics, radiomic features were reproducible, with a difference of 2.5% (0.20–6.7%), 3.75% (0.20–13%) and 4.4% (0.21–20%) for acquisition times of 3, 2 and 1 min per bed position, respectively. **Conclusion:** PET radiomic features are affected by image acquisition time, image reconstruction protocol and performance of the PET scanner. The newly designed inserts for the NEMA-NU2 are useful for simulating different patterns of radiotracer uptake. ¹LIFEx version 4.0 (<http://www.lifexsoft.org/>)

OP-172

Quality Score Guided Correction of Image Derived Arterial Input Function

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Purpose: Kinetic modeling in dynamic PET studies typically requires an accurate arterial input function (AIF). Current gold standard is to obtain AIF invasively by sampling blood from an artery. However, it is desirable to extract an Image Derived Input Function (IDIF) to eliminate arterial blood sampling. The accuracy of IDIF is affected by various physical and biological factors. Ideally, all factors need to be properly corrected to match the

IDIF to blood samples. However, practically, these factors are interconnected. Correction on one factor generally will involve assumptions on other factors, which may lead to overcorrection. The objective of this work is to present a new analytical approach for IDIF generation using a quality score guided corrections. **Methods:** An initial estimation of IDIF was obtained by placing a volume of interest in the descending aorta (DA). We derived quality scores using both dynamic image series and a dynamic-summed image. The quality score was based on five key sources of error: PET/CT misalignment, partial volume effect (PVE), blood spillover, reference region, and quantification biases between dynamic frames and dynamic-summed image. For each of five sources of error, the corresponding correction received a weighted positive score if one connected physical parameter resulted in changes trending towards an ideal solution (e.g. PET/CT realignment changed partial volume factor from 0.71 to 0.86 and thus received a positive score); otherwise, a negative score was assigned. A final quality score was calculated by evaluating all correction combinations and used to derive a priority of needed corrections for each dynamic frame to generate a corrected IDIF. The IDIF generated using the quality score was evaluated on 5 clinical datasets. **Results:** In one of the 5 subjects, the quality score indicated that 23 out of total 32 dynamic PET frames required realignment with CT image. In another subject, according to the quality score, spillover correction was not required because the modeling of PVE sufficiently met the quantification assumption in DA. The relative differences of area under the curve of IDIF as compared to AIF from blood sampling were: IDIF without correction (12% overestimation), with all corrections (5% underestimation), and with proposed method (1% overestimation). The p-value in Two-Sample-Kolmogorov-Smirnov test of time activity curves increased from 0.19 to 0.48. **Conclusion:** In this study, we have shown preliminary feasibility of using the proposed quality score method to further correct the IDIF to more closely match the AIF derived from blood sampling.

OP-173

Stability of image-derived metrics in PET imaging with an emphasis on intrinsic data variability

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Purpose: Quantitative assessment of PET/CT images is useful for treatment personalization, providing the possibility to monitor treatment response and to aid in radiotherapy treatment planning. However, these quantitative measurements are subjected to different types of variation (e.g. instrumental noise, image reconstruction and biology) which reduce reproducibility. In this study, we investigated the impact of instrumental and image reconstruction variability on the stability of commonly used PET image-derived metrics using a list-mode (LM) resam-

pling technique. **Subjects & Methods:** LM resampling was performed by allocating odd and even numbered coincidences to different LM datasets, a process here referred to as count sifting. Count sifting results in two independent LM realizations. This way of splitting LM datasets eliminates the influence of biological effects of *in vivo* measurements, as both datasets represent contemporaneous data. Count sifting was applied to non-parametric LM data of phantom (homogeneous germanium-68/gallium-68 ($^{68}\text{Ge}/^{68}\text{Ga}$) source, as well as the NEMA NU2 PET image quality phantom with fluorine-18 (^{18}F) and zirconium-89 (^{89}Zr) and patient acquisitions (^{18}F fluorodeoxyglucose PET images of 20 lung cancer patients)). The ^{18}F phantom data were reconstructed with 5 different reconstruction algorithms. The difference between LM realizations was quantified by comparing SUV_{max} , SUV_{mean} , SUV_{peak} , coefficient of variation (CoV), metabolic tumour volume (MTV), and the Jaccard index (JI) of the volumes. The relative difference was calculated for the imaging features. **Results:** For the $^{68}\text{Ge}/^{68}\text{Ga}$ images, relative difference in SUV_{max} , SUV_{mean} , and CoV, between the two images were 2.74%, 0.09%, and 1.00% respectively. For the NEMA ^{18}F images (all spheres combined), the SUV_{peak} was least affected by the reconstruction methods (4.16%), whereas the MTV was most affected (13.73%). The smallest relative differences for the image-derived indices were seen using 3D-OSEM with time of flight (5.03%). For the ^{89}Zr images, SUV_{peak} showed the least variation (4.25%) whereas MTV was most affected (21.55%). The relative differences between the images for 20 lung lesions were for the SUV_{max} ($5.87 \pm 4.15\%$), SUV_{mean} ($3.10 \pm 2.80\%$), CoV ($6.99 \pm 6.73\%$), SUV_{peak} ($4.10 \pm 2.60\%$) and MTV ($10.13 \pm 9.26\%$). In addition, the JI was calculated (0.81 ± 0.08). **Conclusion:** Count sifting is a method to study instrumental and image reconstruction variability in PET/CT images, by eliminating the influence of biological variation between generated subsets. Count sifting shows that commonly used image-derived metrics are affected by these types of variation. These results warrant further investigation to study these effects on measurement reproducibility to improve the use of quantitative assessment of PET images for personalized medicine.

OP-174

Determination of appropriate reconstruction parameters for each of 21 PET scanner models from 6 vendors to meet the society phantom criteria for brain amyloid PET imaging.

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Introduction: Brain amyloid PET is an essential tool for clinical trials of therapeutics for Alzheimer's disease. Since PET image quality and quantitative capability depend on the PET scanner model, scanning protocol and reconstruction parameters, it is

essential to standardize the scanning method and to harmonize PET image quality for acquiring reliable multi-center studies. Japanese Society of Nuclear Medicine (JSNM) has issued phantom test criteria of four physical parameters (resolution ≤ 8 mm FWHM and gray-white contrast $\geq 55\%$ with Hoffman phantom, uniformity $\pm 5\%$ (the criteria of uniformity is $\text{SD} \leq 0.0249$ which corresponds to 95% of the ROIs being distributed within 1.00 ± 0.05 assuming normal distribution) and image noise $< 15\%$ with cylindrical phantom) for brain amyloid PET agents (^{11}C -PiB, ^{18}F -florbetapir, ^{18}F -flutemetamol, ^{18}F -florbetaben, see following: <http://www.jsnm.org/archives/3561/>). Because of trade-off between contrast and noise, reconstruction parameters should be optimized for each PET scanner. **Methods:** Based on the JSNM phantom test procedure, the four physical parameters were measured on 21 PET scanner models by 6 vendors (GE, SIEMENS, Philips, Shimadzu, Toshiba and Shanghai United Imaging) for 5 years (2013–2018). The phantom data were acquired in a 30-minute list-mode and multiple images were generated by extracting data corresponding to the brain activity of each amyloid PET drug (^{11}C -PiB, ^{18}F -florbetapir, ^{18}F -flutemetamol, ^{18}F -florbetaben) to find appropriate reconstruction parameters and scanning duration that satisfy the phantom criteria. **Results:** Appropriate reconstruction parameters were determined that satisfied the phantom criteria for almost all PET scanners, providing the physical parameters of 5–8 mm FWHM resolution, 55–65% gray-white contrast, 0.001–0.0249 SD as uniformity, and 6.5–14.9% image noise, under the condition of each amyloid PET drug. Some PET scanner models allowed shortening the scanning duration to half the default standard and still met the phantom criteria. On the other hand, satisfactory reconstruction parameters were not obtained for two oldest PET scanner models under the ^{11}C -PiB phantom test condition. **Conclusion:** JSNM phantom criteria is practicable for almost all currently-used PET scanner models, and the reconstruction parameters for each scanner model obtained in this study is useful information for multi-center brain amyloid PET study.

OP-175

How to harmonize SUV values obtained by two different generation PET/CT tomographs

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Aim: Last generation PET/CT scanners equipped with LSO crystals implemented point-spread function (PSF) and time-of-flight (TOF) data in reconstruction software. These novelties improved image quality but caused an increase of standardized uptake values (SUVs) compared to conventional OSEM reconstruction system of previous generation PET/CT scanners. The EANM identified the problem of SUV harmonization since 2010 when the EARL FDG-PET/CT accreditation programme was established: they suggested to produce two reconstructions, one optimised for maximum lesion detectability and one for harmonized quantitative analysis. In this work we investigated an alternative meth-

odology, using a single reconstruction for both qualitative and quantitative analysis optimised to maximum lesion detectability, and then applying an intrinsic post-reconstruction algorithm for SUV harmonization. **Materials and Methods:** Phantom measurements and subsequent patient data analysis were performed on a Siemens Biograph mCT system equipped with LSO crystals, PSF and TOF algorithms and on a 10-years old General Electric Discovery STE system equipped with BGO crystals. A dedicated algorithm (EQ-filter) quantification technology was tested to harmonize SUV values between scanners and also in relation to the EAMN/EARL specifications. For phantom measurements we used a NEMA IQ phantom and a Jaszczak phantom equipped with small fillable spheres (lesion to background ratios of 8:1 and 4:1). Several different reconstruction settings were used in order to provide a general methodology independent of the specific protocol adopted in our institution. Data obtained by phantom measurements were validated on seven oncologic patients who accepted to perform one-bed extra acquisition on a different scanner. The evaluation regarded 39 small hot lesions (diameters ranging from 0.3 cm to 2.6 cm) and was performed by two experienced nuclear medicine physicians. **Results:** The main benefit of PSF+TOF PET/CT systems is the increased percentage contrast of small lesions. On the other hand, the curves of recovery coefficients (RCs) measured according to NEMA standards exceeded those obtained by the OSEM reconstruction. Discrepancies in SUV_{max} values between the two PET/CT systems were as high as 149%, while they drop below 10% applying the optimized value of EQ.filter. For each scanner and reconstruction setting the optimal value of the EQ.filter was identified in order to minimize these discrepancies. Patient data, analyzed by Wilcoxon statistical test, confirmed phantom measurements. **Conclusion:** the use of a single reconstruction optimized to maximum lesion detectability with EQ.filter is an easy and convenient solution to harmonize semi-quantitative measurements, avoiding a second reconstruction with an additional smoothing filter as suggested by EAMN/EARL.

OP-176

Results of a nationwide phantom based PET-Survey in Switzerland before harmonization

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Aim: To gain an overview about the variability of PET measurements with diverse PET/CT-systems used in Switzerland, and to provide an inventory on acquisition protocol adherence in a multi-centre setting. **Materials and methods:** A total of 28 PET/CT sites in Switzerland was invited to participate in a PET phantom survey. Based on obligatory semiannual phantom measurements as prescribed by the Federal Office of Public Health in Switzerland, a detailed study protocol defined PET acquisitions of two different durations with a homogeneous cylinder phantom (activity concentration (AC) 10 kBq/ml) and a fillable "hot spheres" (18F) phantom (3.5 kBq background AC; sphere to

background ratio 5:1). At least 7 image reconstructions for each acquisition (28 per study site) were requested. Reconstructions included sets of standard (4mm, isotropic) and high resolution (2mm, isotropic) reconstructions, using filtered back-projection (FBP), ordered subset expectation maximization (OSEM) and vendor specific point spread function (PSF) based reconstructions. Data of all sites underwent automatic quality control (QC) utilizing an in-house developed multi-paradigm software and were analyzed with regard to comparability of measured AC. **Results:** Phantom data was provided by 14 of 28 PET sites (5/5 university hospitals, 7/13 cantonal hospitals, 2/9 private hospitals). From 18 PET devices, 459/504 expected datasets (92%) were received and underwent QC. Of these, 6 datasets were not readable, and 31 datasets were not accepted (e.g. no attenuation correction), resulting in 422 evaluated datasets. 257/422 (61%) datasets were of restricted use for quantification because of protocol violations (e.g. strongly anisotropic voxels, filter parameters or AC out of proposed range, faulty exposure and axial or radial offset of phantom spheres), and/or actual background AC was not provided in 160/422 datasets (38 %). We found high variations in prepared actual or presupposed phantom AC and in recovery of AC, latter depending on reconstruction methods and reconstruction parameters (e.g. isotropy of voxels). Device-specific acquisition parameters - in terms of exposure per reconstructed voxel size - had a major influence on inter-site comparability of quantitative PET measurements. Underexposed PET acquisitions lead to faulty quantification of AC. **Conclusions:** As expected from comparable studies, the nationwide Swiss phantom survey also found considerable variation in PET AC quantification. In the context of multi-centre trials, protocol compliance may not be assumed. Thus, a throughout QC of all datasets appears to be mandatory to assure data quality and comparability. In addition, quantitative PET data may only be used after check of adequate image exposure.

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Sunday, October 14, 2018, 16:30 - 18:00, Hall 1

Teaching Session 2 - Interactive Clinical Cases: Lung Anatomy and Patterns of Lung Malignancy

OP-177

Anatomy of the Thorax and Relevant Anatomy of Most Common Metastatic Sites A. Eccles; Guy's and St. Thomas' Hospitals NHS Foundation Trust, London, UNITED KINGDOM.

OP-178a

Patterns of Lung Cancer and False Positive/Negative Patterns

A. Eccles; Guy's and St. Thomas' Hospitals NHS Foundation Trust, London, UNITED KINGDOM.

OP-178b

Patterns of Lung Cancer and False Positive/Negative Patterns

T. Lynch; Belfast, UNITED KINGDOM.

508 Sunday, October 14, 2018, 16:30 - 18:00, Hall 4
Clinical Oncology: PRRT of Neuroendocrine Tumours

OP-179

Markers of the systemic inflammatory response can predict response and improve patient selection in Neuroendocrine Tumours treated with Peptide Radionuclide Receptor Therapy

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Purpose/Introduction: Peptide Receptor Radionuclide Therapy (PRRT) is an effective treatment for certain patients with metastatic neuroendocrine tumours (NETs). Tumour response is highly variable; no biomarker in clinical practice has been demonstrated to reliably predict outcome. An inability to identify non-responsive patients exposes them to 12 months of an expensive therapy with significant side effects and prevents their participation in clinical trials. The Inflammation-Based Index (IBI), derived from serum C-reactive protein and albumin levels, predicts survival and response to treatment in patients in a number of cancer types and was therefore explored in this setting. **Subjects & Methods:** Clinico-pathological data from patients undergoing PRRT for metastatic NETs were collected at baseline and during treatment. The primary endpoint was progression free survival (PFS) with a secondary endpoint of overall survival (OS). Univariate and multivariate Cox regression analyses tested associations between baseline variables and their dynamic changes, and PFS and OS. Decision curve analysis (DCA) was used to determine the net benefit associated with a treatment strategy determined by the baseline IBI and non-response to PRRT. **Results:** Fifty-five patients were recruited. Baseline IBI >0 was associated with inferior PFS (HR 14.2 (95% CI 5.25-38.5), $p < 0.0005$) and OS (HR 5.94 (95% CI 2.21-16.0), $p < 0.0005$). A persistently abnormal IBI through treatment was also associated with inferior PFS (HR 3.07 (95% CI 1.38-6.82), $p < 0.01$) and OS (HR 5.06 (95% CI 1.94-13.2), $p = 0.001$). Multivariate analysis confirmed an independent association between IBI and PFS ($p = 0.001$). DCA indicated a net clinical benefit at risk thresholds between 0.03 and 0.58. **Discussion/Conclusion:** Baseline IBI score and its dynamic change through treatment are associated with both PFS and OS. This reinforces the notion that PRRT may have an immunomodulatory role in NETs. IBI is a minimally invasive, low cost biomarker that is easily calculable from data routinely collected in clinical practice. At a risk threshold equivalent to the currently accepted rate of non-response to therapy, implementation of this score could avoid a significant number of futile future treatments.

OP-180

Impact of baseline liver tumor burden on treatment outcomes with ^{177}Lu -Dotatate in the Netter-1 study

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Background: The liver is the most common site of metastasis in patients with midgut neuroendocrine tumors (NET). We assessed the impact of hepatic tumor burden on treatment efficacy in the NETTER-1 study population. **Methods:** Patients on the phase III NETTER-1 study were randomized to receive either ^{177}Lu -DOTATATE (Lu)(n=117) or high-dose octreotide (Oct) (n=114). Progression-free survival (PFS) was assessed based on liver tumor burden at baseline. The tumor burden was defined as tumor volume/total liver volume by CT, and categorized as low (<25%), moderate (25-50%), and high (>50%), as assessed by central radiology review. Rates of grade 3 or 4 hepatotoxicity were also assessed based on initial tumor burden. **Results:** In total, 141 patients (61%) had low tumor burden (71 Lu, 70 Oct), 50 (22%) had moderate burden (19 Lu, 31 Oct), and 40 (17%) patients had high burden (27 Lu, 13 Oct). Hazard ratios (HR) of PFS were similar across the low, moderate and high liver burden subgroups. Median PFS (months) was 28.35 vs. 11.04 in low (HR= 0.218, 95% confidence interval [CI] 0.120 to 0.394); Not Reached (NR) vs. 8.67 in moderate (HR=0.202, 95% CI 0.077 to 0.525); 19.38 vs. 5.52 in high liver burden (HR= 0.193, 95% CI 0.079 to 0.474), respectively. In the ^{177}Lu -DOTATATE arm, grade 3/4 (CTCAE v 4.03) AST and ALT toxicities occurred in the low burden group in 2 and 3 patients, respectively and in the high burden group in 3 and 1 patients, respectively. Grade 3/4 hyperbilirubinemia occurred in one patient from the low burden group and one from the moderate burden group. All hepatic toxicities were resolved without sequelae. In the high-dose octreotide arm, there were no treatment-related grade 3/4 AST, ALT or bilirubin toxicities. **Conclusion:** Treatment with ^{177}Lu -DOTATATE resulted in significant PFS improvement regardless of baseline liver tumor burden in patients with well-differentiated, metastatic midgut NET.

OP-181

Personalized ^{177}Lu -octreotate peptide receptor radionuclide therapy of neuroendocrine tumours: preliminary dosimetry, efficacy and safety results from the P-PRRT trial

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Purpose: To report the preliminary results from the prospective P-PRRT trial (NCT02754297), a phase 2 study in which the injected activity (IA) of ¹⁷⁷Lu-octreotate is adjusted to deliver a prescribed absorbed radiation dose to the kidney. **Methods:** In the P-PRRT trial, eligible patients with progressive and/or symptomatic neuroendocrine tumour (NET) are given a four-cycle induction course of ¹⁷⁷Lu-octreotate with quantitative SPECT (QSPECT)-based dosimetry, during which the prescribed renal dose is 23 Gy, with 25–50% reduction in cases of significant haematological or renal impairment. This is delivered by personalizing IA according to body surface area and glomerular filtration rate for the first cycle, and prior cycle renal Gy/GBq for the subsequent cycles. Consolidation and/or maintenance cycles are offered to responders only. Radiological (RECIST) and molecular response (¹¹¹In/⁶⁸Ga-octreotide/octreotate scans) were assessed three months after the induction course, in addition to per-PRRT molecular response (¹⁷⁷Lu-QSPECT/CT). Safety was evaluated according to CTCAE. **Results:** Fifty-two patients underwent 171 cycles. In 34 patients who completed the induction course, a median cumulative IA of 36.1 (range: 6.3–78) GBq was administered, which yielded median cumulative kidney and tumour_{max} doses of 22.1 (range: 8.3–24) Gy and 186 (range: 15.2–443) Gy, respectively. Twenty-nine patients (85%) received a personalized IA and a cumulative tumour_{max} dose that were higher than those that would have been received under a fixed-IA PRRT regime of 7.4 GBq/cycle, representing a median 1.26-fold (range: 0.47–2.7-fold) increase in tumour_{max} dose ($P < 0.0001$). In 39 assessable patients, the best response was partial in 9 (23%), minor in 14 (36%), stable disease in 13 (33%), and progressive disease in 3 (7.7%) patients. In 13 patients with pancreatic NET, 11 (85%) had partial/minor response, while the two others (15%) had stable disease. Acute and subacute side effects were of grade 1/2 only, nausea and fatigue being the most frequent, in 33% and 31% of patients, respectively. Grade 3/4 subacute toxicities were lymphocytopenia in 52% of patients, followed by anaemia (7.7%), leukopenia, thrombocytopenia, worsening of liver function tests (5.8% each), and neutropenia (3.8%). Grade 3/4 chronic toxicities were lymphocytopenia (19.0%), anaemia and neutropenia (4.8% each). No patient developed significant renal toxicity. **Conclusion:** As compared to the common fixed-IA PRRT regime, personalized PRRT allows to significantly increase IA and tumour dose, while controlling renal dose. Personalized PRRT yields promising response rates, particularly in patients with pancreatic NET, with a favourable safety profile that appears similar to that of empiric PRRT.

OP-182

The Role Of Adding Somatostatin Analogues To [¹⁷⁷Lu]Lu-Octreotate As A Combination And Maintenance Therapy

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Purpose: Although somatostatin analogues (SSA) and peptide receptor radionuclide therapy (PRRT) are validated therapies in patients with advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs), it remains unclear whether SSA combined with PRRT or as maintenance therapy can provide prolonged survival compared to patients treated with PRRT alone. In this retrospective study, we aimed to investigate whether there is a survival benefit to adding SSA to PRRT as a combination therapy and/or maintenance therapy. **Subjects and Methods:** The investigation included 168 patients with unresectable GEP-NETs treated at the University Hospital Bonn, Germany. The patients were divided into two main groups: PRRT with [¹⁷⁷Lu]Lu-Octreotate monotherapy (N=81, group 1) and PRRT plus SSA (N=87, group 2) as combined therapy with PRRT and/or as maintenance therapy after PRRT. **Results:** Data for overall survival (OS) were available from 168 patients, of whom 160 had data for progression-free survival (PFS). The median PFS was 27 months in group 1 vs. 48 months in group 2 ($p = 0.012$). The median OS rates were 47 months in group 1 and 91 months in group 2 ($p < 0.001$). The death-event rates were lower in group 2 (26%) than in group 1 (63%). SSA as a combination therapy with PRRT and/or as a maintenance therapy showed a clinical benefit rate (objective response or stable disease) of 95%, which was significantly higher than group 1 (79%). **Conclusion:** SSA as a combination therapy and/or maintenance therapy may play a significant role in tumor control in patients with GEP-NET who underwent a PRRT with [¹⁷⁷Lu]Lu-Octreotate.

OP-183

¹⁷⁷Lu-DOTATATE Peptide Receptor Radionuclide Therapy; Gender Differences in Small Intestinal and Pancreatic Neuroendocrine Tumors

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Purpose/Introduction: In a study of patients with small intestinal NETs (SI-NETs) (n=25) undergoing ¹⁷⁷Lu-DOTATATE peptide receptor radionuclide therapy (PRRT), men required more administered activity than women to reach their best response (RECIST 1.1) as opposed to patients in a study on pancreatic NETs (P-NETs)(n=24). In the present study these findings were analyzed in a larger group of patients. **Subjects & Methods:** Among patients undergoing PRRT at Uppsala University Hospital November 2005 to October 2014, data on administered

activity, best response (BR) according to RECIST 1.1, percent tumor reduction (RECIST 1.1), weight, height, age and body mass index (BMI) were available for 151 SI-NET patients and 82 P-NET patients. Cycles of 7.4 GBq ^{177}Lu -DOTATATE were administered at 6–8 weeks interval. To achieve BR on CT (RECIST 1.1) SI-NET patients required 2–7 cycles while P-NET patients required 2–10. After the last therapy cycle the SI-NET patients were followed with CT for 4 to 125 months and the P-NET patients for 9 to 132 months. **Results:** In the SI-NET group, the percentage tumor reduction on CT according to RECIST 1.1 was similar in men and women (mean $\pm$ SD 14.9 $\pm$ 14.5% versus 15.3 $\pm$ 13.1%, $P=0.9$). Consistent with previous results in the small patient cohort, men with SI-NETs required more administered activity than women to reach their best (and similar) response on CT according to RECIST 1.1 (mean $\pm$ SD) 31.7 $\pm$ 11.7 GBq versus 27.1 $\pm$ 8.8 GBq. This gender difference was not found in P-NET patients, similar to the previous smaller study. In search for possible concurrent factors in the SI-NET patients, gender age, lean body mass (LBM), body mass index (BMI) and administered activity was tested by using multilinear regression. Gender was the most significant factor in this test ($P=0.04$), however, with a very low explanation value ($R^2=0.08$). Neither BMI nor weight correlated to the administered activity in any analyses. **Conclusion:** In this study, we could confirm that men require more administered activity than women to achieve the same best percentage response on CT according to RECIST 1.1, neither BMI nor LBM could explain this gender difference.

OP-184

Combined ^{177}Lu -DOTATATE and metronomic capecitabine in Gastro-entero-pancreatic Neuroendocrine Tumors with high glucose metabolism: preliminary data of a Phase II prospective trial.

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Background and purpose: Radiometabolic therapy with ^{177}Lu -DOTATATE (PRRT) is active and well tolerated in patients affected by gastro-entero-pancreatic neuroendocrine tumors (GEP-NET). However, GEP-NET are very heterogeneous and patients with FDG PET positive tumor respond less to PRRT than FDG negative ones. In this setting a combination of PRRT and a chemotherapy drug such as capecitabine may offer a better chance of tumor control. The aim of this prospective phase II study was to evaluate the activity and toxicity of ^{177}Lu -DOTATATE associated to metronomic capecitabine as radiosensitizer agent, in patients with advanced FDG positive GEP-NET. **Patients and methods:** From August 2015 to December 2016, 37 patients with advanced GEP NET, G1–G2 and G3 with Ki67<50%, were consecutively enrolled. All patients showed progression disease to conventional imaging, positivity to somatostatin receptor imaging (Rotterdam score >2) and FDG PET positive lesions (SUV> 2.5). A cumulative activity of 22.2 GBq or 27.5 GBq of ^{177}Lu -DOTATATE was administered in five cycles 8 weeks apart,

according to kidney and bone marrow reserve. All patients performed the dihydropyrimidine dehydrogenase (DPD) test to evaluate tolerability to capecitabine, that was administered in the inter-cycle period between ^{177}Lu -DOTATATE infusions, with a metronomic schedule of 1500 mg/die. According to IRST protocol all patients who received 1 cycle therapy were evaluated for toxicity (CTCAE criteria) while at least 2 cycles were requested for activity. **Results:** All 37 patients were evaluable for toxicity that was predominantly G1/G2, referred to hematological problems or mucositis and asthenia. Four patients (10.8%) discontinued after the first cycle for G3/G4 toxicity (2 hematological and 2 asthenia and vomiting all recovered after capecitabine interruption), 2 (5.4%) patients discontinued after the fourth cycle for G3 toxicity (1 asthenia, 1 thrombocytopenia). Thirty-three patients were evaluable for response to therapy. Of these, 30 completed the treatment, 2 stopped after the fourth cycle for toxicity and 1 after the third for progression disease. The median administered activity was 27.5 GBq in 5 cycles. The 3 months response has been assessed according to RECIST criteria. Overall response was PR in 9 pts (27%), SD in 18 pts (55%) with a DCR of 82%. **Conclusions:** This phase II study showed that the combination of ^{177}Lu -DOTATATE and metronomic capecitabine is active and well tolerated in GEP-NET patients with aggressive disease (G1–G3 FDG positive). A randomized trial (LU-CA) comparing standard ^{177}Lu -PRRT vs ^{177}Lu -PRRT plus metronomic capecitabine is ongoing at IRST (Eudract number: 2014-003067-38).

OP-185

Induction PRRT With CAPTEM Chemotherapy in a High-risk Population of Metastatic Neuroendocrine Neoplasia (NEN): Balancing Efficacy With Risk

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Introduction: Recognizing the adverse prognosis of non-G1/FDG-avid NEN, we intensified our standard Lu-177-DOTA-octreotate (LuTate) peptide receptor radionuclide therapy (PRRT) protocol by adding capecitabine/temozolamide (CAPTEM) chemotherapy in such patients. Capitalising on 'sink effect', we also selectively use Y-90-DOTA-octreotate (YTate) followed by LuTate +/- CAPTEM in patients with bulky disease. We audited the efficacy and toxicity of this approach. **Subjects and methods:** Patients who received one or more cycles of CAPTEM chemotherapy during induction PRRT were identified, and haematological safety and efficacy were reviewed and correlated with other clinical parameters. **Results:** 35 patients (17 male) fulfilled our inclusion criteria, mean age 56 yrs (range 16–78). 30 patients (86%) had pancreatic NET's (of which 26 were grade 2/3). Prior systemic therapies included chemotherapy (12) and sunitinib/everolimus (6). 124 cycles of induction PRRT were administered, 81 combined with CAPTEM. 108 cycles were LuTate (mean 8.3 GBq) and 16 were Y-Tate (mean 3.2 GBq) alone or combined with LuTate. By RECIST 1.1 criteria, the disease control rate (DCR) was 86%; 2 (6%) CR, 14 (40%) PR, 14 (40%) SD, and 5 (14%) PD. Acute grade 3/4 cytopenia (excluding lymphopenia) occurred in 19.4% of LuTate cycles vs 37.5% of YTate cycles. Addition of

CAPTEM appeared to increase myelotoxicity with YTate (16.7% without versus 50% with CAPTEM) but not with LuTate. Grade 4 thrombocytopenia occurred in 8 cycles (6.5%), with 7 being in association with CAPTEM (including 3 with YTate). There was one febrile neutropenia (urological sepsis), and two bleeding episodes requiring transfusion support. At three months, there was no persistent G4 cytopenia, two G3 neutropenia, and one G3 thrombocytopenia. At median follow-up of 18.5 months (range 9–50), 4/35 patients (11.4%) developed myelodysplasia (3), or acute leukaemia (1). All had also received YTate at some stage during therapy. Baseline GaTate PET and other parameters (spleen SUV_{max}/mean/volume, liver volume, liver metastatic burden, volume of bony metastatic disease, liver synthetic function, baseline cytopenias) were not clearly predictive of toxicity but limited by the small sample size. **Conclusion:** In this patient cohort with adverse prognostic factors, PRRT plus CAPTEM chemotherapy achieved a high DCR but with greater myelotoxicity than generally seen with PRRT alone. The combination of YTate and CAPTEM appears particularly toxic and should be avoided or reserved for patients otherwise at highest risk of disease-related mortality. The combination of PRRT with alkylating chemotherapy (temozolamide) may increase the risk of myelodysplasia and warrants careful observation in ongoing trials of this combination.

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Thyroid: Endocrine Oncology

OP-186

Adrenal Tracer Uptake by ¹⁸F-FDOPA PET/CT in Patients with Pheochromocytoma and Disease Controls

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Purpose: (1) To determine reference maximum Standardized Uptake Values (SUV_{max}) values for normal adrenal ¹⁸F-DOPA tracer uptake. (2) To determine the optimal diagnostic approach for pheochromocytoma localization by using ¹⁸F-DOPA SUV_{max} across a series of cut-off points: the affected adrenal gland (inter-individual analysis), the difference in SUV_{max} between the affected adrenal gland and the contralateral normal adrenal gland (intra-individual analysis), or a combination of these two.

Subjects and methods: All patients with histologically confirmed pheochromocytoma diagnosed between November 2009 and December 2017 were retrospectively analysed. Only those patients who underwent an ¹⁸F-FDOPA PET/CT-scan for localization purposes before adrenalectomy, were included for further analysis. The disease control group consisted of patients who underwent ¹⁸F-FDOPA PET/CT for other indications, and who had no genetic susceptibility for developing a pheochromocytoma. SUV_{max} of a volume of interest surrounding the adrenal glands was determined on EARL reconstructed images. Receiver operating characteristic (ROC) analysis was performed for adrenal gland SUV_{max}, and intra-individual difference in SUV_{max} between affected and normal adrenal gland. In addition, binary

logistic regression was performed for ROC analysis of the combined parameters. **Results:** In total, 49 histologically confirmed pheochromocytomas were diagnosed in 47 patients, and 217 disease control patients were identified. In the disease control group, no differences between the SUV_{max} of left and right adrenal glands were observed, and uptakes in both adrenal glands correlated significantly with each other ($r=0.865$, $p<0.001$). Median (range) adrenal gland SUV_{max} in pheochromocytomas and in the disease control group was 14 (2.2–50) and 3.1 (1.1–6.6), respectively ($p<0.001$). ROC analysis revealed 91% sensitivity and 84% specificity at a SUV_{max} cut-off value of 4.1 (area under the curve (AUC)=0.934), and 93% sensitivity and 96% specificity at an intra-individual SUV_{max} difference between the affected and normal adrenal gland of 1.0 (AUC=0.977). The combination of both variables slightly increases the AUC to 0.983. **Conclusions:** ¹⁸F-FDOPA PET/CT distinguishes pheochromocytoma from normal adrenal glands with the highest diagnostic accuracy when combining the SUV_{max} of the affected adrenal gland with the difference in SUV_{max} between affected and normal adrenal gland.

OP-187

Comparison of ⁶⁸Ga-DOTA-JR11 PET/CT with (dosimetric) ¹⁷⁷Lu-DOTA-JR11 SPECT/CT in patients with metastatic neuroendocrine tumors undergoing peptide receptor radionuclide therapy

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Purpose/Introduction: ⁶⁸Ga-DOTA-JR11 and ¹⁷⁷Lu-DOTA-JR11 are a new pair of somatostatin receptor antagonists for imaging and therapy of somatostatin receptor positive tumors. The aim of this study was to compare tumor uptake of ⁶⁸Ga-DOTA-JR11 and ¹⁷⁷Lu-DOTA-JR11 in order to determine if PET imaging with ⁶⁸Ga-DOTA-JR11 could predict uptake of ¹⁷⁷Lu-DOTA-JR11. **Subjects & Methods:** As part of a prospective clinical trial, 19 patients with metastatic neuroendocrine tumors underwent both, pre-therapeutic whole-body ⁶⁸Ga-DOTA-JR11-PET/CT imaging (acquisition 60–70 minutes postinjection; 173 MBq (median) ⁶⁸Ga-DOTA-JR11) and dosimetry with ¹⁷⁷Lu-DOTA-JR11 SPECT/CT (1940 MBq (median) ¹⁷⁷Lu-DOTA-JR11). Volumes of interest were placed over up to 6 ⁶⁸Ga-DOTA-JR11 avid lesions (uptake greater than liver). Standardized uptake values (SUV_{max}, SUV_{mean}, SUV_{peak}) were measured on ⁶⁸Ga-DOTA-JR11 PET. Additionally, target-to-normal tissue ratios (TNR spleen/liver) were calculated. The same lesions were identified on the dosimetry study and the same parameters calculated on the SPECT/CT images acquired 18–24 h post-injection. For a subset of lesions tumor-absorbed dose per injected activity (D/A_0) was calculated using planar imaging for 7 days to determine the clearance of the activity from the lesions. **Results:** A total of 85 lesions were analyzed. On ⁶⁸Ga-DOTA-JR11 PET/CT, median SUV_{peak} was 9.74 (1.18–82.44), TNR spleen 6.53 (1.02–47.64) and TNR liver 10.25 (1.31–99.08). On ¹⁷⁷Lu-DOTA-JR11 SPECT/CT, SUV_{peak} was 40.75 (4.87–256.7), TNR spleen 4.09 (0.26–74.83) and TNR liver 23.23 (2.07–104.48). SUVs

and tumor-to-organ ratios on PET and SPECT were significantly correlated ($p < 0.001$), but the degree of correlation was modest with Spearman correlation coefficients ranging from 0.41–0.53. Mean absorbed dose ($\pm$ SD) was 6.46 (± 4.03) Gy/GBq (41 lesions). Correlation of SUV_{peak} to absorbed dose (Gy/GBq) was modest $r = 0.38$, $p < 0.0157$. Subgroup analyses showed a better correlation for lesions with SUV_{peak} on PET of > 10 ($r = 0.5056$) than for lesions with a lower SUV_{peak} ($r = 0.0803$). Nevertheless, in all patients, the lesion peak uptake ratio for ^{177}Lu -DOTA-JR11 vs ^{68}Ga -DOTA-JR11 was high, even in those with low uptake on PET (SUV ≤ 10) a ratio of 7.7 ± 5.39 was noted. **Discussion/Conclusion:** SUV_{peak} and tumor-to-normal-tissue-ratios determined on ^{68}Ga -DOTA-JR11 PET correlate with ^{177}Lu -DOTA-JR11 on SPECT. Though variation is noted, high lesion uptake of ^{177}Lu -DOTA-JR11 is seen, even in patients with low uptake on ^{68}Ga -DOTA-JR11 PET, probably related to the higher affinity of ^{177}Lu -DOTA-JR11 for somatostatin receptors. These findings support the feasibility of its use as diagnostic/therapeutic pair for patient selection and PRRT and that low uptake should not preclude patients from treatment with ^{177}Lu -DOTA-JR11.

OP-188

^{68}Ga -DOTATOC PET Uptake in Non-Functioning Pituitary Adenomas -A Longitudinal Case-Controlled Pilot Study

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Introduction: Magnetic resonance imaging (MRI) is an excellent diagnostic tool for the detection of lesions in the pituitary gland. However, since MRI only provides morphological information, small hormone secreting tumors may be difficult to detect. ^{68}Ga -DOTATOC PET, targeting the somatostatin receptors (SSTR), has successfully been used for diagnosing neuroendocrine tumors. Pituitary tumor cells also express SSTR, enabling visualization using ^{68}Ga -DOTATOC PET. So far, this technique has however not been evaluated in pituitary tumors, likely because normal pituitary cells also harbors SSTR. Our aim was to systematically assess the role of ^{68}Ga -DOTATOC PET in the management of pituitary adenomas. **Materials and methods:** This was a longitudinal study of nine patients with non-functioning pituitary adenoma (NFPA) examined with ^{68}Ga -DOTATOC PET/CT pre- and post-operatively. Thirteen healthy controls were also included. The PET-examinations were performed as a 0–45 minutes dynamic list mode scan. A 1.5 T T1 MRI of the pituitary was performed for co-registration. Tracer uptake was analyzed in manually outlined volumes of the tumor as well as in the five hottest voxels in the pituitary region. Data from the

35–45 minute frames were chosen for the statistical analysis. The Mann-Whitney U-test was used to compare ^{68}Ga -DOTATOC uptake in the patients and controls. Here we report the pre-operative data. **Results:** The median Standardized uptake value (SUV)_{max} in the hottest five voxels after 45 minutes was 3.67 (interquartile range 3.12–8.37) in patients compared to 13.20 (12.19–13.55) in controls ($P = 0.0043$). In the manually drawn volume of interest (VOI), the median SUV_{max} was 3.89 (3.42–8.53) in patients and 14.06 (12.48–15.85) in the controls ($P = 0.0026$). ROC-analysis showed an area under the curve of 0.85 for the hottest five voxels ($P = 0.0056$), and 0.87 for the manually outlined VOIs ($P = 0.0037$). Sensitivity was 78% and specificity was 92% for both VOI definitions. **Conclusion:** This is the first study evaluating NFPA pathology with ^{68}Ga -DOTATOC PET. Our preliminary results revealed a statistically different functional ^{68}Ga -DOTATOC tracer uptake between NFPA and normal pituitary gland. This is an important step forward in the diagnostic workup for tumor verification and localization.

OP-189

Dual tracer ^{68}Ga -DOTATOC and 18F-FDG PET/CT for risk stratification in pancreatic neuroendocrine neoplasms

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Introduction: Combined 18F-FDG and ^{68}Ga -DOTA-peptides PET/CT are commonly used for a better characterization of tumour heterogeneity in metastatic pancreatic neuroendocrine tumours (PanNENs). The use of these combined modalities is still controversial. The present study aims to assess the prognostic role of 18F-FDG and ^{68}Ga -DOTA-TOC for risk stratification in localized PanNENs. **Subjects and methods:** 45 patients with localized PanNENs undergoing both 18F-FDG and ^{68}Ga -DOTA-TOC PET/CT prior surgery were included in the analysis, retrospectively. Two expert nuclear medicine physicians evaluated PET images. SUV_{mean} and SUV_{max}, metabolic tumour volume (MTV) and tumour lesion glycolysis (TLG) for FDG and DOTA-TOC tumour volume (DOTATOC-TV) and tumour lesion (DOTA-TOC-TL) have been derived for both scans. ROC curves were used to investigate the performance of PET-derived parameters in predicting tumor status. Logistic regression analysis was used to assess whether PET parameters categorized with optimal cut-off could predict the corresponding tumor characteristic. **Results:** 14 patients had G1, 28 G2 and 3 had G3 PanNEN, according to 2010 WHO classification. Mean lesion diameter was 39 mm (range: 8–200). Considering 18F-FDG PET/CT, SUV_{max}, SUV_{mean}, MTV and TLG could discriminate between pT1/pT2 PanNEN versus pT3/pT4. Cut-off thresholds and correspondent sensitivities and specificities were 3.45, 66.7% and 73.9% for SUV_{mean} ($p = 0.119$), 7.45, 61.1% and 87% for SUV_{max} ($p = 0.0028$),

8.95, 66.7% and 91.3% for MTV ($p=0.0007$) and 32.4, 66.7% and 87% for TLG ($p=0.0011$). SUVmax and MTV were predictive for distant metastases (threshold: 7.45 and 8.9, respectively; equal sensitivity and specificities of 71.4 and 73.5%, respectively ($p=0.357$)). Regarding ^{68}Ga -DOTATOC PET/CT, DOTATOC-TV and DOTATOC-TL were predictive for differentiating pT1/pT2 PanNENs versus pT3/pT4. Cut-off threshold and correspondent sensitivity and specificity were 37.75, 70% and 79.2% for DOTATOC-TV ($p=0.0018$) and 1088.4, 60% and 91.7% for DOTATOC-TL ($p=0.0012$). DOTATOC-TL was predictive for distant metastases (threshold: 1088.4; $p=0.0258$), with 71.4% sensitivity and 75.7% specificity. 12 patients had lymphnodal involvement at histological examination, ^{68}Ga -DOTATOC PET/CT resulted positive in 5/12 (41.6%). Multivariate analysis showed ^{68}Ga -SUVmean and DOTATOC-TL as the only predictors for lymphnodal involvement with a threshold, sensitivity and specificity of 17.5, 66.6% and 75% ($p=0.0172$) for ^{68}Ga -SUVmean and 347.76, 75% and 60.7% ($p=0.0466$) for DOTATOC-TL. **Conclusion:** In localized PanNENs, PET-derived parameters obtained from combined ^{18}F -FDG PET/CT and ^{68}Ga -DOTATOC have a prognostic role for risk stratification. The dual tracer approach can be reliably considered as a support for tailored treatment approaches, by identifying patients with localized PanNENs that might benefit from neoadjuvant treatment strategies and tighter follow-up.

OP-190

Detection of insulinoma using Glucagon-like peptide-1-receptor imaging with $^{99\text{m}}\text{Tc}$ -EDDA-HYNIC-exendin-4

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Background and aim: Most insulinomas are solitary and benign. They are rather small in size, typically less than 1,5 cm, and therefore accurate preoperative localization is of paramount importance, since the definite therapy is pancreas-sparing surgery to preserve exo-endocrine function. In about 10% of insulinomas, conventional imaging (CT, EUS, MRI, somatostatin receptor scintigraphy) are negative. Glucagon-like peptide-1 receptors (GLP-1R) were found to be expressed in virtually 100% of benign insulinoma cases. The aim of this study was to evaluate GLP-1R imaging with the use of $^{99\text{m}}\text{Tc}$ -EDDA-HYNIC-exendin-4 in localization of insulinoma, where conventional imaging was negative or inconclusive. **Materials and methods:** Whole-body GLP-1R SPECT/CT was performed 4-hours after administration of $^{99\text{m}}\text{Tc}$ -EDDA-HYNIC-exendin-4 in patients with suspected insulinoma and negative or inconclusive conventional imaging (CT/ EUS/MRI/SRS). Blood pressure and glucose values were monitored at several time points. The results of GLP-1R scintigraphy were evaluated by experienced nuclear medicine physician and the diagnostic performance analysed using histopathology as the gold standard. **Results:** Seven patients (all women, mean age 60 years) were enrolled in our study. In all focal uptake in pancreas (3 in the body, 3 in the tail and 1 in the neck) was found and surgery performed. Histopathology confirmed insulin-producing neuroendocrine tumors (G1 and G2). Thus, sensitivity and specificity of GLP-1R scintigraphy were assessed to

be 100%. **Conclusion:** In our experience GLP-1R imaging with the use of $^{99\text{m}}\text{Tc}$ -EDDA-HYNIC-exendin-4 is an efficient diagnostic modality in localization of insulinomas, especially where the results of available conventional imaging are inconclusive.

OP-191

Comparison evaluation of the diagnostic potential of PET/MRI and PET/CT using mIBG-lod-124 in neuroendocrine and neuroectodermal tumors

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Purpose: To compare the diagnostic potential of PET/MRI and PET/CT using mIBG-lod-124 in neuroendocrine and neuroectodermal tumors. **Methods:** A total of 20 patients (12 m, 8 w, age 53 ± 16 y) with histopathologically confirmed pheochromocytoma ($n=15$), paraganglioma ($n=2$) and ganglioneuroblastoma ($n=3$) underwent both a whole-body contrast-enhanced PET/CT and PET/MRI approximately 1 day after injection of 48 ± 9 MBq mIBG-lod-124. Image analyses included the detection and delineation capacity of malignant lesions. Morphological components: transversal maximal tumor diameter and conspicuity (4-point scale (not visible=0 - high contrast=3)). PET images: tumor conspicuity (4-point scale), SUVmax and SUVmean using VOI technique. **Results:** 58 malignant mIBG-positive lesions (peritoneal and mesenteric $n=22$, bone $n=15$, lymph node $n=8$, liver $n=8$, lung $n=2$, pleural space $n=2$, adrenal $n=1$) were detected with both PET/CT and PET/MRI with strongly positive correlated mean SUVmax (18.3 ± 11.4 vs. 17.5 ± 9.8 ; Pearson's correlation $r=0.84$) and SUVmean (12.1 ± 7.7 vs. 11.1 ± 6.7 ; $r=0.91$). Comparable high lesion conspicuity in the PET component of PET/CT (2.9 ± 0.4) and PET/MRI (2.9 ± 0.3 ; $p=0.46$) could be assessed with significant higher lesion conspicuity in MRI (2.8 ± 0.6) compared to CT (2.6 ± 0.8 ; $p=0.01$). On both imaging modalities tumor delineation of the most lesions was successful, but two small lung lesions were not visible on MRI and five osseous metastases could not be assessed on CT, but showed an unequivocal hyperintensity on MRI. **Conclusions:** Integrated mIBG-lod-124-PET/MRI shows high potential as diagnostic procedure in neuroendocrine and neuroectodermal tumors with in comparison to PET/CT comparable detection rate and high lesion conspicuity in PET. A significant higher lesion conspicuity could be found in MRI compared to CT. PET/MRI may serve as a powerful alternative to PET/CT.

OP-192

Significance of Quantitative Analysis on pre-operative ^{68}Ga -DOTATOC PET/CT in Paraganglioma and Pheochromocytoma: First Experience

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Introduction: Studies have been reported that histologic and biochemical factors have prognostic utilities in Paraganglioma (PGL) and Pheochromocytoma (PCC). In this study, we evaluated quantitative indexes of pre-operative ^{68}Ga -DOTATOC PET/

CT of PGL and PCC and searched correlation with other known prognostic factors; anatomic volume, histopathologic (PASS; Pheochromocytoma of Adrenal gland Scaled Score and Ki-67), and biochemical factors. **Subjects & Methods:** Thirteen patients diagnosed as PGL or PCC were retrospectively enrolled. All patients underwent biochemical laboratory test (24-hour urine vanillylmandelic acid (VMA), epinephrine (EPI), norepinephrine (NE), dopamine (DA), and plasma/urine normetanephrine (NM) and metanephrine (MN)) and ^{68}Ga -DOTATOC PET/CT before surgery. Metabolic tumor volume (MTV) of each lesion with increased DOTATOC uptake on PET/CT was analyzed. Moreover, we performed macroscopic and histopathologic evaluations of resected lesions. **Results:** Seven patients were diagnosed with PGL and 6 patients were diagnosed with PCC; Total 17 lesions were pathologically confirmed. Comparing with histopathologic data, MTV was significantly correlated with anatomical volume (mL), PASS, and Ki-67 (%) of resected lesions (volume; $r = 0.620$, $P = 0.01$, PASS; $r = 0.630$, $P = 0.01$, Ki-67; $r = 0.650$, $P = 0.01$). Moreover, MTV exhibited significant correlation with urine VMA ($r = 0.910$, $P < 0.01$), EPI ($r = 0.630$, $P = 0.03$), NE ($r = 0.636$, $P = 0.03$), DA ($r = 0.789$, $P < 0.01$) and plasma/urine NM level (plasma; $r = 0.562$, $P = 0.04$, urine; $r = 0.757$, $P < 0.01$). On the other hand, plasma/urine MN did not show any correlation with MTV (plasma; $r = 0.358$, $P = 0.20$, urine; $r = 0.409$, $P = 0.15$). Finally, MTV and anatomical volume were the major factor for biochemical and functional status in multivariable analysis. (all $P < 0.01$). **Conclusion:** This is the first experience reporting MTV of ^{68}Ga -DOTATOC PET/CT is strongly related to both anatomical volume and biochemical function of the lesions, limited to PGL and PCC. Through the study, we suggest that DOTATOC uptake analysis with morphologic volume has potential to evaluate malignancy and estimate risk factor. Further study with a large cohort is warranted regarding prognostic significance of ^{68}Ga -DOTATOC PET/CT in PGL and PCC.

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Comparison of ^{68}Ga -DOTANOC PET/CT, ^{131}I -MIBG SPECT/CT and conventional imaging in uncommon primary and metastatic paragangliomas

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Purpose: To compare the diagnostic accuracy of ^{68}Ga -DOTANOC PET/CT, ^{131}I -MIBG SPECT/CT and conventional imaging (CIM) in patients with uncommon primary and metastatic paragangliomas. **Material and methods:** Total 90 patients (Mean age: 35.7 ± 14.6 years; Male-40/Female-50) with known or suspected paraganglioma were prospectively included. All patients underwent ^{68}Ga -DOTANOC PET/CT and ^{131}I -MIBG scan within 2 weeks of each other. Histopathology and/or clinical/imaging follow up (minimum-6 months) were used as reference standard. **Results:** In 90 paraganglioma patients, a total of 152 lesions (115 primary and 37 metastatic lesions) were evaluated. 10 patients (11%) had paraganglioma lesions at uncommon sites. 15 patients (16%) had metastatic involvement (including regional lymph nodes, lung, liver and skeletal metastases). Lymph node metastases were noted in 11, skeletal in 8, lung in 3 and

liver in 1 patient. On lesion wise analysis ^{68}Ga -DOTANOC PET/CT was positive in 132 and negative in 20 lesions. Among these 131 were true positive, 1 false positive, 3 false negative and 17 true negative with overall sensitivity of 97.7%, specificity of 94.4%, PPV of 99.2%, NPV of 85%. ^{131}I -MIBG planar was positive in 44 lesions with sensitivity of 32.85% and SPECT/CT in 50 lesions with sensitivity of 37.3%. Comparable conventional imaging was true positive for 115 lesions where as falsely negative for 19, showing sensitivity of 85.2%. On a lesion wise comparison PET/CT was superior to ^{131}I -MIBG SPECT/CT and CIM ($P < 0.0001$). Among patients with uncommon sites of paraganglioma involvement (11 lesions, including 5 mediastinal, 1 tracheal, 1 sternum, 2 urinary bladder, 1 vaginal and 1 pararectal), all patients were correctly identified with ^{68}Ga -DOTANOC PET/CT, however MIBG scintigraphy could pick up only 2/11 lesions (18%). Only one patient had MIBG positive uncommon site of involvement (mediastinal mass with sternal lesion). Among 15 patients with metastatic involvement, 53 lesions including (16 primary sites and 38 metastatic sites) were evaluated. ^{68}Ga -DOTANOC PET/CT was true positive for 51 lesions, one false positive and one false negative with overall sensitivity of 98%. However, MIBG scintigraphy showed significantly lower sensitivity of 34% for planar and 40% for SPECT/CT in this group of patients. Conventional imaging showed sensitivity of 75% in this group. PET/CT was superior to ^{131}I -MIBG SPECT/CT and CIM in this group of patients ($P < 0.0001$). Metastatic paraganglioma patients were screened for respective radionuclide therapy based on diagnostic imaging results. **Conclusion:** ^{68}Ga -DOTANOC PET/CT showed high diagnostic accuracy in patients with uncommon primary and metastatic paraganglioma patients.

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Sunday, October 14, 2018, 16:30 - 18:00, Hall 28

Inflammation & Infection: New Trends in Imaging Infection & Inflammation

OP-194

Usefulness of simultaneous FDG PET/MRI for assessing therapeutic response in pyogenic spondylodiscitis - prospective pilot study

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Background: Although MRI is highly sensitive and specific for detection of pyogenic spondylodiscitis, MRI is of limited value in reassessing effectiveness of antibiotic treatment. In addition, FDG has high sensitivity and specificity for detection of osteomyelitis. Although, limited data, FDG PET is considered more promising in assessing therapeutic response than MRI. The objective of the study was to determine if FDG PET/MRI can assess the response of patients with pyogenic spondylodiscitis to antibiotic treatment in a clinically useful time frame. **Methods:** From Jan to Dec in 2017, patients with diagnosed of pyogenic spondylodiscitis were prospectively included. Patients were treated with parenteral antibiotics for more than 3 weeks and

then scanned with integrated PET / MR machine. The patients were divided into responder and non- responder according to clinical symptom and blood test (ESR & CRP). PET/MR results were compared to the final clinical diagnosis and follow-up data.

Results: Twenty-four patients (65.8 y-o, 16 males) with diagnosis of pyogenic thoraco-lumbar spondylodiscitis were enrolled and 31 examinations were taken. Nine non-responders were identified, 7 of them were added to responder after additional treatment. Finally, 9 non- responders and 22 responders were registered. All of the patients were controlled with antibiotic therapy, and there was no recurrence during the follow-up periods at least 3 months. Non-responders had sustained elevations of ESR (74.11 ± 30.84 vs 48.45 ± 29.77 mmHg), CRP (3.25 ± 3.18 vs 1.04 ± 1.53 mg/dL), and SUVmax (6.61 ± 1.17 vs 3.89 ± 1.18) compared to responders ($p < 0.05$). There was difference in FDG distribution between non-responder and responder. Responders showed limited FDG uptake around endplate and disc space whereas the non-responder showed widespread uptake over the vertebral body. On the other hand, diagnostic MRI findings of bone marrow edema, destruction of the affected vertebrae and contrast enhancement pattern were not different between 2 groups. **Conclusion:** FDG PET/MRI could be helpful to determine the end of parenteral antibiotic therapy and pattern of activity is critical to distinguishing between responders and non-responders.

OP-195

A Radiomic approach for successful distinction of infection versus inflammation in patients treated with reparative orthopaedic surgery: a pilot study

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Purpose/Introduction: The purpose of this pilot study is to assess the value of PET in differentiating infection from inflammation in patients with joint prosthesis implant (JP) or post-traumatic synthesis interventions (SI) using a Radiomic approach. Due to this new algorithm for patients affected by inflammation, a frequent cause of false positives, FDG PET CT images could avoid unnecessary bone resections, prosthetic components explants and use of antibiotic spacers. **Subjects & Methods:** 29 Patients (11 women, 18 men) with JP or SI were included in the study. All patients were treated surgically to remove suspicious areas identified by FDG PET CT as possible foci of infection or inflammation. MicroDTTect features a patented processing antibiofilm compound (dithithreitol, DTT), that allows to dislodge bacteria embedded in biofilms, without affecting their viability and cultural examination. MicroDTTect closed system was used to collect and process removed tissues. Based on this, patients were assigned to the inflammation or infection class. FDG PET CT Image analysis consisted in a first semi-automatic segmentation step carried out by an expert nuclear medicine physician on FDG SUV images. Segmentation was done using the level tracing effect module, which defines an outline where the pixels all have the same background value as the current

background pixel. A SUV over 3 g/ml was considered an indicator of suspicious uptake and the SUV of the analysed areas was included in further analysis. Intensity, shape and texture-based image features were calculated on segmented regions by using the PyRadiomics software. Totally 196 features were calculated from CT and PET images for each patient. Feature selection was carried out using a custom genetic algorithm. Features subsets, with sizes ranging from 2 to 5, were scored by their classification accuracy using 3 different machine learning (ML) systems: kNN, LDA and NaiveBayes classifier (NB). Models validation was carried out by leave-one-out and, additionally, by 5- and 10-fold cross-validation (20 repetitions). **Results:** 16 out the 29 patients were positive at the post-surgery bacterial isolation test. For the remaining 15 inflammation was diagnosed. The best diagnostic performance was obtained analysing 4 features, comprising one CT-based and three PET-based features, using the NB classifier with average accuracy of 92% in the three validation tests. **Discussion/Conclusions:** This pilot study suggested that ML systems applied to Radiomic data from FDG PET and CT can discriminate bone infection from inflammation. Selected features confirm that the two imaging techniques provide complementary information.

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EARL-Standardized ¹⁸F-FDG PET/CT Quantification in Suspected Prosthetic Heart Valve Endocarditis

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Introduction: ¹⁸F-Fluorodeoxyglucose (FDG) Positron-Emission Tomography/Computed Tomography (PET/CT) was recently introduced as a new tool for the diagnosis of prosthetic heart valve endocarditis (PVE). Quantification of FDG uptake has mostly been non-standardized in previous literature, which resulted in widely spread standardized uptake values (SUV) and diagnostic thresholds. The aim of this study was to determine a diagnostic cut-off using a standardized measurement method on EARL-accredited (EANM Research Ltd.), calibrated reconstructions. **Subjects & methods:** From a larger multicentre retrospective study comprising 160 patients who underwent PET/CT for suspicion of PVE, 111 patients who had a scan with EARL-accredited reconstructions were included. Quantitative analyses were performed by two experienced observers blinded to all clinical data. The maximum SUV (SUV_{max}) was measured in an automated VOI using a 40% threshold isocontour, while the SUV ratio was calculated by dividing the SUV_{max} by the mean SUV in the blood pool of the descending aorta. Based on a bi-

nomial regression model of positive or negative confounders, scans that had visually been interpreted as false positive or false negative due to low inflammatory activity at time of imaging (CRP < 40 mg/L) or prior use of surgical adhesives (i.e. BioGlue), respectively, were excluded. Residual myocardial FDG uptake was not a confounding factor in this study thanks to patient preparation with a 24h low-carbohydrate diet and a > 6h fast. A final diagnosis of PVE was determined by expert team consensus based on all clinical data and follow-up. **Results:** After exclusion of possible confounders, 64 EARL-standardized scans remained that had been acquired in 30 patients with a definite final diagnosis of PVE, and in 34 patients without PVE. The mean SUV_{max} in the PVE group was 5.3 ± 1.6 versus 3.0 ± 0.6 in the no-PVE group ($p < 0.001$). The mean SUV_{ratio} in the PVE and no-PVE group was 3.2 ± 0.8 and 1.7 ± 0.3 , respectively ($p < 0.001$). SUV_{ratio} was the most reliable diagnostic predictor, with an optimal cut-off of 2.0 (sens. 100%/spec. 91%/PPV 91%/NPV 100%/AUC 0.99). A SUV_{ratio} of 2.6 had a specificity and PPV of 100% for PVE. **Conclusion:** Standardized quantification on EARL-accredited reconstructions is a reliable diagnostic tool in the assessment of perivascular FDG uptake in patients suspected of PVE. In patients with sufficient inflammatory activity for a diagnostic PET/CT (CRP ≥ 40 mg/L) and without prior use of FDG-avid surgical adhesives, a SUV_{ratio} of 2.0 was a 100% sensitive and 91% specific predictor of PVE, while a SUV_{ratio} of 2.6 or higher was 100% specific for PVE.

OP-197

Comparison of ^{99m}Tc -HMPAO-leukocyte scintigraphy and ^{18}F FDG-PET-TDM for diagnosis and therapy monitoring of skull base osteomyelitis

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Introduction: Skull base osteomyelitis (SBO) is a rare but life threatening disease observed in elderly diabetic patients, with high risk of recurrence, and difficult therapeutic management. CT and MRI are accurate for the diagnosis but not for the therapeutic response assessment. Some studies pointed out the usefulness of ^{99m}Tc -HMPAO-Leucocyte-Scintigraphy (LS) for initial diagnosis and treatment response assessment in SBO. ^{18}F FDG-PET/CT is highly sensitive in detecting inflammation and infection, with a better spatial resolution than LS, but has never been evaluated in skull base osteomyelitis. The aim of this study was to compare ^{18}F FDG-PET/CT and LS for i) initial diagnosis and ii) healing confirmation in SBO. **Subjects & methods:** We retrospectively reviewed from February 2014 to October 2016 all patients ($n=12$) with confirmed SBO (osteolysis on CT) who underwent LS and ^{18}F FDG-PET/CT twice, at initial diagnosis and after six weeks of antibiotherapy. All patients were followed at least 17 months after the end of antibiotherapy. Clinical, biological, CT, LS, FDG and follow-up data were recorded. LS images (planar and SPECT/CT performed 4h and 24h after intravenous injection of autologous ^{99m}Tc -HMPAO-leucocytes), and ^{18}F FDG-PET/CT images were visually assessed and quantified. Quantitative variables were SUV_{max} for PET and lesion-to-contralateral non lesion activity ratio (N/NL) for LS. **Results:** One patient had

missing follow up data and was excluded. At initial diagnosis, LS and ^{18}F FDG-PET/CT were positive in 11/11 (N/NL ratio : 3.84 ± 0.90) and 11/11 (SUV_{max} : 6.03 ± 2.93) patients respectively. After 6 weeks of antibiotherapy, according to follow-up data, 6 patients were cured and 5 had residual disease. Amongst the cured patients, 6/6 had a truly negative second LS, and 4/6 had a falsely positive second ^{18}F FDG-PET/CT (SUV_{max} : 4.37 ± 3.6). For patients with residual disease, 4/5 second LS were truly positive (L/NL ratio : 2.23 ± 0.96), 1/5 second LS was falsely negative (with CT signs of an abscess), and 5/5 second ^{18}F FDG-PET/CT were truly positive (SUV_{max} : 6.65 ± 3.76). LS and FDG had 100% sensibility at initial diagnosis. However, after 6 weeks of treatment, LS was accurate for 10/11 patients and FDG was accurate for only 7/11 patients to assess whether the patient was fully cured or not. **Conclusion:** ^{18}F FDG-PET/CT is powerful for initial diagnosis of SBO but is less specific than LS for healing assessment at the end of antibiotic therapy. We conclude it is less accurate than LS in therapeutic monitoring of SBO.

OP-198

Utility of 18F-fluoro-deoxyglucose positron emission tomography for the diagnosis of rheumatic disease especially polymyalgia rheumatica: a retrospective study

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Purpose: The aim of the study was the evaluation of 18F-FDG PET/CT scores to identify polymyalgia rheumatica (PMR) among patients suffering from rheumatic diseases. Secondly, it aimed to define PET/CT semiology of rheumatic diseases and evaluate the accuracy to diagnose large vessel vasculitis (LVV). **Subjects and methods:** We retrospectively included 216 patients with suspicion of rheumatic disease, unexplained biological inflammatory syndrome or suspicion of LVV, who underwent 223 PET/CT between April 2011 and December 2015 in our institution. Analysis of the images demonstrate articular and periarticular FDG uptake at different locations as well as associated vasculitis. Thus, we calculated articular uptake specificity among various diseases: PMR, LVV, spondyloarthropathy (SA) and rheumatoid arthritis (RA) and the proportion of LVV. A semi-quantitative analysis of FDG uptake (from 0 to 3 according to liver uptake) was performed on 17 hotspots suggestive of PMR. Scores reflecting mean FDG uptake and number of sites with significant uptake (superior to liver) were assessed. For both scores, sensitivity, specificity and optimal cutoffs, determined by ROC curves, were calculated. **Results:** In this study, 162 PET/CT were realized in patients who suffered from inflammatory rheumatism, 32 rheumatic diseases without inflammatory rheumatism, 29 without rheumatic diseases. Among 162 PET/CT realized in patients who had inflammatory rheumatism, 57 were PMR (ten associated with LVV), 50 RA, 18 SA, ten LVV, five psoriatic arthritis, five microcrystalline arthritis, four RS3PE, four paraneoplastic syndromes, three SAPHO and six unclassified rheumatism. On visual reading, in PMR group, we found 73.7% and 57.9% uptake

for shoulders and spinous process, specificity was respectively 57.8% and 61.4%. Sacroiliac uptake in SA and peripheral joints uptake in RA were highly specific, respectively 97.5% and 88.6%; 55% (11/20) of LVV patients showed a significant uptake on vascular wall. Four rheumatic diseases were labelled as paraneoplastic syndromes. Significant differences between 57 PMR PET/CT and 162 inflammatory rheumatism PET/CT were found for mean FDG uptake score (1.32 vs 0.87) and for the number of sites with significant uptake: 6.82 sites vs 3.5 sites. The presence of three or more sites with significant uptake was correlated with the diagnosis of PMR with 86% sensitivity and 85.5% specificity. For the mean FDG uptake score, the cut-off was 0.824 (78.7% sensitivity and 75.6% specificity) to distinguish PMR from other diagnosis in our study. **Conclusion:** In addition to visual reading, uptake scores are relevant for distinguishing polymyalgia rheumatica among other patients suffering from rheumatic diseases.

OP-199

Uveitis-related sarcoidosis detected by FDG-PET/CT in patients with negative CT scan

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Introduction: Sarcoidosis, an inflammatory systemic disease of unknown etiology, may appear in some cases as an ophthalmic disorder such as uveitis. Meanwhile, in patients with uveitis, the diagnosis of sarcoidosis, probably underestimated, depends on the extent of the workup, however, a prompt diagnosis is not frequent. The aim of this study was to estimate the role of FDG-PET/CT in the diagnostic workup of patients affected by potential uveitis-related sarcoidosis and with a negative CT scan. **Material and Methods:** Sixty-nine consecutive patients (47 females, median age 55 years old) affected by chronic uveitis and with a negative CT scan were enrolled. Patients underwent FDG-PET/CT and all scans were analyzed by a nuclear physician blinded to data of patients' follow up. PET/CT was dichotomized in positive or negative for thoracic sarcoidosis based on pulmonary or mediastinal pathological FDG uptake. PET data were combined with clinical and biological features (such as ACE levels and bronchoalveolar lavage (BAL), while other imaging modalities were silent) to establish the diagnosis of the sarcoidosis based on modified Abad Criteria: patients had proven or probable sarcoidosis if histologically proven or if all criteria were fulfilled, presumed sarcoidosis if two criteria were positives and indeterminate uveitis or other diagnosis if only one of the following criteria was satisfied: typical changes on a FDG/PET-CT, predominantly CD4 lymphocytosis in BAL fluid or elevated serum ACE levels. Univariate and multivariate analysis were used to establish the impact of each clinical, biological or imaging feature. **Results:** Uveitis was anterior in 24, intermediate in 8, posterior in 9 and panuveitis in 28 patients. FDG-PET/

CT was suggestive of thoracic sarcoidosis in 22 patients (32%) showing 22 abnormal mediastinal FDG uptakes and 2 abnormal pulmonary FDG uptakes. Furthermore, in 19 out of 22, the modified Abad Criteria were upgraded. Sarcoid uveitis according to modified Abad criteria was established proven or probable in 15, presumed in 19 and indeterminate uveitis or other diagnosis in 35 patients. According to univariate analysis, age ($p<0.05$), FDG-PET/CT ($p<0.05$), ACE levels ($p<0.05$), Interferon Gamma Releasing-Assay ($p<0.05$), and intermediate localisation of uveitis ($p=0.077$) were predictive of sarcoid uveitis, while in multivariate analysis only FDG-PET/CT and ACE were significant predictors ($p<0.05$) of uveitis-related sarcoidosis. **Conclusion:** Our study showed the high potential of FDG-PET/CT in order to correctly diagnose uveitis-related sarcoidosis. In particular, patients in which all other imaging modalities, including CT scan, were negatives, FDG-PET/CT changed modified Abad Criteria in more than one fourth.

OP-200

¹⁸F-FDG PET/CT versus ^{99m}Tc-HMPAO-WBC SPECT/CT in Diagnosis of Suspected Left-Ventricular-Assist-Device or Prosthetic Vascular Graft Infection

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Aim: The number of left ventricular assist device (LVAD) implants for the treatment of advanced heart failure as well as the use of prosthetic vascular grafts (PVG) for various indications is increasing tremendously. A rare but severe complication following insertion of these devices is infection, which remains a diagnostic challenge. Recently, radionuclide imaging of infectious processes has gained a pivotal role in diagnosis of prosthetic valve endocarditis, but for other device related infections the role yet needs to be established. The aim of our study was to compare two competing molecular imaging techniques - ¹⁸F-FDG PET/CT and ^{99m}Tc-HMPAO-WBC SPECT/CT in patients with suspected LVAD or PVG infection. **Materials and methods:** Between September 2015 and April 2018 patients with suspected LVAD or PVG infection underwent both ¹⁸F-FDG PET/CT (1 hour after injection) and ^{99m}Tc HMPAO-WBC-SPECT/CT (4 and 20 hours after reinjection), preferably within 7 days. 6 patients had LVAD and 21 patients had PVG suspected infection. The results of ¹⁸F-FDG PET/CT and ^{99m}Tc HMPAO-WBC-SPECT/CT were analysed separately by experienced nuclear medicine physicians. The final diagnosis was based on a positive haemoculture, positive bacteriological culture from the site of infection and patient follow-up. **Results:** 27 patients (5 women and 22 men, mean age 62 years) were included in our prospective study. 17 of them had infection. With ¹⁸F-FDG PET/CT 6 patients were correctly diagnosed as positive, 1 patient as false positive (FP), 1 patient as false negative (FN), 4 patients as true negative (TN) and 15 results were equivocal. With ^{99m}Tc- HMPAO-WBC SPECT/CT 15 patients were correctly diagnosed as positive, 1 patients as FP, 1 patient as FN, 9 patients as TN and 1 result was equivocal. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of each imaging modality were 88%, 60%, 79%, 90% and 78%, respectively, for ¹⁸F-FDG PET/CT; and 88%, 90 %, 94

%, 82 % and 89%, respectively, for ^{99m}Tc - HMPAO-WBC SPECT/CT in patient-based analyses. **Conclusion:** ^{99m}Tc - HMPAO-WBC SPECT/CT offers higher specificity than ^{18}F -FDG PET/CT, therefore a sequential strategy for the diagnosis of suspected LVAD or PVG infection has been proposed and consists of performing ^{18}F -FDG PET/CT first, following ^{99m}Tc - HMPAO-WBC SPECT/CT when results of ^{18}F -FDG PET/CT are inconclusive. Larger studies are needed.

OP-201

T2 Mapping As An Adjunct Diagnostic Tool In Patients Undergoing Hybrid 18F-FDG PET/MR Imaging For The Evaluation Of Cardiac Sarcoidosis

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Introduction: Sarcoidosis is a systemic inflammatory disease, pathologically defined by noncaseating granulomas in multiple organs, including the heart in up to 60% of cases. Endomyocardial biopsy is the gold standard for the diagnosis of cardiac sarcoidosis (CS), but sensitivity is low because of the patchy nature of the disease. Current guidelines support the implementation of advanced and complementary cardiac imaging modalities that can detect pathological hallmarks of CS, namely inflammation (^{18}F -FDG PET) and scar tissue (MR with late gadolinium enhancement (LGE)). Nevertheless, diagnosis remains unclear in case of discordant PET and MR results, when PET is positive in the absence of LGE. In those cases, dynamic quantitative analysis of the PET signal has proven useful to distinguish between false positive (PET+MR-) and true positive scans (PET+MR+). Our aim is to understand the additive role of cardiac T2 mapping in patients with unlikely diagnosis of CS or PET+MR-. **Subjects and methods:** 89 patients with clinical suspicion of active CS underwent PET/MR with gadolinium and ^{18}F -FDG to assess the pattern of injury and disease activity. Patients were diagnosed with active CS when LGE and increased FDG uptake co-localized (PET+LGE+). In case of discordant results, lesions were qualitatively and quantitatively defined as quiescent scar tissue (PET-LGE+) or as false positive (PET+LGE-). T2 maps were generated with data acquired in the basal, mid-ventricular and apical short-axis planes with three T2 preparation times (=0, 25, 50 ms). Maximum T2 values of PET+LGE+ and PET+LGE- patients were

compared with independent-sample t-test. **Results:** Of the 89 patients that underwent PET/MR scan, 26 were diagnosed with active CS (PET+LGE+), 23 had no imaging evidence of cardiac involvement (PET-LGE-), 16 showed quiescent scar tissue (PET-LGE+), and 24 were considered false positive (PET+LGE-). On visual assessment, color-coded T2 maps and short-axis PET images of overlapping myocardial sections (base, mid, apex) were concordant in PET+LGE+, but discordant in PET+LGE-. Likewise, maximum T2 values of PET+LGE+ patients (48.1 ± 2.4) was significantly greater than those of PET+LGE- patients (43.7 ± 1.8) ($p=0.006$). **Conclusion:** T2 mapping may prove useful in the characterization of patients with uncertain diagnosis of active CS due to discordant PET and MR findings. In particular, T2 mapping could exclude active inflammation when PET findings are unreliable because of failed suppression of basal myocardial uptake of FDG. To our knowledge, this is the first report where simultaneous myocardial tissue characterization using MR-based T2 mapping and PET were systematically evaluated. transit that could limit colonic transit measurements performed via oral tracer administration.

404c Sunday, October 14, 2018, 17:00 - 18:00, Hall 5

Mini Course 3 - Interactive: PET Patient Preparation: Pitfalls & Artefacts

OP-202

PET Patient Preparation: Artefacts and Pitfalls

D. Vriens; University of Leiden, Leiden, NETHERLANDS.

601 Monday, October 15, 2018, 08:00 - 09:30, Plenary Hall

CME 5 - Radiopharmacy / EDQM: Validation of Radioanalytical Methods

OP-203

General Principles on Validation of (Radio)Analytical Methods

S. Todde; University of Milano-Bicocca – Tecnomed Foundation, Department of Medicine and Surgery, Monza, ITALY.

OP-204

EANM Guidelines – Practical Examples

N. Gillings; PET & Cyclotron Unit, Copenhagen University Hospital, Rigshospitalet, Copenhagen, DENMARK.

OP-205

European Pharmacopoeia Guide for the Elaboration of Monographs for Radiopharmaceutical Preparations – Validation of Radioanalytical Methods

E. Pel; European Pharmacopoeia Department, European Directorate for the Quality of Medicines and HealthCare, Strasbourg, FRANCE.

602 Monday, October 15, 2018, 08:00 - 09:30, Hall 2

Joint Symposium 9 - Inflammation & Infection / ESVS:
Inside the Aorta: Vascular Inflammation, Infection and
Atherosclerosis

OP-207**Vascular Inflammation, Infection and Atherosclerosis - The Vascular Surgeon's View**

*N. Chakfe; Les Hopitaux Universitaires de Strasbourg, Nouvel
Hopital Civil, Service de Chirurgie Vasculaire et Transplantation
Rénale, Strasbourg, FRANCE.*

OP-208**Vascular Inflammation, Infection and Atherosclerosis - The Radiologist's View**

*P. A. de Jong; University Medical Center Utrecht and Utrecht
University, Department of Radiology, Utrecht, NETHERLANDS.*

OP-209**Vascular Inflammation, Infection and Atherosclerosis - The Nuclear Medicine Physician's View**

*X. Li; Medical University of Vienna, Vienna General Hospital,
Division of Nuclear Medicine-Department of Biomedical Imaging
and Image-guided Therapy, Vienna, AUSTRIA.*

603 Monday, October 15, 2018, 08:00 - 09:30, Hall 3

Joint Symposium 10 - Oncology / ESMO:
Radioisotope Therapies in Prostate Cancer and
Position in Oncological Treatment Paradigms

OP-212**Current Treatment Landscape of mCRPC**

*S. Gillissen; Division of Cancer Sciences, University of Manchester
and The Christie Hospital, Manchester, UNITED KINGDOM and
Kantonsspital St. Gallen, Division of Oncology/Haematology and
University of Bern, SWITZERLAND.*

OP-213**Radium-223 and Concomitant Therapy for mCRPC - Lessons Learned**

*O. Sartor; Tulane Cancer Center, Department of Medical
Oncology/Urology, New Orleans, UNITED STATES OF AMERICA.*

OP-214**PSMA Radioligand Therapy - Ready for Prime Time?**

*M. Hofman; Peter MacCallum Cancer Centre, Cancer Imaging and
Theranostics, Melbourne, AUSTRALIA.*

604 Monday, October 15, 2018, 08:00 - 09:00, Hall 5

Technologists: Oral Presentations 1

OP-216**Usefulness of SPECT for the semiquantitative assessment of regional ^{123}I MIBG myocardial uptake in heart failure: comparison between iterative reconstruction (OSEM) versus filtered back projection**

*A. Ruzza, I. Andreoli, G. Romagna, P. Basile, L. Filippi, O. Bagni;
Santa Maria Goretti Hospital, Latina, ITALY.*

Purpose: SPECT with ^{123}I -metaiodobenzylguanidine (^{123}I -MIBG) has been introduced for the imaging of the regional adrenergic denervation in heart failure (HF). Nevertheless, the added value of SPECT semiquantitative analysis for the identification of patients with high risk of arrhythmia is still few explored. The purpose of this study was to evaluate the usefulness of SPECT semiquantitative analysis for the assessment of regional ^{123}I -MIBG myocardial uptake in HF, also comparing the results of 2 types of SPECT reconstructions (iterative reconstruction methods based on ordered-subset expectation maximisation - OSEM - vs filtered back projections -FBP-) applied for the semiquantitative analysis of regional ^{123}I -MIBG uptake in patients with HF. **Methods:** After injection of ^{123}I -MIBG, twenty-one patients with HF underwent the same day planar images at 15 min and planars and SPECT at 4 h by using a dual headed variable angle gamma camera equipped with low/energy high resolution collimators (Infinia, GE Medical Systems). Heart to mediastinum (H/M) ratio was calculated on planar images according to the international guidelines. SPECT images were reconstructed by using both FBP and OSEM (2 iterations, 10 subsets). Emory Cardiac Toolbox™ was applied to obtain 17-segment regional polar (bull's-eye) maps both for OSEM and FBP images. The summed defect score (SDS) was calculated on SPECT 17-segment regional polar map. The SDS values obtained with OSEM and FBP were compared by using Student's t-test. **Results:** ^{123}I -MIBG SDS calculated for FBP and OSEM reconstructed images resulted of 22 ± 8.8 and 22.2 ± 8.2 , respectively. No significant difference was found between the values obtained with the 2 methods ($p = 0.43$). Of note, nine patients presented H/M ratio values significantly higher than the 1.6 threshold identified by the ADMIRE HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) multicenter study and severely increased SDS. Among these patients with $\text{H/M} > 1.6$ and elevated SDS, six subjects presented inducible ventricular tachycardia on electrophysiology testing and received prophylactic implantable cardioverter defibrillator (ICD). **Conclusions:** The assessment of regional myocardial uptake with ^{123}I -MIBG SPECT may be helpful to identify patients with high arrhythmogenic risk. As concerns SPECT semiquantitative analysis, in our series OSEM and FBP offered comparable diagnostic performance for the assessment of regional myocardial uptake with ^{123}I -MIBG.

OP-217**Usefulness of SMARTZOOM collimators: zoom out of MPIs**

*A. I. P. Queiroz, G. C. Paixão; Queen Elizabeth Hospital,
Birmingham, UNITED KINGDOM.*

Introduction: Smartzoom collimators are a Siemens® product with magnifying properties of a cone-beam collimator near the center of field of view which has been widely used in our Department for MPI SPECT. The shape of this collimator increases the counts which reduces the time of the SPECT and increases the sensitivity. Could we use this sensitivity for other scans in Nuclear Medicine? And reduce the time of other scans? The aim of this study is to test the usefulness of these collimators when applied in other scintigraphy's. **Materials and methods:** We used Smartzoom and Low Energy High-Resolution LEHR collimators; Sensitivity Phantom circle shaped with 9.9 cm of diameter; William Phantom square shaped phantom with 21.5x14.4 cm; $^{99m}\text{TcO}_4^-$ with activities ranged between: 0.5 to 20MBq; 5-15min statics pictures with each phantom at 11 cm distance from the collimator. **Preliminary Results:** ROIs were drawn on the acquired images to measure the diameter of the cold and hot areas. This revealed that the area has an increased diameter in the images acquired with the Smartzoom Collimators. This is expected due to the pinhole effect of the central area of the FOV. One of the parameters used with LEHR on small organs, is digital zoom (eg.2.29). Whereas with the Smartzoom collimators there is an increase in zoom by the mechanical direction of the collimator septum's. Therefore it is possible to say that, the statics acquired with Smartzoom collimators have double the amount of counts when compared with the respective one acquired with LEHR. An increased sensibility can lead to a decrease in the acquisition time and efficient usage of the Gamma Cameras. For the preliminary results and based only in a qualitative analysis, the hot and cold areas are more delineated in the statics acquired with the Smartzoom than the ones acquired with LEHR. **Conclusion:** This study is an ongoing project at the moment. Unfortunately, there is no conclusion to present but, in our Department we are very keen in developing the project in order to achieve the goals above.

OP-218

Comparison of Myocardial Perfusion Scores [SSS/SRS] calculated by manufacturer's normal database provided by QPS versus Institutional personalized normal database

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Objectives: In SPECT semiquantitative analysis of myocardial perfusion [SSS/SRS scores] proved to be important for diagnosis of coronary artery disease [CAD]. Most laboratories use pre-installed database provided with quantitative software package. However characteristics of Manufacturer's normal database [M-NDBs], created from patients with a low likelihood of cardiac disease [<5%], often don't fit Institutional local population: use of an inappropriate database could influence performance of any quantitative software. Indeed studying normal population in different geographic areas significant physical differences may be found. Hence the need to create an Institutional local database [I_NDB] for each/many laboratories. **Aim:** We evaluated the effect of body mass index [BMI] as a significant variable in diagnostic performance on quantitative myocardial perfusion SPECT results using QPS M_NDB versus I_NDB. **Methods:** Forty

male_patients [45±10yrs] and forty female_patients [40±12yrs] scheduled for Tc^{99m}-Sestamibi SPECT during 2013-2016 period were selected to generate a gender specific I_NDB using Cedars Sinai Suite AutoQuant[PFQ]. All patients referred in suspicion of CAD with a pretest low likelihood of cardiac disease [at least 1 risk factor] had BMI >30; underwent stress exercise on a bicycle ergometer; Gated_SPECT was performed using double-head Siemens Symbia-S equipped with LEHR collimators. Myocardial Perfusion scores [SSS,SRS,SDS] and coronary territory extent[LAD,LCx,RCA] were calculated both at stress and rest using QPS. Exclusion criteria were diabetes, ECG abnormalities[LBBB, PM] and history of CAD [revascularization, infarction]. **Results:** In males only SDS differed significantly [$p<0.03$] between M_NDB and I_NDB [2.4 vs 3.5 mean values respectively]; perfusion defect extent PDEx was larger as Total Value both at stress and rest [0.017, 0.002]; specifically in RCA territory [$p<0.011$] at stress and LCx [$p<0.002$] at rest. In females SRS [$p<0.043$] and SDS [$p<0.043$] were significantly different between M_NDB and I_NDB. As regards coronary territories PDEx was larger in LAD both at stress [$p<0.027$] and rest [$p<0.02$]; and LCx at rest [$p<0.047$]. **Conclusions:** In our experience I_NDB, as compared to M_NDB, seem to better identify extent and severity of perfusion defects in a specific subgroup of patients with BMI >30. In particular significant differences were observed in myocardial segments / coronary territories in which soft tissue attenuation is relevant: inferior/inferolateral in males and anteroseptal wall in females.

OP-219

ATLAAS - Investigation into the Incorporation of Morphological Data on Automated Segmentation

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Background: Radiotherapy treatment planning requires the accurate delineation of the metabolic tumour volume (MTV). However, work done by our group has shown how ¹⁸F-FDG PET automated segmentation (PET-AS) algorithms can be influenced by PET imaging features. Further, MTV delineation in ¹⁸F-FDG PET imaging is limited by low-spatial resolution due to the partial volume effect (PVE). Nonetheless, machine-learned automated segmentation (ML-AS) algorithms have shown promise for the accurate delineation of the MTV. The decision-tree based ML-AS algorithm ATLAAS includes PET imaging features in a machine-learned model to best predict the most accurate PET-AS method for MTV delineation. However, the inclusion of morphological PET imaging features in machine-learned models is potentially influenced by spatial resolution. Our aim was to investigate resampling PET imaging to associated CT coordinate systems and resolution grids for the inclusion of morphological features in the development of the ATLAAS machine-learned model. **Methods:** The ATLAAS machine-learned model contains 200 simulated ¹⁸F-FDG PET scans (ATLAAS_{ORIG}). A high-resolution machine-learned model (ATLAAS_{HD}) was developed by re-sampling ATLAAS_{ORIG} on the coordinate system and resolution grid of the associated CT. For simulated PET data, ground truth (GT)

contours were obtained from a PET template with a matrix size of 512x512. A validation dataset, consisting of 96 simulated and fillable phantoms with known GT contours was used to assess MTV delineation accuracy. GT contours for the inserts used in fillable phantoms were obtained from CT imaging. The morphological feature surface to volume ratio (S2VR) was included in the ATLAAS_{ORIG} (ATLAAS_{ORIG-S2VR}) and ATLAAS_{HD} machine-learned models (ATLAAS_{HD-S2VR}). The Dice Similarity Coefficient (DSC) of ATLAAS_{ORIG}, ATLAAS_{ORIG-S2VR}, ATLAAS_{HD} and ATLAAS_{HD-S2VR} was calculated in comparison to the GT contours. **Results:** The mean DSC (+/- SD) for ATLAAS_{ORIG}, ATLAAS_{ORIG-S2VR}, ATLAAS_{HD} and ATLAAS_{HD-S2VR} was 0.75(+/- 0.16), 0.78 (+/- 0.14), 0.79(+/- 0.13) and 0.82(+/- 0.10) respectively. A Kruskal-Wallis test, showed a significant difference ($P = 0.017$) between the DSC of ATLAAS_{ORIG}, ATLAAS_{ORIG-S2VR}, ATLAAS_{HD} and ATLAAS_{HD-S2VR}. **Conclusion:** This study investigated extending the ATLAAS machine-learned model to include morphological features. This was done following resampling of PET data on the coordinate system of associated CT scans. The resampled ATLAAS machine-learned model incorporating morphological features had the highest DSC and smallest STD in comparison to other developed models. This study demonstrates how resampling PET data to CT coordinate systems can potentially improve the accuracy of MTV delineation through the inclusion of advanced PET imaging features in machine-learned models.

OP-220

Influence of voxel size for localization of parathyroid adenomas with ¹⁸F-choline PET/CT

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Introduction: Primary hyperparathyroidism (PHP) is one of the most common endocrine disorders. ^{99m}Tc-MIBI SPECT/CT is the most widely used imaging technique for localization of hyperfunctioning parathyroid tissue. Recently, ¹⁸F-choline PET/CT has been introduced as a potential replacement for ^{99m}Tc-MIBI SPECT/CT. Even though superior over SPECT/CT, the relatively poor spatial resolution of PET/CT renders the detection of small lesions limited. The relatively low spatial resolution introduces the partial-volume effect which negatively affects the image both visually and quantitatively. One possible approach to reduction of partial-volume effect is the use of smaller voxel size.

Aim: The aim of our research was to investigate the effect of 4 mm and 2 mm voxel size on detection of small parathyroid adenomas. **Materials and methods:** For the preclinical analysis we used the NEMA phantom with six fillable spheres. The spheres and background was filled with a solution of ¹⁸F-choline, in ratio of 5:1. For clinical analysis we included 32 patients with biochemically and histologically proven primary hyperparathyroidism (dual-phase ¹⁸F-choline PET/CT). For the preclinical and clinical part, identical reconstructions were used and quantitative (lesion SUV, contrast-to-noise ratio [CNR], contrast recovery coefficient [CRC]) and qualitative analyses (lesion presence/absence) were performed. **Results:** When comparing

NEMA phantom reconstructions with 4 mm and 2 mm voxel size, the target-to-background contrast increases, particularly for small lesions. The median volume of parathyroid adenomas was 1,77±3.87 ml. The difference between average SUV (mean and max), CNR (mean and max) and CRC (mean and max) when using the 2 mm and 4 mm voxel size were statistically significant ($P < 0.001$) in both imaging phases. After visual analysis, agreement between two physicians was high (0.86). Using the 4 mm voxel size the sensitivity decreased by 9% in the first phase and 6% in the second phase. **Conclusion:** The use of 2 mm voxel size can improve diagnostic accuracy.

OP-221

Harmonization of reconstruction parameters between PET/MR (SIGNA) and PET/CT (Discovery STE)

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Objective: The purpose of this study was to harmonize standardized uptake values (SUV) between two hybrid systems: PET/MR GE SIGNA and PET/CT GE Discovery STE. Despite of having different technologies on each system (attenuation correction methods, reconstruction algorithms and detectors), we achieved comparable results in both scanners. **Methods and Materials:** In order to correct for partial volume effect and reduce the variability of SUV values, the harmonization protocol of the European Association of Nuclear Medicine (EANM) was used. Cross-calibration of PET/MR and PET/CT was carried out using a 5.640 ml cylindrical water phantom. The NEMA NU2-2001/2007 image quality phantom was used to harmonize parameters for data acquisition, image processing and analysis. Different methods were applied to assess the impact of changes on SUV and mean and maximum sphere recovery coefficients (RC), according to the EANM established limits. The harmonized reconstruction factors were determined as well as the minimum acquisition time for each scanner. Finally, the correlation between SUV (max) and SUV (mean) was measured in 32 tumour tissue locations. **Results:** The harmonization of the reconstruction parameters decreased the variation of the expected RC in both technologies. For PET/CT, the average variation changed from 5,29%, to 0,47%, whereas for PET/MR the average decreased from 40,40% to 14,30% after harmonization, respectively. However, mean RCs for 37, 28 and 22 mm spheres fell outside tolerance limits. A minimum bed-time of three minutes for both PET/CT and PET/MR satisfied the coefficient of variation (CV) criteria (<15%). CV was higher for PET/CT (9,39%) in comparison to PET/MR (9,09%). Therefore, noise in the PET/MR was slightly lower than PET/CT when acquisition time decreases, which is expected since our PET/MR is more sensitive than our PET/CT scanner. From these measurements, the harmonized reconstruction parameters for both systems were: 2 iterations, 28 subsets, 6,7 mm Gaussian axial standard smoothing filter, with Time of Flight (TOF) in the case of PET/MR. Hence, whole-body PET/CT and PET/MR ¹⁸F-FDG clinical images were reconstructed with harmonized parameters obtaining a higher correlation between SUV(max) and SUV(mean)(r_{Pearson} of 0.986 and 0.977 versus 0.976 and 0.966 before harmonization, respec-

tively). **Conclusion:** After harmonization of the reconstruction parameters, variation of the expected RC decreased in 4,82% in average for PET/CT and in 26% in average for PET/MR. This strategy looks forward to using both technologies with comparable and reproducible results, for centres with different PET systems and also for performing multicentric trials.

OP-222

Bayesian Penalised Likelihood (BPL) vs Ordered Subset Expectation Maximisation (OSEM) Reconstructions: A case study in solitary pulmonary nodules (SPN) assessed with 18F-FDG PET-CT

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Introduction: A Bayesian penalised likelihood (BPL) PET reconstruction algorithm has been recently introduced as a commercial product (Q.Clear, GE Healthcare). This BPL algorithm acts by suppressing the noise on each iteration, allowing the reconstruction to run to full convergence up to 25 iterations improving contrast and suppressing image noise [1]. These improvements can be useful in assessing various pathologies, specifically in SPN [2].

Aim: Our aim is to analyse two cases of subjects with diagnosed SPN who underwent 18F-FDG PET-CT and evaluate the differences of the retrospective use of Q.Clear in SUVmax values in comparison with OSEM reconstruction and consequent implications on the patient cancer care pathway. **Methods and Mate-**

rials: Two patients diagnosed with SPN were selected, patient A with an 8mm left upper lobe nodule and patient B with a 26mm right upper lobe nodule. The images were retrospectively reconstructed using Q.Clear and compared with the standard-of-care OSEM reconstruction using the same PET acquisition data after IV administration of 18F-FDG. For both reconstructions, image quality was visually assessed, SUVmax calculated and images scored in accordance with BTS (British Thoracic Society) guidelines in order to calculate the Herder risk score (% of estimate risk of malignancy in the nodules). **Discussion:** It is shown for patient A, when compared with OSEM Q.Clear increases the SUVmax of the lesion from 0.9 to 1.9, leading to an increase of the BTS score from 2 to 3. Therefore the Herder score for that patient is affected (risk of malignancy is 19% with OSEM and 69% with Q.Clear) with potentially major consequences on patient management decisions. For patient B the choice of reconstruction does not appear to influence the BTS score, which is 4 on OSEM (SUVmax 7.5) and remains BTS score 4 on Q.Clear (SUVmax 9.4). This change does not influence the Herder score, maintaining the risk of malignancy at 96%. **Conclusion:** As expected, Q.Clear does not appear to affect the management of patient B where the BTS score was already 4 (intense uptake). But for the lower BTS score of patient A, Q.Clear shows an increase of score from faint to moderate uptake impacting his cancer care pathway. In order to be able to extrapolate this result a more detailed study is already taking place. Preliminary results suggest that Q.Clear reconstruction, compared to standard OSEM, increases the Herder score in approximately 25% of SPNs with the potential to affect subsequent management decisions [2].

OP-223

Practical learning simulator of nuclear medicine imaging artifacts: a tool to teach future nuclear medicine technologists about imaging artifacts and its role in resolving

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Introduction and Aim: Artifacts in nuclear medicine imaging are a problem for diagnosis. The theoretical teaching of these problems is not enough, sometimes due to the lack of images representing these artifacts, published or from clinical practice, and because it's not possible to reproduce these problems. The aim of this work was to develop a practical learning simulator that allows to students to learn about image artifacts and to correlate with the techniques necessary to solve or avoid them, being able to reproduce these artifacts as often as necessary.

Material and methods: To reach our aim it was used a video camera. Twenty four students represented a situation that could correspond to artifacts like the movement of the patient, patient collaboration, soft-tissue attenuation or non-target uptake overlap, overlying non-anatomical structures, contamination artifacts, the failure of the equipment, inadequate selection of the instrumentation, poor preparation and positioning of the patient, low radiopharmaceutical activity, previous exams with administration of radiopharmaceuticals. A platform was developed with application of four tasks: 1º to take a picture or video that simulates an artefact, 2º apply image processing tools to highlight artifacts, 3º to search an image in the bibliography of a real case of the artefact, to make an analysis and to discuss ways to solve or avoid these artifacts, 4º evaluate the satisfaction on a scale of 0 to 10 regarding to the accomplishment of the task. **Results:** Regarding the evaluation of the satisfaction of the simulation of each of the artifacts and execution of the tasks proposed in the platform, the average varied between 7.3 ± 1.3 and 8.4 ± 1.1 , corresponding the lowest value to the simulation of a situation of low radiopharmaceutical activity administration and the highest value to a situation of patient movement. In general students were able to respond to all tasks, were able to work with several image processing tools, discussed in group and analyzed the images or videos obtained, considering the great variability and creativity to simulate each of these artifacts and presented several solutions to avoid or solve these artifacts.

Conclusion: With the platform developed and a video camera it was implemented a practical learning simulator that allowed students to learn about the most common imaging artefacts in Nuclear Medicine, became aware of the loss of image quality and the consequences for image interpretation and analysis and developed the knowledge to apply techniques to solve or avoid these artifacts.

OP-224

Patient and Public Involvement and Engagement in Nuclear Medicine

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Introduction: Patient, carer and public involvement/engagement (PPI/E) refers to incorporating and integrating patients' or users' perspectives. Members of the public, patients and carers collaborate in research instead of only participating in studies. Today's research landscape prioritizes research themes to align with the patients - the ultimate beneficiaries of our research. PPI/E in Imaging, particularly in nuclear medicine is a relatively new concept across Europe. However, combined with the fact that ionizing radiation in medical imaging is not widely understood patient involvement is of increasing importance. **Subjects & methods:** A literature review conducted using Medline and Embase research databases in March 2018, combining subject headings & keyword searches for "nuclear medicine; diagnostic techniques; patient involvement; patient engagement and research" identified no articles, whereas several articles can be found in other fields such as Alzheimer, lung cancer and others. This demonstrates the need for PPI/E to be recognised and promoted in nuclear medicine across Europe and worldwide. At The Royal Marsden Hospital two dedicated patient representatives work alongside the Imaging Department professionals to support studies in nuclear medicine and magnetic resonance. **Results:** With the inclusion of patient representatives in the teams, overall PPI/E awareness within the hospital increased substantially over the past 8 years and PPI/E inclusion is now compulsory to obtain ethical approval. PPI/E members are involved in various aspects such as early phase study concept meetings and study design, research documentation review, leading on training sessions for researchers; inclusion as investigators or leading on studies and contributing to applications for research funding for imaging studies. As a result of the PPI/E program in imaging, two imaging funding applications with a substantial involvement from PPI/E. were awarded. PPI/E not only provides substantial support to studies and applications (e.g. Masters imaging study and PhD application), but also has contributed substantially to presentations at national conferences on the role of patients in imaging led studies. **Conclusion:** The role of PPI/E in nuclear medicine is crucial, warranting efforts to increase awareness. PPI/E provides knowledge and experience to professionals who in turn contribute to PPI/E personal development and empowerment to promote imaging health research. With a good understanding of the patients' needs and interests we can tailor research and make it more valuable, acceptable and understandable to potential participants. This is particularly important for nuclear medicine where terminology and technology is complex and patient input can help to provide a more positive patient experience.

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Monday, October 15, 2018, 08:00 - 09:00, Hall X

M2M: It's All About Peptides

OP-225

Selective Imaging of $\alpha v\beta 8$ -Integrin With Ga-68-Labelled Peptide Conjugates

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Because no selective small-molecule ligands for $\alpha v\beta 8$ -integrin have been available, this subtype is the least studied among the 8 RGD-binding integrins. Unlike these, $\alpha v\beta 8$ -integrin features a unique structure in that it does not possess a cytoplasmic tail. It plays a key role for fundamental processes of tumor cell development and differentiation, for example, activation of TGF β , and is involved in tumor progression and invasion. Furthermore, it mediates the cellular entry of certain viruses, such as Foot-and-Mouth (FMDV) Herpes Simplex (HSV) or Epstein-Barr (EBV). We present the first ^{68}Ga -labelled PET probes for in-vivo study of tissue distribution and biological functions of $\alpha v\beta 8$ -integrin. Recently, we developed a cyclic octapeptide with subnanomolar ($\text{IC}_{50}=0.93\text{ nM}$) affinity for $\alpha v\beta 8$ and a high selectivity (IC_{50} for all other RGD-binding integrins $>210\text{ nM}$). On this basis, we synthesized monomeric and trimeric TRAP chelator conjugates by means of click-chemistry coupling. The ^{68}Ga -labelled compounds were characterized in vitro and evaluated in-vivo, using SCID mice bearing subcutaneous MeWo ($\alpha v\beta 8+$ human melanoma) xenografts, by μPET imaging and ex-vivo biodistribution 60 min p.i.. Expression density of $\alpha v\beta 8$ -integrin was assessed by $\beta 8$ -immunohistochemistry (IHC) for tumor and various other tissues. The trimer exhibits a 37fold higher $\alpha v\beta 8$ -integrin affinity than the monomer ($\text{IC}_{50}=0.89\text{ vs. }33\text{ nM}$, respectively) resulting in a higher tumor uptake ($1.9\pm 0.3\text{ vs. }1.0\pm 0.3\text{ \%ID/g}$, respectively, in biodistribution), while blockade resulted in the same baseline ($0.25\pm 0.16\text{ and }0.25\pm 0.09\text{ \%ID/g}$, respectively). Both tracers are excreted renally, consistent with high polarity ($\log D = -3.1\pm 0.1\text{ and }-3.9\pm 0.1$, respectively). IHC showed intermediate $\beta 8$ -expression in the tumor while most organs and tissues were found $\beta 8$ -negative, resulting in low uptakes ($<0.4\text{ \%ID/g}$) confirming a low degree of unspecific binding. A slight $\beta 8$ -expression in the lung was detectable with the trimer but not with the monomer ($0.68\pm 0.19\text{ \%ID/g vs. }0.35\pm 0.16\text{ \%ID/g}$, respectively), showcasing a higher sensitivity of the trimer. Favorable tumor/tissue ratios (t/blood: 6.7 and 5.5; t/liver: 6.8 and 6.6; t/muscle: 29 and 24 for trimer and monomer, respectively) are reflected by PET images with low background and excellent delineation of the $\alpha v\beta 8$ -positive tumor. In conclusion, both $\alpha v\beta 8$ -integrin-targeted probes possess favorable pharmacokinetics and are suitable for mapping $\alpha v\beta 8$ -integrin in vivo by means of PET, while the trimer is preferred due to higher sensitivity and higher absolute uptake in $\alpha v\beta 8$ -positive tissues.

OP-226

[^{18}F]RPS-534: A novel CXCR4 specific imaging agent

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Aim: Following our recent identification of [^{18}F]RPS-544 as a CXCR4-specific agent for PET imaging, we sought to develop new structural leads via in silico screening and evaluate these leads for CXCR4 specific targeting using in vitro and in vivo models.

Materials and Methods: A full High Throughput Virtual Screening was performed on a 17.3 million compound database to identify the best 50k structures docked against human CXCR4.

Next, the lead compound library was supplemented with CXCR4 ligands with known affinity, and a Standard Precision docking experiment was performed to select the top 500 structures. Structures were modified to include a fluorine atom at a logical site for radiofluorination and further evaluated in an Extra Precision Docking Experiment. Three lead candidates (RPS-533, 534 and 545) were identified and synthesized along with their corresponding precursors for radiofluorination. The compounds were evaluated by competitive binding assay against [^{68}Ga]Pentixafor, and K_d and internalization were determined using PC3-CXCR4 cells. [^{18}F]Fluorinated ligands were synthesized by a click reaction with 2-[^{18}F]fluoroethylazide and evaluated in a bilateral (CXCR4/CXCR4⁺) PC3 tumor model at 1 h post intravenous injection by $\mu\text{PET}/\text{CT}$ ($n=2$) and biodistribution ($n=5$). Specificity was confirmed by differential tumor uptake and blocking with AMD-3100 (5 mg/kg). **Results:** Cyclam-containing compounds (e.g. AMD-3100) had the best docking scores, but a common feature in the top structures was a 1,4-benzenedimethanamine moiety. The inclusion of a fluoroethyltriazole improved docking scores. A 3 step radiosynthesis was designed consisting of (1) the synthesis of 2-[^{18}F]fluoroethylazide; (2) a click reaction with an alkyne precursor; and (3) deprotection. The manual, non-optimized radiosynthesis was completed in 2 h with a radiochemical yield of $34.7\pm 15.6\%$ ($n>10$) and molar activity $>185\text{ GBq}/\mu\text{mol}$. In spite of their superior docking scores, RPS-533, -534 and -545 showed modest IC_{50} values ($\text{IC}_{50} = 356\pm 100\text{ nM}$, $218\pm 38\text{ nM}$ and $398\pm 41\text{ nM}$, respectively) against [^{68}Ga]pentixafor relative to RPS-544 ($\text{IC}_{50}=4.9\pm 0.3\text{ nM}$). However, imaging and biodistribution studies confirmed superior tumor uptake for [^{18}F]RPS-534 and faster clearance via kidneys at all time points relative to [^{18}F]RPS-544. Uptake in PC3-CXCR4 tumors was 2.1 times greater ($p<0.0001$) than [^{18}F]RPS-544. Co-injection of AMD-3100 decreased PC3-CXCR4 tumor uptake by 60–70%, and uptake in bone and spleen was completely blocked. **Conclusions:** [^{18}F]RPS-534 was identified from an *in silico* screen and demonstrated high and specific uptake in PC3-CXCR4 tumors. Rapid clearance via the kidneys leads to high tumor-to-tissue ratios. On this basis [^{18}F]RPS-534 is the most promising [^{18}F]fluorinated CXCR4 imaging agent reported to date.

OP-227

Can $^{68}\text{Ga}(\text{HP}_3\text{-RGD}_3)$ image early onset of rheumatoid arthritis preclinically?

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Purpose: Manifesting as joint pain and swelling, stiffness and fatigue, rheumatoid arthritis is an autoimmune disease characterized by systemic inflammation. If identified early, it can be treated successfully in a proportion of patients with disease-modifying anti-rheumatic drugs. Imaging could detect disease early-on and allow monitoring of disease progression thus maximising disease suppression. Here, we investigated $^{68}\text{Ga}(\text{HP}_3\text{-RGD}_3)$ as a PET imaging tool to detect arthritis early-on by targeting integrin $\alpha_v\beta_3$, found on osteoclasts, macrophages and new blood vessels. **Methods:** Preclinical studies using the K/BxN serum trans-

fer model of arthritis were carried out. Control groups were PBS alone or co-injection with a blocking dose of c(RGDfK). C57Bl/6 mice were injected with arthritogenic serum ($n=10\text{--}20/\text{group}$) and imaged by PET/CT with $^{68}\text{Ga}(\text{HP}_3\text{-RGD}_3)$ at 1 h p.i. on day 6 (9–16 MBq/4 μg) or used for biodistribution only (1.5–6 MBq/4 μg). Separately, mice presenting mild or established, severe arthritis were imaged on day 8 with $^{68}\text{Ga}(\text{HP}_3\text{-RGD}_3)$, culled and used for biodistribution studies ($n=3$ per group). In a final study, ankle joints were removed from healthy and arthritic mice on day 10 for staining with H+E and flow cytometry was used to identify immune cell populations in the joints and joint-draining lymph nodes at the peak of disease (Day 5). **Results:** Mice imaged at day 6 did not have external signs of arthritis nor could PET/CT visualise early signs of arthritis. In biodistribution studies, a difference in joint uptake of $^{68}\text{Ga}(\text{HP}_3\text{-RGD}_3)$ was seen between mice receiving arthritogenic serum and PBS. For example, tracer uptake in the feet and ankles was $0.84\pm 0.16\%$ ID and $0.67\pm 0.22\%$ ID ($p=0.007$), respectively. At day 8, imaging could differentiate between severely arthritic joints (increased diameter $>0.5\text{mm}$) and joints with little inflammation, even within the same mouse. In biodistribution data, tracer uptake in severely arthritic joints was $0.26\pm 0.02\%$ ID in wrists and $0.68\pm 0.18\%$ ID in ankles, whereas wrists measured $0.14\pm 0.02\%$ ID and ankles $0.29\pm 0.03\%$ ID in non-arthritic mice. In blockade studies, radiotracer uptake in severely arthritic joints measured $0.08\pm 0.01\%$ ID in wrists and $0.24\pm 0.02\%$ ID in ankles ($p=0.0005$). Joints and joint-draining lymph nodes from arthritic mice showed enhanced cell infiltration and erosion as well as a greater number of T cells, monocytes, dendritic cells and neutrophils, respectively, compared to healthy mice. **Conclusion:** In mice, $^{68}\text{Ga}(\text{HP}_3\text{-RGD}_3)$ is an excellent and specific tracer to image arthritis but only where disease is established. **Acknowledgements:** Funding for the project was in part provided by the Rosetrees Trust.

OP-228

Targeted optical imaging of the GLP-1R using exendin-IRDye800CW

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Background: While pre-operative imaging is essential for tumour detection before surgical cancer treatment, translating this information into the operating room is challenging. Intra-operative optical imaging can provide real-time detection of tumour lesions and thereby contribute to optimal surgical procedures. Insulinomas and focal lesions in congenital hyperinsulinism (CHI) are GLP-1-receptor (GLP-1R) positive pancreatic lesions. Although surgical treatment is the therapy of choice, the procedure can be challenging because of the small size of these lesions and the necessity to conserve healthy pancreatic tissue. The stable GLP-1 analogue exendin specifically binds the GLP-1R on pancreatic beta cells. GLP-1R imaging using [^{68}Ga]Ga-labelled exendin is a successful pre-operative imaging technique for insulinomas and is under investigation in CHI. We

hypothesize that exendin-4 labelled with the near-infrared (NIR) dye IRDye800CW enables specific targeting of pancreatic beta cells and thereby intra-operative visualization of GLP-1R positive lesions. **Methods:** Exendin-IRDye800CW was characterized *in vitro* and *in vivo*. A competitive binding assay was performed using CHL-cells transfected with the human GLP-1R. In mice bearing subcutaneous GLP-1R positive tumours, biodistribution studies were performed, as well as *in vivo* fluorescence imaging using an IVIS optical imaging system. The applied fluorescent biodistribution method was validated by combined radioactive and fluorescent biodistribution studies using the dual-labelled tracer [^{111}In]In-DTPA-exendin-4-Cy5.5. In healthy mini pigs, *in vivo* fluorescence imaging of the pancreas was performed using a laparoscopic NIR imaging system. **Ex vivo** fluorescence imaging of pancreatic tissue was performed with a flatbed scanner and fluorescence microscopy. **Results:** Exendin-IRDye800CW has a high affinity for the GLP-1R with an IC_{50} of 4 nM, which is comparable to unlabeled exendin. Injection of 3 μg exendin-IRDye800CW in BALB/c nude mice with subcutaneous GLP-1R positive tumours resulted in a tumour uptake of 3.2 ± 1.4 %ID/g, which decreased with increasing peptide doses to 2.5 ± 0.2 %ID/g, 1.4 ± 0.1 %ID/g and 0.6 ± 0.3 %ID/g for 10, 30 and 100 μg , respectively. Tumours were successfully detected by fluorescence imaging. In mini pigs after injection of 1.4 $\mu\text{g}/\text{kg}$ exendin-IRDye-800CW, a clear fluorescent signal was detected in the pancreas. Specific uptake in the pancreatic islets was shown by detection of individual islets in pancreas tissue by flatbed fluorescence scanning and fluorescence microscopy. **Conclusion:** These data indicate that exendin-IRDye800CW is a promising tracer for intra-operative optical imaging of GLP-1R positive lesions.

OP-229

Preclinical comparison of the new GRPR-antagonist ^{111}In -SB13 vs. ^{111}In -labeled native GRP(17-27) with focus on stability and biodistribution patterns in mice

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Aim: The overexpression of the gastrin-releasing peptide receptor in human tumors has been exploited for delivering diagnostic/therapeutic radionuclides to pathological lesions by bombesin (BBN)-like carriers. The biosafety and attractive pharmacokinetics of radiolabeled GRPR-antagonists led to the development of promising candidates for human use. As a part of this effort, we report on the GRPR-antagonist SB13 (DOTA-[His²⁵-NHCH(CH₂CH(CH₃)₂)]GRP(17-25)), suitable for labeling with ^{111}In . Preclinical results are presented herein from direct comparison of ^{111}In -SB13 with the previously reported GRPR-agonist ^{111}In -DOTA-GRP(17-27) in PC-3 cells and mouse models. It should be noted that the two tracers differ only in the C-terminus. Stability and biodistribution changes during neprilysin (NEP) inhibition induced after phosphoramidon (PA) coinjection are discussed. **Materials and Methods:** Competition binding

assays with SB13 against [^{125}I -Tyr⁴]BBN were conducted in GRPR-positive PC-3 cell membranes. Blood samples collected 5 min post-injection (pi) of ^{111}In -SB13 or ^{111}In -DOTA-GRP(17-27) in healthy mice without or with PA-coinjection were analyzed by HPLC for radiometabolites. Biodistribution of ^{111}In -SB13 and ^{111}In -DOTA-GRP(17-27) was performed without or with PA-coinjection in PC-3 xenograft-bearing SCID mice at 4 h and 24 h pi; additional 4-h animal groups received excess [Tyr⁴]BBN for *in vivo* GRPR-blockade. **Results:** SB13 displayed single-digit affinity for the GRPR ($\text{IC}_{50} = 2.6 \pm 0.4$ nM vs. $\text{IC}_{50} = 19.2 \pm 2.9$ nM of DOTA-GRP(17-27)). In peripheral mouse blood ^{111}In -SB13 showed notably superior stability (78% intact) compared with ^{111}In -DOTA-GRP(17-27) (<27% intact) at 5 min pi; PA-coinjection fully stabilized ^{111}In -SB13 in mouse circulation, with only partial stabilization achieved for ^{111}In -DOTA-GRP(17-27) (<78% intact). Higher uptake in the PC-3 xenografts was exhibited by ^{111}In -SB13 (8.1 ± 1.4 %ID/g) compared to ^{111}In -DOTA-GRP(17-27) (4.3 ± 0.3 %ID/g) at 4 h pi, increasing to similar levels (29.4 ± 4.6 %ID/g and 29.2 ± 5.3 %ID/g, respectively) after PA-coinjection. Notably, ^{111}In -SB13 cleared much faster from background than ^{111}In -DOTA-GRP(17-27) even after PA-coinjection, including the GRPR-rich mouse pancreas (3.6 ± 1.0 %ID/g and 65.8 ± 6.5 %ID/g at 4 h pi in the respective PA-groups). **Conclusions:** The new GRPR-antagonist based radiotracer ^{111}In -SB13 displayed higher bioavailability, stronger tumor-targeting and more attractive pharmacokinetics in mice compared with the respective GRPR-agonist, structurally differing only in the C-terminus. These qualities were enhanced during *in-situ* NEP inhibition providing good opportunities for clinical translation.

OP-230

Selection of the most optimal ADAPT6-based probe for imaging of HER2 using PET and SPECT.

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Aim: Radionuclide molecular imaging may solve the problem of discrimination between metastases with high and low level of expression of HER2, which is necessary for selection of patients potentially responding to HER2-targeting therapy. ADAPT6 is an engineered affinity protein based on the scaffold of albumin-binding domain of protein G. ADAPT6 variants bind to HER2 with low nanomolar affinity. Small size of ADAPT6 (6 kDa) permits good contrast in imaging of HER2 expression. Several optimisation studies demonstrated that N-terminal sequences DEAVDANS and (HE)₃DANS, C-terminal sequence GSSC and positioning DOTA chelator at C-terminus improved the tumour-to-organ ratio of ^{111}In -labelled variants. Thus, DOTA-C⁶¹-(HE)₃DANS-ADAPT6-GSSC and DOTA-C⁵⁹-DEAVDANS-ADAPT6-GSSC should be the most promising variants for labelling with trivalent radiometals. The aim of this study was to select the best ADAPT6 variant providing good discrimination between tumours with high and low HER2 expression and the best contrast in PET and SPECT imaging. **Methods:** C⁵⁹-DEAVDANS-ADAPT6 and C⁶¹-(HE)₃DANS-ADAPT6-GSSC were site-specifically con-

jugated with maleimido-DOTA. The conjugates were labelled with ^{111}In and ^{68}Ga . Disposable size-exclusion columns were used for purification. HER2-expressing SKOV-3 and BT474 cell lines were used to study specificity and cellular processing. Female BALB/C nu/nu mice bearing SKOV-3 (1.6×10^6 receptors/cell) and DU 145 (5.1×10^4 receptors/cell) xenografts were used to evaluate capacity of radiolabelled ADAP variant to discriminate between tumours with high and low HER2 expression. PET/CT imaging was performed to show discrimination between xenografts with high and low HER2 expression. **Results:** Labelling with both ^{68}Ga and ^{111}In provides radiochemical yields over 90%. The radiochemical purity of all conjugates was over 99%. All variants demonstrated specific binding to HER2-expressing cells and equally slow internalization. Tumour uptake of ^{111}In -labeled variants was slightly but significantly higher than ^{68}Ga -labeled ones, and clearance of ^{111}In -labeled variants was rapid. All variants had several-fold higher uptake in SKOV-3 than in DU-145 xenografts. Both ^{111}In - and ^{68}Ga -labeled DOTA- C^{61} -(HE)₃DANS-ADAPT6-GSSC had rapid clearance from blood compared to DOTA- C^{59} -DEAVDANS-ADAPT6-GSSC. DOTA- C^{61} -(HE)₃DANS-ADAPT6-GSSC provided approximately twice higher tumour-to-blood ratios at 3 h p.i. (208 ± 36 for ^{111}In and 109 ± 17 for ^{68}Ga) than DOTA- C^{59} -DEAVDANS-ADAPT6-GSSC (93 ± 19 for ^{111}In and 50 ± 18 for ^{68}Ga) in mice bearing SKOV-3 xenografts. The tumour-to-organ ratios for ^{68}Ga -DOTA- C^{61} -(HE)₃DANS-ADAPT6-GSSC are sufficiently high to provide high-contrast PET imaging in major metastatic sites (tumour-to-liver ratio of 48 ± 7 , tumour-to-bone-ratio of 147 ± 70 and tumour-to-lung ratio of 104 ± 34). **Conclusions:** [^{68}Ga]Ga-DOTA- C^{61} -(HE)₃DANS-ADAPT6-GSSC and [^{111}In]In-DOTA- C^{61} -(HE)₃DANS-ADAPT6-GSSC are the best variants for imaging of HER2 expression using PET and SPECT, respectively.

OP-231

Comparative studies of 4-(*p*-iodophenyl)butanoic acid acylated acidic amino acids as effective albumin binders by PET imaging and biodistribution using ^{18}F -labeled trifluoroborate derivative of PSMA-617 as a targeting vector

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Introduction: Conjugation of an albumin binder to extend blood retention time of radiotherapeutic agents is an attractive strategy to enhance tumor uptake and treatment efficacy. However, the most investigated albumin-binding motif, N^{ϵ} -[4-(*p*-iodophenyl)butanoyl]-D-Lys, contains only one carboxylate group. For conjugation to peptides on solid phase, this albumin binder has to be anchored at the C-terminus. Otherwise, modifications for conjugation to peptides such as via click reaction are needed. In this study, we exploited the replacement of D-Lys with various acidic amino acids that contain two carboxylate groups: one for coupling to peptides and the other as part of albumin-binding motif. **Methods:** HTK01160, HTK01171, HTK01190 and HTK01192 containing 4-(*p*-iodophenyl)butanoic

acid acylated Glu, Asp, Glu, and Aad (L-2-aminoadipic acid), respectively, were synthesized via the solid phase approach. After assembling the PSMA-617 pharmacophore (tranexamic acid-2-Nal-Lys-ureido-Glu), Lys was coupled to the C-terminus, followed by sequential coupling of albumin-binding components (the acidic amino acid and 4-(*p*-iodophenyl)butanoic acid) to the α -amino group of Lys. For HTK01160 and HTK01190, Glu was coupled to the PSMA targeting vector via the α - or γ -carboxylate group, respectively. After coupling azidoacetic acid to the ϵ -amino group of Lys, peptides were cleaved off the resins and clicked with *N*-propargyl-*N,N*-dimethyl-ammoniomethyltrifluoroborate to obtain the desired standards. Radiofluorination was conducted via ^{18}F - ^{19}F isotope exchange reaction. PET imaging and biodistribution studies were performed in mice bearing PSMA-expressing LNCap prostate cancer xenografts. **Results:** ^{18}F -HTK01160, ^{18}F -HTK01171, ^{18}F -HTK01190 and ^{18}F -HTK01192 were obtained in 0.5–4.0% average decay-corrected radiochemical yields with >99% radiochemical purity and $\geq 57\text{GBq}/\mu\text{mol}$ average specific activity. All ^{18}F -labeled compounds showed prolonged blood retention and good PSMA targeting as hearts and tumors were clearly visualized in PET images acquired at both 1- and 4-h post-injection. The changes on blood uptake values from 1- to 4-h post-injection for ^{18}F -HTK01160, ^{18}F -HTK01171, ^{18}F -HTK01190 and ^{18}F -HTK01192 were 19.9 ± 11.8 to $11.2 \pm 1.58\% \text{ID/g}$, 21.5 ± 2.29 to $18.1 \pm 1.99\% \text{ID/g}$, 25.9 ± 7.10 to $20.8 \pm 2.93\% \text{ID/g}$, and 18.6 ± 0.92 to $14.9 \pm 1.10\% \text{ID/g}$, respectively. The changes on LNCap tumor uptake values from 1- to 4-h post-injection were 14.2 ± 1.27 to $33.1 \pm 8.34\% \text{ID/g}$ for ^{18}F -HTK01160, 7.26 ± 0.78 to $16.4 \pm 3.16\% \text{ID/g}$ for ^{18}F -HTK01171, 3.87 ± 1.13 to $9.51 \pm 1.56\% \text{ID/g}$ for ^{18}F -HTK01190, and 5.49 ± 0.48 to $15.9 \pm 2.93\% \text{ID/g}$ for ^{18}F -HTK01192. **Conclusion:** We designed and compared four albumin-binding motifs that can be directly constructed on solid phase to anywhere in the sequences of peptides and peptidomimetics without additional chemical modifications. The *N*-[4-(*p*-iodophenyl)butanoyl]-Glu motif in ^{18}F -HTK01160 greatly enhanced tumor uptake and showed relatively faster blood clearance; thus it is promising for conjugation to radiotherapeutic agents to improve treatment efficacy.

OP-232

Development and evaluation of a new Interleukin-2 PET radioligand [^{18}F]AIF-RESCA-IL2: comparison with [^{18}F]FB-IL2

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Introduction: Interleukin-2 is a 15.5 kDa glycoprotein that binds with high affinity to IL2 receptors (IL2R) that are overexpressed on activated T-cells, which are involved in various pathological diseases, such as autoimmune diseases, but also play a major role in the tumor immune response. We have developed [^{18}F]

FB-IL2 which has been successfully used for detecting activated T-cells in rodents [1]. Recently, a GMP-compliant production of [^{18}F]FB-IL2 for clinical use was implemented, but the production method proved to be complex and time-consuming. Therefore, we now developed a simplified method to label IL2 with ^{18}F -fluoride. Here we present the synthesis of [^{18}F]AIF-RESCA-IL2 and its comparison to [^{18}F]FB-IL2. **Methods:** The [^{18}F]AIF-RESCA-IL2 synthesis was automated on the Eckert&Ziegler PharmTracer synthesis module. An [^{18}F]AIF $^{2+}$ solution was freshly prepared by adding ca. 10 GBq of ^{18}F -fluoride in 400 μl of NaCl 0.9% to 50 nmol AlCl_3 in 200 μl of NaOAc buffer (0.1 M, pH 4.5). This solution was added to RESCA-TFP (50 nmol, 12 min, RT). [^{18}F]AIF-RESCA-TFP was purified using an HLB cartridge. Purified [^{18}F]AIF-RESCA-TFP was conjugated with human recombinant IL2 (Proleukin $^{\circ}$, 17.2 nmol, 50°C, 12 min, pH 8.4) and purified using a TC2 cartridge. The stability of [^{18}F]AIF-RESCA-IL2 was tested in human serum (TCA precipitation) at 60 min. **Ex-vivo** biodistribution [^{18}F]AIF-RESCA-IL2 (1.21 ± 0.95 MBq) and [^{18}F]FB-IL2 (4.20 ± 0.8 MBq) was studied in male immunocompetent BALB/c mice ($n=6$) at 60 min p.i. **Results:** The [^{18}F]AIF-RESCA-TFP complex was formed at room temperature with excellent yields (>80%). The subsequent conjugation of IL2 with [^{18}F]AIF-RESCA-TFP provided the final product, [^{18}F]AIF-RESCA-IL2 with a radiochemical yield ($2.4 \pm 1.6\%$) and radiochemical purity (>95%) within 90 min. [^{18}F]AIF-RESCA-IL2 showed high stability in human plasma with >90% of the tracer remaining intact after 60 min. Preliminary biodistribution of [^{18}F]AIF-RESCA-IL2 in mice (60 min, p.i) showed high uptake in kidneys (49 ± 23 %ID/g), spleen (43 ± 25 %ID/g), liver (31 ± 6 %ID/g) and bone marrow (27 ± 12 %ID/g), which was comparable to the biodistribution of [^{18}F]FB-IL2 (kidneys 22 ± 11 %ID/g; spleen 17 ± 14 %ID/g; liver 12 ± 11 %ID/g; bone marrow 11 ± 12 %ID/g). **Conclusion:** [^{18}F]AIF-RESCA-IL2 can be obtained in similar yields as [^{18}F]FB-IL2, but in a substantially shorter time (90 vs. 150 min). In addition, substitution of the 4- ^{18}F fluorobenzoyl group with Al ^{18}F -RESCA increased significantly the uptake in kidneys spleen and liver. Further studies are ongoing to evaluate the selectivity [^{18}F]AIF-RESCA-IL2 binding to IL2R on activated T-cells. **References:** [1] Di Galleonardo et al., *J. Nuc. Med.*, **2012**, 53(5):679–86

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Introduction: This presentation summarizes an upcoming ICRP Publication on the development and intended use of a series of ten computational phantoms representing the reference male and female newborn, 1-year-old, 5-year-old, 10-year-old, and 15-year-old as defined in Publication 89. These phantoms have been formally adopted by the ICRP for use within Committee 2 in the development of age-dependent dose coefficients following the 2007 Recommendations. They are presented in the very same voxelized structures and tissue ID numbers as given in Publication 110 for the adult reference computational phantoms. **Methods:** The pediatric reference phantoms were constructed along 9 steps in their development: (1) selection of CT tomographic data, (2) segmentation of those CT images, (3) body contour and organ modeling via NURBS/PM surfaces, (4) adjustments of outer body contour to match total body mass, (5) adjustments of individual organ values to match reference masses, (6) subdivision of the skeletal tissues, (7) voxelization of the NURBS/PM surfaces, (8) voxel retagging for lymphatic nodes and skeletal muscle, and (9) further modifications to bring the series of pediatric phantoms into a structure identical to that original established for the adult phantoms of Publication 110. **Results:** The upcoming ICRP Publication will include a variety of annexes similar to those given in Publication 110 to include tissue IDs, elemental compositions, surface depth distributions, organ pair chord-length distributions, and cross sectional images. **Discussion:** These pediatric phantoms have been used by Task Group 90 of Committee 2 in the development of age and sex dependent dose coefficients representing external exposures to contaminated air, water, and soil. They have also been used by Task Group 96 of Committee 2 in the development of age and sex dependent specific absorbed fractions for internally emitted photons, electrons, alpha particles, and neutrons, in a manner similar to the adult SAF values given in Publication 133. These SAF values are currently being utilized by Task Group 96 in the preparation of dose coefficients for radionuclide ingestion and inhalation as part of the forthcoming EIR (Environmental Intakes of Radionuclide) publication series which updates the dose coefficients of ICRP Publications 56, 67, 71, and 72. Finally, the new pediatric SAF values will be used to assemble radionuclide S values for use by Task Group 36 in their revision of nuclear medicine organ and effective dose coefficients.

606 Monday, October 15, 2018, 08:00 - 09:00, Hall Y

Do.MoRe: Radiation Exposure & Protection

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The ICRP Reference Pediatric Phantoms - Design, Construction, and Applications to Nuclear Medicine Dosimetry

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OP-234

FAPI-PET/CT: normal tissue biodistribution and a preliminary dosimetry estimate of two DOTA-containing FAP-targeting agents compared to FDG in cancer patients

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Purpose: Fibroblast activation protein (FAP) is overexpressed in cancer associated fibroblasts of several tumor entities. Recent

development of quinolone based positron-emission-tomography (PET)-tracers that act as FAP-Inhibitors (FAPi), demonstrated promising results pre-clinically and already also in few clinical cases. Consecutively this novel tracer is now applied in our hospital to amend the diagnostics of cancer patients which were facing limitations of standard exams. Here we analyze the normal tissue biodistribution of this new class of PET-radiopharmaceuticals in comparison to the current standard Onco-PET based on Fluorodesoxyglucose (FDG). **Methods:** A preliminary dosimetry estimate was based on three patients examined at 0.2h, 1h and 3h after tracer injection using the QDOSE dosimetry software suit. Further PET/CT scans of tumor patients were acquired only 1 h after injection of either FAPI-2 (n=25) or FAPI-4 (n=25); for 5 patients an intra-individual related FDG-scan (also acquired 1h p.i.) was available. For the normal tissue of 16 organs, a 2cm Spheric-VOI was placed in the parenchyma, for pathological lesions a threshold segmented VOI was used to quantify $SUV_{mean/max}$. **Results:** Very similar to literature values for FDG, an exam with 200 MBq ^{68}Ga -FAPI-2/4 corresponds to an equivalent dose of approx. 6/7 mSv. Targeting of both FAPI-tracers was fast, except of clearance from blood-pool and renal calices the normal tissue biodistribution between 10 min and 3 h p.i. changes minimally over time. In FAPI-2 the tumor uptake from 1h to 3h p.i. decrease by 75%, the tumor retention was slightly prolonged with FAPI-4 (50% washout). At 1h p.i. both FAPI-tracers performed equally. In comparison to FDG the tumor uptake was almost equal (average SUV_{max} -FDG 7.41; SUV_{max} -FAPI-2 7.37; n.s.); the background uptake in brain (1.01 vs 0.32), liver (2.77 vs 1.69) and oral/pharyngeal mucosa (4.88 vs 2.57) was significantly lower with FAPI; other organs were not relevantly different between FDG and FAPI. **Conclusion:** FAPI-PET/CT is a new diagnostic mean in imaging cancer patients. In contrast to FDG no diet/fasting in preparation of the exam is necessary. Tumor-to-background contrast ratios equal or even improved in comparison to FDG. Fast tracer kinetics seems appropriate to image patients even <1 h pi.

OP-235

Evaluation of the administrated dose and image quality of pediatric patients

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Aim: To evaluate the effective dose and image quality obtained with different image reconstruction methods when reducing the injected activity in pediatric imaging with [18F]FDG PET/CT.

Material and Methods: In this retrospective study, data from ten pediatric patients with epilepsy (age 3-15 years old) and five oncological patients (7-18 years old) were used. Patients underwent [18F]FDG-PET/CT examination with injected activities of 4.2 MBq/kg (epilepsy patients) and 5.1 MBq/kg (oncology patients) on a Siemens Biograph TPTV PET/CT system. The acquired list mode data was preprocessed to virtually reduce the number of counts to 75%, 50%, 35%, 20% and 10% of the total

counts. The data was reconstructed using the STIR framework. Reconstructions were performed for every patient and activity alteration with two reconstruction methods: standard OSEM with Gaussian filter (FWHM = 0, 2, 4 mm) and Maximum-A-Posteriori (MAP) reconstruction with median root prior (MAP-MRP) (prior values $\beta = 20, 100, 200$). Tracer avid lesions (i.e. tumors and lymph nodes) were delineated using a 50% threshold region growing and lesion-to-background ratios (LBR) were calculated. For hypo-metabolic regions in epilepsy patients the figure of merit was the LBR between the epileptic focus and the corresponding contralateral side of the brain. Further, the uniformity within a background region was evaluated. Relative deviations of the LBR at reduced number of counts were calculated by comparison with the values obtained with all the counts. The patient effective dose (ED) was estimated from the CT and PET acquisitions. **Results:** Relative deviations below 10% were obtained for count reductions down to 50% and the reconstruction methods OSEM+4mm filter (7.0%) and MAP-MRP with $\beta = 200$ (6.7%). The noise level for these cases was 15.4% and 17.6% respectively (14.3% and 14.6% with all the counts). Using 50% of counts ED for PET could be reduced from 4.7 to 2.4 mSv (epilepsy patients) and from 5.8 to 2.9 mSv (oncological patients). Given the calculated ED from CT (0.3 mSv epilepsy, 3.6 mSv oncology), this results in a reduction of the total ED up to 53% and 68% of the standard ED, respectively. **Conclusion:** A potential reduction of the injected PET activity up to 50% can be achieved without compromising the image quality (relative deviations of the LBR values below 10%) by applying a suitable reconstruction method. **Acknowledgments:** The financial support of the Austrian FWF Project I3451-N32 is gratefully acknowledged.

OP-236

130, 110 or 80 kV tube voltage for the low-dose CT at lung V-/P-SPECT-CT: Trade-off between radiation exposure and image quality

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Introduction: V-/P-SPECT-CT is a sensitive and specific technique to detect or rule out pulmonary embolism. In a previous study there was evidence that by reducing the CT's tube voltage from 130 to 110 kV radiation exposure could be lowered significantly without loss of imaging quality. Aim of the current study was to test a further reduction of the CT's tube voltage to 80 kV and its consequences on imaging quality. **Subjects & methods:** V-/P-SPECT/CT with Technegas and about 150 MBq ^{99m}Tc -MAA (Siemens SymbiaT) including a low dose CT was performed in 25 patients. Three matched pairs (12 male, 13 female) concerning gender, height, weight and body mass index (BMI) for 130, 110 and 80 kV were identified. Image quality of the acquired low dose CT was visually analysed using a 6 point scale (grade 1-6). Radiation exposure of the low dose CT was calculated using CT-EXPO. T-test for paired samples concerning height, weight, BMI and radiation exposure of the low dose CT - according to ICRP 103 - was performed. **Results:** Height, weight and BMI of the 130, 110 and 80 kV collectives did not differ significantly: $0.37 < p < 0.86$ (height 170.0 ± 10.5 (130kV) vs. 170.5 ± 8.8

cm (110kV) vs. 169.1 ± 9.3 cm (80kV); weight 77.2 ± 16.0 (130kV) vs. 77.8 ± 18.4 kg (110kV) vs. 75.8 ± 16.9 kg (80kV); BMI 26.7 ± 5.1 (130kV) vs. 26.7 ± 5.6 (110kV) vs. 26.4 ± 4.8 (80kV)). For the low dose CT according to ICRP 103 the following radiation exposure was calculated for 130 kV: 0.69 ± 0.15 mSv, for 110 kV: 0.51 ± 0.12 mSv and for 80 kV: 0.34 ± 0.11 mSv, significant differences were found for all comparisons ($p < 0.0005$). Image quality using 110 kV (2.44 ± 0.51) was not worse than using 130kV (2.48 ± 0.51), resulting $p > 0.7$. Image quality using 80 kV (3.28 ± 0.74) was significantly ($p < 0.0001$) worse in comparison to the two other options. **Conclusion:** By reducing the CT's tube voltage from 130 to 110 kV within V-/P-SPECT/CT radiation exposure can be lowered by about 25% without relevant loss of image quality. A further reduction to 80 kV results namely in lower radiation exposure but image quality worsens significantly so that we recommend 110 kV.

OP-237

Nordic-wide Survey of CT Exposures in Hybrid PET-CT and SPECT-CT Examinations

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Introduction: A growing number of CT scans are performed by Nuclear Medicine facilities in combination with PET or SPECT scans, yet reference data for radiation doses in hybrid imaging is sparse. CT scans can be performed in hybrid imaging for attenuation correction (AC), localisation, lesion characterisation or fully diagnostic purposes. Third quartile doses for a population are used to generate diagnostic reference levels (DRLs), and median doses used to demonstrate 'achievable doses', to be used for benchmarking practice. In this first Nordic-wide multi-centre study of CT doses in hybrid imaging, third quartile and median doses are presented for PET-CT and SPECT-CT examinations specific to the clinical purpose of CT, and the scope for further optimisation of CT doses is evaluated. **Materials and Methods:** Data on hybrid imaging CT exposures (CTDIvol, DLP, exposure settings) and clinical purpose of CT (AC only, localisation, characterisation, diagnostic) was gathered for 5 PET examinations (wholebody oncology, infection/inflammation, brain, cardiac and bone) and 8 SPECT examinations (bone, cardiac, lung, parathyroid, mIBG, Octreotide, thyroid post-ablation and sentinel node). Data were submitted by 43 Nuclear Medicine facilities. Data from a given system in a given department was included if $n(\text{number of patients}) \geq 10$ (or if $n < 10$ but mA modulation was not used). Each included dataset was normalized to give CTDIvol and DLP for a 75kg person. Third quartile and median doses were determined for DLP and CTDIvol according to clinical purpose of CT. Ratios of maximum to minimum weight-normalised doses

between facilities were also calculated for each examination and clinical purpose. **Results:** Submitted data was considered sufficient for reliable reference data for: PET wholebody oncology and inflammation/infection (localisation/characterisation); PET brain (AC only); cardiac PET and SPECT (AC only); SPECT bone, lung and parathyroid examinations (localisation/characterisation). There was a wide range of weight-normalised doses between facilities: maximum to minimum weight-normalised DLP ratios between facilities for the same examination type and clinical purpose of CT were up to: PET wholebody oncology 9:1; PET inflammation / infection 19:1; PET brain 17:1, SPECT and PET cardiac 21:1; SPECT lung 27:1; SPECT bone 10:1; and SPECT parathyroid 8:1. **Conclusions:** CT doses are presented for the Nordic region for 4 PET-CT and 4 SPECT-CT examinations, specific to clinical purpose of CT. Furthermore, the wide range of weight-normalised doses between facilities (for the same examination type and clinical purpose of CT) demonstrates good scope for further optimisation of CT exposures.

OP-238

Why should we take care about occupational dosimetric impact when routine use of gallium-68 in nuclear medicine? A preliminary study.

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Introduction: Medical research in PET/CT diagnosis involving new gallium-68 radiolabelled pharmaceuticals is steadily rising in the last years thanks to the combined improvement of both radionuclide production and radiolabelling. Publications demonstrate benefits for the patient but few studies evaluate the occupational dosimetric impact when use the gallium-68 in routine, in terms of effective and equivalent dose. **Subjects & Methods:** In this study, extremities, crystallin and whole body exposure are evaluated for three technologists when use of the gallium-68 radiolabelling with DOTATOC peptide (10 runs) requiring handmade steps and PSMA-11 peptide (5 runs) that is an automated process. Electronic dosimeter ED3 (APVL) is used to access to instantaneous dose-rate that can be afterward related to steps of handling. OSL pellets (LANDAUER) are used to measure the cumulative dose. Dosimeters are placed on fingers, protection eyeglass and chest. During the production runs, we separate radiolabelling phase from injection handmade phase to the patient (150 MBq/patient). The annual equivalent and effective doses are extrapolated on a mean of 2.5 patients per day during 52 weeks of 5 days with ⁶⁸Ga-PSMA-11 or ⁶⁸Ga-DOTATOC lonely. **Results:** The measurements show high exposures heterogeneity, confirmed with ED3 measurements that present high punctual peaks during the production runs. For ⁶⁸Ga-PSMA-11, the median equivalent dose to extremities, per production run and per syringe, is 228 µSv [208; 493] and, at the injection time, the median equivalent dose to extremities per

syringe is 212 μSv [188; 278]. For 68Ga-DOTATOC, the median equivalent dose to extremities, per production run and per syringe, is 315 μSv [28; 875] and, at the injection time, the median equivalent dose to extremities per syringe is 493 μSv [111; 1225]. The extrapolated annual equivalent dose to extremities lead to 288 mSv [257; 501] and 525 mSv [90; 1365], respectively for 68Ga-PSMA-11 and 68Ga-DOTATOC. The extrapolated annual equivalent dose to crystallin lead to 6,5 mSv [4,9; 11,7] and 1,3 mSv [background; 113,1], respectively for 68Ga-PSMA-11 and 68Ga-DOTATOC. The extrapolated annual effective dose lead to 1,3 mSv [background; 16,9] and 1,3 mSv [background; 53,3], respectively for 68Ga-PSMA-11 and 68Ga-DOTATOC. **Conclusion:** This study highlights that the use in routine of radiolabelled gallium-68 could lead to significant equivalent doses for technologist, especially since the protocol is not automated. This advocates strongly for a specific attention when routine use of a new radiopharmaceuticals, particularly on radiation optimisation of radiolabelling protocol and injection phase, also on high practical training of technologist.

OP-239

Skin dose saving of the staff following the acquisition of an automated multidose injection system in $^{90}\text{Y}/^{177}\text{Lu}$ peptide receptor radionuclide therapy

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Purpose: Significant staff exposure can be a critical issue in Molecular Radiotherapy, particularly when handling unsealed beta emitters-labelled radiopharmaceuticals. Taking into account the amounts of administered activity and the physical properties of therapeutic radionuclides, the skin of the hands is the riskiest organ. The aim of this work was to evaluate the equivalent dose saving of the staff involved in $^{90}\text{Y}/^{177}\text{Lu}$ -labelled radiopharmaceuticals administration (physicians), using an automated multidose injection system (IRIS, Comecer). IRIS is designed for diagnostic/therapeutic purposes. **Methods:** Before the clinical use, IRIS was properly calibrated to guarantee accurate measures of β -emitters. The desired patient dose is automatically drawn from the radiopharmaceutical vial, then measured and directly injected to the patient. Staff dosimetry was carried out with a series of thin active layer ultrasensitive MCP-Ns (LiF: Mg, Cu, P) dosimeters fixed at the operator's fingertips to evaluate the skin equivalent dose. The skin dose of the physician was assessed by 6 dosimeters positioned over the first three fingers of each hand, replaced after each procedure. 100 procedures (600 fingertip doses) were considered. Shielded aprons, anti-X gloves to improve the protection against radiation were used. Physicians wore also direct reading personal devices to monitor the external body radiation exposure during dispensing. The analysis was carried out through the comparison of the data collected before the introduction of the automated device, when the radiopharmaceutical was administered systematically (intravenous injection) using a traditional infusion system. The mean handled activity/session was 40.2 GBq (^{177}Lu) and 12.2 GBq (^{90}Y). **Results:** To equally compare procedures involving different

amounts of handled activities, fingertip dose data were normalized to the single activity used. The mean skin dose values (95th percentile) of Hp(0.07) before and after IRIS introduction were respectively 0.035 (0.136) and 0.006 (0.017) mSv/GBq. The Wilcoxon-Mann-Whitney test proved a reduction in extremity dose due to IRIS use ($P=0.0114$). Mean personal body equivalent doses absorbed by the physicians before and after IRIS introduction were 3.3 uSv (range: 1-11 uSv), and 2 uSv (range: 1-13 uSv), respectively in terms of Hp(10), and 7.1 uSv (range: 1-31 uSv), and 2.6 uSv (range: 1-8 uSv), respectively in terms of Hp(0.07). **Conclusions:** The introduction of an automated dispensing and injection system during beta-emitters labelled therapy has led to a significant decrease in the dose to the physicians' fingertips in radiopeptides administration (up to 8 times). In addition, IRIS allowed to further reduce mean personal body equivalent doses.

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Monday, October 15, 2018, 08:00 - 09:30, Hall 1

Pitfalls & Artefacts 3 - Interactive Clinical Cases: Dosimetry: Advantages and Limitations of Voxelized Dosimetry for Intra-Arterial Liver Therapy

OP-240

Visualisation of the Activity in the Liver After Radioembolisation: Is it Noise or a Real Indication of the Arterial Distribution?

S. Walrand; Université Catholique de Louvain, Nuclear Medicine, Brussels, BELGIUM.

OP-241

Voxelized Dosimetry Options from Mean Dose to Voxel Dose Distributions and Beyond or Room for Improvement in Image Reconstruction?

M. Ljungberg; Lund University, Department of Medical Radiation Physics, Lund, SWEDEN.

OP-242

Voxel-Based Dosimetry Treatment Planning for Intra-Arterial Liver Cancer Therapy - What are the Options?

M. Lam; University Medical Centre Utrecht, MS Radiology, Utrecht, NETHERLANDS.

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Monday, October 15, 2018, 08:00 - 09:00, Hall 4

Clinical Oncology - Rapid Fire Session: It's in the Blood!

OP-243

Prospective Evaluation Of FDG PET/CT As A Predictor Of Prognosis In Newly Diagnosed Transplant Eligible Multiple Myeloma Patients

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IRCSS, Reggio Emilia, ITALY, ³Santa Croce e Carle Hospital, Cuneo, ITALY, ⁴AOU S.Maria della Misericordia, Udine, ITALY, ⁵AO Città della Salute e della Scienza, Torino, ITALY, ⁶Research and Innovation Department A Lacassagne Cancer Center, Nice, FRANCE, ⁷University of Torino, Torino, ITALY.

Aim of the study was to prospectively evaluate FDG-PET/CT IN Multiple Myeloma at diagnosis, after induction and prior to maintenance in a sub-group of patients enrolled into EMN02/HO95 MM international phase III trial. The end-point was to define the most prognostic cut-off for IMPETUS criteria in the light of follow-up data. 103 pts were included in the PET/CT imaging sub-study, and followed for a median of 24 months. PET/CT was performed at baseline, after induction and prior to the start of maintenance. Each PET scan was a posteriori re-interpreted in a blinded independent central review process, managed by WIDEN®, by a panel of 5 expert nuclear medicine physicians. They described: bone marrow metabolic state (BM), number (Fx) and score (Fs) of focal PET positive lesions, osteolysis (Lx), presence and site of extramedullary disease (EM), and fractures (Fr), according to the IMPETUS criteria (Nanni et al, EJNM 2018). Moreover, a global score (GS), from 1 to 5, was given to each patient, considering the highest score among BM, Fx, Fs and EM. Each parameter was considered interpreted when 3/5 reviewers were concordant. Baseline characteristics of the patients were the following: median age 58 years, ISS and R-ISS stage III 15% and 10%, high-risk cytogenetics (t(4;14) ± del(17p) ± del(1p) ± 1q gain detected by FISH) 42%. At baseline, 78% of the patients had FLs, with a median SUVmax of 6.0. Of all parameters, only Fx ≥ 4 was associated with worse PFS and OS (P = 0.06). Following 4 cycles of VCD, PET/CT remained positive in 59% of the patients, with a median SUVmax of 3.7. Of all parameters, only Fs ≥ 4 was predictive of worse OS (P = 0.05). Prior to maintenance, PET/CT remained positive in 34% of the patients, with a median SUVmax of 3.4. Normalization of PET/CT before maintenance (66%) was associated with a significant improvement in the outcome, for different parameters: PFS: presence of FLs (P=0.03), Fx ≥ 4 (P=0.001), Fs ≥ 2 (P=0.03), 3 (P=0.03) and 4 (P=0.006) and SUVmax ≥ 3.4 (p=0.002). GS was also predictive for PFS if ≥ 3 (P=0.033), 4 (P=0.0001) and 5 (P=0.004). The same parameters were also predictive for OS. In conclusion, PET/CT was confirmed to be a reliable predictor of outcome in newly diagnosed transplant eligible MM patients. Normalization of PET/CT before maintenance was associated with a significant improvement for PFS and OS.

OP-244

Evaluation of chemokine receptor 4 expression by 68Ga Pentixafor PET/CT in patients with multiple myeloma

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Purpose: To demonstrate the CXCR4 expression, which is a potential target for myeloma-specific therapy and negative prog-

nostic factor, in patients with multiple myeloma with 68Ga-Pentixafor PET/CT, compared with standard clinical parameters and 18F-FDG PET/CT findings. **Material-method:** Twenty-four (17 women, 7 men; mean age: 58.9±12.7; range:39-82 years) multiple myeloma patients who had undergone 18F-FDG PET/CT scan to evaluate the disease activity were included in the study. 68Ga-Pentixafor PET/CT scans were performed also with in average of 12 days. Scans were compared on a patient and on a lesion basis. Both PET/CT findings of patients were correlated with standard clinical parameters of disease activity. **Results:** 68Ga-Pentixafor PET and 18F-FDG PET were detected focal pathologic lesions in 13/24 (54.2%) and 16/24 (66.6%) patients, respectively. In 19/24 patients, both tracers showed concordant findings [(CXCR4 + / FDG + in 12 pts); (CXCR4 - / FDG - in 7 pts)] and in the remaining 5 patients, findings were discordant. Number of focal lesions for 68Ga-Pentixafor and 18F-FDG were 89 (44%) and 113 (56%), respectively. 68Ga-Pentixafor PET detected more lesions in 2/12 (17%) patients, 18F-FDG PET proved superior in 7/12 (58%). In the remaining 3/12 (25%) patients, both tracers detected an equal number of lesions. There was no significant difference in appendicular and axial skeletal and extramedullary distribution ratios for both examinations (p>0.05). There was no statistically significant correlations between the 68Ga-Pentixafor PET and 18F-FDG PET positivity and disease activity, MM subtype, ISS phase, light chain disease, beta2microglobulin, albumin, creatinine, LDH, FLC and M protein levels in during scans. **Conclusion:** Chemokine receptor expression is accepted as a negative prognostic factor in patients with multiple myeloma. Although it doesn't replace FDG PET/CT in diagnosis, demonstration of receptor expression by Ga-68 PET/CT for CXCR4-targeted therapies may guide appropriate patient selection, determination of prognosis and patient selection for potential Pentixather (CXCR4) therapy.

OP-245

Prevalence and clinical significance of incidental extra-skeletal findings detected on the unenhanced CT portion of PET/CT performed in Multiple Myeloma patients

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Aim: 18F-FDG-PET/CT is a useful tool to image Multiple Myeloma (MM), to evaluate the extent of whole-body disease and to distinguish between active or inactive disease after therapy. The unenhanced CT portion may provide additional independent diagnostic information not apparent on PET. The aim of this study was to evaluate the added value and the frequency of potentially clinically significant incidental findings (IF) from the independent reading of the unenhanced CT portion of PET/CT studies. **Material and Methods:** From June 2016 to July 2017, 112 patients (66 men and 46 women; mean age 65.8 y) affected by MM underwent to 18F-FDG-PET/CT at our Nuclear Medicine Department. The unenhanced CT portion of PET/CT was performed with the following parameters: acquisitions

from the skull to the mid-thigh (5–7 bed positions), 120 kV and mA with automatic modulation system. All CT studies were retrospectively reviewed on a dedicated workstation, with 3.75 slice thickness and equipped with MPR/VR reconstructions, by an expert CT radiologist. Each IF, not related to MM, was categorized in a body region/system and classified according to MM-Reporting and Data System (MM-RADS), a 5-point significance score system inspired by C-RADS. **Results:** 153 IF were detected in 112 patients (mean value: 1.4). 53.6% of IF would have required further clinical investigation (MM3+MM4); while (28/153) 18.3% were potentially clinically significant (MM4) and categorized as follows: 9/153 (5.9%) in the abdomen (8 liver solid lesions >1cm and 1 peritoneal carcinomatosis), 8/153 (5.2%) in the lung (3 pulmonary nodules >1 cm, 3 calcified pleural plaques >1cm, 2 non-calcified pleural plaques >1cm), 6/153 (3.9%) in the cardiovascular system (aortic aneurysmal dilations), 3/153 (2.0%) in the gastrointestinal tract (2 rectal thickening, 1 appendicular mucocoele), 1/153 (0.7%) in the genitourinary system (1 kidney solid nodule >1cm), 1/153 (0.7%) in the breast (1 breast solid nodule >1cm). **Conclusion:** ^{18}F -FDG-PET/CT is now considered the method of choice in MM. To date, co-registration CT images become diagnostic, thanks to specific dose reduction protocols. Our study showed that the independent reading of the unenhanced CT portion of PET/CT studies found a considerable number of IF (1.4/pts), probably due to the high mean age of MM patients. Particularly, the evidence that 18.3% (MM4) was severe enough to warrant significant change in the clinical management of patient, leads us to believe that the combined radiologist-nuclear physician report, may improve the diagnostic value of ^{18}F -FDG PET/CT and the management of these patients.

OP-246

Post-Treatment ^{18}F -FDG PET/CT in Patients with Hodgkin's Lymphoma: Setting the Best Threshold of Deauville Scale

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Purpose: The aim of this study was to evaluate metabolic tumor response in patients with Hodgkin's lymphoma using the Deauville 5-point scale and to correlate the results with clinical outcome and biopsy using different values of threshold for PET-positivity. **Subjects & Materials:** Fifty-seven patients (29 male and 28 female; mean age $\pm$ SD, 33.4 y $\pm$ 14.8y) with histologically confirmed classic Hodgkin's lymphoma who had undergone ^{18}F -FDG PET-CT scan at baseline and after first line of standard chemotherapy before radiotherapy, were included in this retrospective study. Four patients were in stage I, 27 patients in stage II, 9 patients in stage III and 17 patients were in stage IV. Post-treatment ^{18}F -FDG PET-CT scans were evaluated according to the Deauville criteria and based on Lugano classification, patients were allocated to classes of complete metabolic response (CMR) partial metabolic response (PMR), no metabolic response (NMR) and progressive metabolic disease (PMD). In a subgroup of 26 patients, biopsy was performed immediately af-

ter ^{18}F -FDG PET-CT, on residual masses or lesions that remained metabolically active after therapy and results were compared to the Deauville score. Patients were then subjected to follow-up and the median follow-up period was 41 months. **Results:** All patients were positive at the baseline scan. The analysis of post-treatment scans assigned a Deauville score (DS) as follows: DS1 to 17 patients, DS2 to 7 patients, DS3 to 16 patients, DS4 to 7 patients and DS5 to 10 patients. Forty patients were in CMR, 10 in PMR, 3 in NMR and 4 in PMD. All patients with DS4 were in PMR and achieved complete remission after radiotherapy. Using DS ≥ 4 as a cut-off to define a positive scan, failure-free survival (FFS) was 95% for PET-negative and 59% for PET-positive ($\chi^2 = 9.179$, $p = 0.0024$). Increasing the threshold for positivity to DS5, FFS was 95% for PET-negative and 30% for PET-positive ($\chi^2 = 22.088$, $p < 0.0001$). Biopsy of 26 lesions (2 DS1, 2 DS2, 7 DS3, 5 DS4 and 10 DS5) showed the presence of residual disease in 8 lesions with DS5 belonging to 4 patients with PMD, 2 with PMR and 2 with NMR. All five DS4 lesions were negative at biopsy. **Conclusions:** Our findings suggest that in Hodgkin's lymphoma, patients with DS4 in PMR at the end of treatment may be considered PET-negative thus avoiding overtreatment of those patients.

OP-247

Response Evaluation To Checkpoint Inhibitors by ^{18}F -FDG PET/CT In Patients with Hodgkin Lymphoma

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Introduction: Encouraging results with checkpoint inhibitors have induced FDA to approve Nivolumab and Pembrolizumab for patients with relapsed or refractory Hodgkin Lymphoma (HL). Nevertheless, not all patients benefit from these new agents and definite markers of response are still argument of discussion, as well early detection of therapy response. Our aim was to evaluate tumor response to checkpoint inhibitors by ^{18}F -FDG PET/CT at the baseline, 8 and 17 weeks after treatment start. **Subjects and Methods:** Overall, 43 HL patients (M:F= 26:17; median age 31 years) treated with checkpoint inhibitors (42 nivolumab; 1 pembrolizumab), were enrolled between November 2014 and August 2017. The study was approved by the IRB. For each patient, ^{18}F -FDG PET/CT was evaluated at three time points: before immunotherapy, 8 weeks and 17 weeks after treatment start. According to Cheson response criteria, we documented the best clinical response and identified four categories: progression disease (PD), stable disease (SD), partial response (PR) and complete response (CR). PET scans were reviewed and changes in metabolic parameters, visually and semi-quantitatively, were analyzed. All parameters were statistically analyzed with respect to treatment response and progression-free survival (PFS). **Results:** At a median observation time of 13 months (range 3-31 months), the best clinical responses were CR in 26 patients, PR in 5 patients, SD in 8 patients and PD in 4 patients. Overall, 31 out

of 43 (72%) patients reached an objective response. PET scan at the 8 weeks of treatment, performed in 22 patients, showed lower Deauville Score (DS) in patients with CR compared to the other response types ($p=0.011$). Likewise, SUVmax was significantly different ($p=0.002$), with a progressive reduction in the four response categories, while no significant modification in the tumor burden parameters (TLG and MTV) were detected. After 17 weeks, DS confirmed being different among responder groups. In addition, significant decrease in metabolism activity (SUVmax, $p=0.034$) and tumor burden (TLG and MTV, $p=0.025$ and 0.019 , respectively) were observed in the responder patients. Finally, patients evaluated by PET/CT as responders (CR, PR) had a significantly longer PFS (median not reached vs 23.3 months; HR 0.158, 95% CI, 0.031 to 0.792; $p=0.01$). **Conclusion:** In our study, we demonstrated that ^{18}F -FDG PET/CT is able to detect HL patients responding to checkpoint inhibitors already at early assessment 8 weeks after treatment start. Reduction of tumor burden appears evident later, probably due to the re-activation of immune system and increased glucose consumption in the lymphocytes.

OP-248

Combining Anthropometric and Radiomic Parameters Measured on ^{18}F -FDG PET/CT Improves the Prognosis of Diffuse Large B-Cell Lymphoma

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Introduction: Our aim was to study the prognostic value of models combining anthropometric parameters (describing patient's morphology) and radiomic parameters (describing tumour characteristics) determined on pre-therapeutic ^{18}F -FDG PET/CT in diffuse large B-cell lymphoma (DLBCL). **Subjects & methods:** We retrospectively included 215 patients with DLBCL. Patients underwent initial ^{18}F -FDG PET/CT before R-CHOP (73%) or intensified R-CHOP (R-ACVBP) regimens (27%). Tumours were segmented using a fixed threshold value of 41% of SUVmax. Two in-house softwares, Anthropometer3D and Oncometer3D, were used to automatically extract anthropometric parameters (lean body, muscle, fat body, visceral adipose tissue and sub-cutaneous adipose tissue masses) from the CT and radiomic parameters (describing tumour burden, fragmentation, dispersion and massiveness) from the segmented PET, respectively. The Spearman's rank correlation coefficient (ρ) was computed between the parameters to determine correlated parameters. All possible models combining uncorrelated parameters ($|\rho| < 0.8$) were evaluated using a random forest analysis with a five-fold cross-validation process. Known prognostic factors, the International Prognostic Index (IPI) and the type of chemotherapy could be combined in the models. The models were compared

by their mean area under the curve (AUC) of the ROC analysis. For a selection of models, accuracy and AUC of the five-fold cross-validations were compared by a paired t-test with $p < 0.05$ considered significant. **Results:** The model giving the best results was the one combining IPI, the type of chemotherapy, the total metabolic tumour volume (TMTV), the ratio between TMTV and its surface corresponding to the tumour volume surface ratio (TVSR) and the fat body mass (FBM) with a mean accuracy of 0.79 ± 0.08 and mean AUC of 0.82 ± 0.13 . The model combining only IPI and the type of chemotherapy had a lower accuracy (mean 0.70 ± 0.11 , $p=0.04$) and AUC (mean 0.75 ± 0.13 , $p < 0.001$), while the one combining IPI, the type of chemotherapy and TMTV had a lower AUC (mean 0.77 ± 0.15 , $p=0.0498$) with a non significantly different accuracy (mean 0.75 ± 0.10 , $p=0.26$). **Conclusion:** The prognosis of DLBCL can be improved by using a model combining three well recognized parameters (IPI, type of chemotherapy and TMTV) with two others parameters measured on the pre-therapeutic ^{18}F -FDG PET/CT: TVSR describing the tumour fragmentation and FBM describing the patient's adiposity.

OP-249

The prognostic role of final end of treatment FDG-PET-CT can be improved by absolute monocyte count in patients with diffuse large B cell lymphoma

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It is well established that some of the patients with diffuse large B-cell lymphoma (DLBCL) and negative end of treatment PET-CT (EOT-PET-CT) will relapse, while a proportion with positive uptake can still obtain long term event free survival (EFS). For these reasons it is very important to improve the prognostic value of the EOT-PET-CT. In our earlier studies, we demonstrated the additional significant prognostic value of absolute monocytes count (AMC) in DLBCL. Thereafter, we planned a multicenter, retrospective study to assess whether combining the most utilized prognostic criteria at the time of diagnosis, such as International Prognostic Index or AMC with EOT-PET-CT, would impact the already strong predictive value of EOT-PET-CT even further. We reviewed clinical and laboratory data of 200 consecutive, previously untreated patients with DLBCL recorded at Modena Cancer Center, S. Andrea Hospital, Rome and Bnai Zion Medical Center Haifa from 2007 to 2015, who were uniformly treated with R-CHOP or R-CHOP-like regimens. Our results show that patients with negative EOT-PET-CT, but with AMC $> 630/\text{mmc}$ have a 3-years EFS of 72%, while patients with negative EO-PET-TC but with AMC $\leq 630/\text{mmc}$ have a 3-years EFS of 84%. Furthermore, considering patients with positive EOT-PET-CT, those with AMC $> 630/\text{mmc}$ have a 3-years EFS of 8%, while those with AMC $\leq 630/\text{mmc}$ have an EFS of 38%. In conclusion, it appears that combining the gold standard for response evaluation - EOT-PET-CT with a simple and inexpensive parameter like

AMC at diagnosis, further improves prognostication in DLBCL, allowing for progress towards personalized medicine. While still waiting for more refined methods based on genomic investigation applicable to clinical practice, we believe that this simple method can be useful for all doctors working in lymphoma clinical practice.

OP-250

Lesion Based Analytics On Pretherapy FDG PET/CT Radionics To Predict Ibrutinib-resistant Mantle Cell Lymphoma

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Background: Ibrutinib was approved to treat mantle cell lymphoma (MCL), an aggressive and incurable B-cell lymphoma subtype, with an overall response rate of 68%. However, the 1-year survival rate is only 22% in ibrutinib resistant MCL. Meanwhile, ibrutinib is costly: \$164,141/new and \$566,002/relapsed patient as first-line treatment. To facilitate selecting appropriate patients for ibrutinib therapy, it is desirable to have a model that can predict patient's response to ibrutinib base on pretherapy FDG-PET/CT. **Methods:** MCL patients' response to ibrutinib were retrospectively analyzed using Lugano and LYRIC criteria. Complete and partial response were grouped as sensitive (S), stable and progression disease were combined as resistant (R). All lymphoma lesions on pretherapy FDG-PET/CT were retrospectively identified and separated using MIM software with threshold of SUV_{max} ≥ 2. We used machine learning and pattern-recognition techniques to analyze pretherapy FDG-PET/CT texture and shape features, and routine clinical used PET features such as SUV_{max}, TLG and tumor volume. Radiomics results were correlated with available whole transcriptome sequencing (WTS) data from clinical specimens. **Results:** Total 19 MCL patients (6 R and 13 S) with 719 lymphoma lesions were analyzed. Our training set included 359 lesions (177 S and 182 R); our test set had 360 lesions (178 S and 182 R). Among the selected 189 imaging features, combined CT Hounsfield unit features of "CT.Std.Dev.Mean.Ratio" and "CT.Max.Mean.Ratio", with PET feature of "SUV Min/Mean Ratio" demonstrated best performance. The model reached lesion based prediction F1 score (integrative measure of precision and recall) of 0.866 in R group patients, and 0.918 in S group patients, with overall F1 score of accuracy of 0.898. The F1 score for both S and R groups, as well as the prediction accuracy using the combined three features are significantly higher than each of a single feature ($p < 1e-10$). These results indicated intratumor heterogeneity played an important role in ibrutinib resistance. WTS results are available in 7S and 6R patients, showed that expression of glucose metabolism related gene (Glucose transporters, Hexokinase and G6Pase gene) were not significantly different between R and S groups, but there were a significant enrichment of genes in mTOR signaling, cell cycle regulation, and MYC targets in ibrutinib-resistant tumors. **Conclusions:** Based on pretherapy FDG-PET/CT, tumor heterogeneity imaging features with underlying

other altered metabolic pathways, rather than routinely used SUV_{max}, volume, TLG features and associated glucose metabolism, played an important role in predicting ibrutinib resistance in MCL lesions.

OP-251

Prognostic Role Of pre-treatment 18F-FDG PET/CT Metabolic Parameters In Burkitt Lymphoma

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Purpose: Burkitt's lymphoma (BL) is an aggressive lymphoma with high 18fluorine-fluorodeoxyglucose (18F-FDG) avidity but no validated criteria for 18F-FDG positron emission tomography/computed tomography (PET/CT) in treatment evaluation and prediction of outcome are currently available. The aim of this study was to investigate whether the metabolic pre-treatment 18F-FDG PET/CT parameters can predict treatment response (at interim and end of treatment) and prognosis in BL.

Subjects and methods: Between January 2007 and January 2017, 65 patients with histologically proven BL were retrospectively enrolled; all patients underwent basal 18F-FDG PET/CT, interim PET/CT after 2 cycles of chemotherapy and end of treatment PET/CT after 6 cycles of chemotherapy. The PET images were analyzed visually and semi-quantitatively by measuring the maximum standardized uptake value body weight (SUV_{bw}), the maximum standardized uptake value lean body mass (SUV_{lbm}), the maximum standardized uptake value body surface area (SUV_{bsa}), lesion to liver SUV_{max} ratio (L-L SUV R), lesion to blood-pool SUV_{max} ratio (L-BP SUV R), total metabolic tumor volume (tMTV) and total lesion glycolysis (TLG). For the entire population, receiver operating characteristic curve analysis was used to identify the optimal cutoff point of semiquantitative parameters in the light of progression free survival (PFS) and overall survival (OS). Survival curves were plotted according to the Kaplan-Meier method. **Results:** All PET/CT scans were positive showing increased 18F-FDG uptake in nodal and extranodal lesions. At a median follow up of 40 months, the median PFS and OS were 34 and 39 months with 3-year and 5-year PFS of 62% and 52% and 3-year and 5-year OS of 70% and 60%. Baseline MTV and TLG were significantly higher in patients with partial response compared to complete response group at end of treatment ($p = 0.018$ and $p = 0.027$), while no significant differences were found at interim ($p = 0.979$ and $p = 0.510$). Other metabolic PET/CT features showed no statistically significant difference among complete response and partial response group both on interim and end of treatment. In univariate analysis, SUV_{bw}, SUV_{lbm}, SUV_{bsa}, L-L SUV R and L-BP SUV R were not related to outcome survival. Instead, MTV and TLG were confirmed to be independent prognostic factors both for PFS ($p = 0.008$ and $p = 0.009$) and OS ($p = 0.005$ and $p = 0.012$). **Conclusion:** In conclusion, in our study we demonstrated that metabolic tumour features (MTV and TLG) were significantly correlated with outcome survival, both for PFS and OS and were significantly lower in patient with complete response after therapy compared to partial response group.

OP-252

Tumor Absorbed Dose and Changes in FDG PET Parameters in Non-Hodgkin Lymphoma Patients Treated With ¹⁷⁷Lu-Lilotomab Satetraxetan

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Introduction: ¹⁷⁷Lu-lilotomab satetraxetan is a novel anti-CD37 antibody-radionuclide conjugate for treatment of non-Hodgkin lymphoma (NHL) patients. Patients from four treatment arms with different pre-treatment and pre-dosing regimens in the phase 1 part of the LYMRIT-37-01 trial were included. Patients were injected with 10, 15 or 20 MBq/kg of ¹⁷⁷Lu-lilotomab satetraxetan. The aim of this work was to calculate changes in FDG-PET parameters at a lesion level and investigate correlations with tumor absorbed doses. **Subjects and Methods:** A total of 40 tumours from 15 patients (1-5 tumours per patient) were included, based on eligibility for dosimetry. Tumour absorbed doses were calculated from post therapy SPECT/CT-images as previously described (Blakkisrud et. al, JNM 58(1) 2017). FDG PET/CT was performed at baseline and three months after treatment. The following PET parameters were measured: Standardized uptake value (SUV) max, SUVpeak, metabolic tumour volume (MTV) and total lesion glycolysis (TLG). MTV and TLG were calculated according to EANM guidelines for tumour imaging v2. The relative change at three months compared to baseline was calculated for each parameter. **Results:** Mean baseline values (range) for SUVmax, SUVpeak, MTV and TLG were 9.5 (4.6 - 19.4), 8.0 (3.5 - 16.8), 13.0 (1.9 - 112.8) ml and 91.2 (7.6 - 1071.1). A full reduction in SUVmax, SUVpeak, MTV and TLG was observed in 18, 25, 26 and 26 tumours, respectively. Average change in FDG PET-parameters for SUVmax, SUVpeak, MTV and TLG were 56, 64, 78 and 75 %, respectively. The tumour absorbed doses ranged from 35 to 859 cGy, with a mean value of 299 cGy. No significant linear correlation was found between tumour absorbed dose and the relative change in PET-parameters. However, when inspecting each patient individually (excluding patients that had a complete reduction in all included tumours), higher tumour absorbed doses resulted in more reductions in SUVmax for 6 of 8 patients. **Conclusion:** Using a generalized linear model, no clear overall correlation between tumour absorbed dose and relative change in the FDG PET parameters were observed. This could possibly be attributed to the fit model and individual differences, as most lesions demonstrated either a complete reduction in SUVmax or an intra-patient increased reduction for higher absorbed doses.

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Monday, October 15, 2018, 08:00 - 09:00, Hall 6

Thyroid: Endocrine Molecular Imaging

OP-253

Comparison of Glucagon-like Peptide-1 (GLP-1) receptor PET/CT, SPECT/CT and 3T MRI for the localisation of occult Insulinomas: evaluation of diagnostic accuracy in a prospective crossover imaging study

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Purpose: Benign insulinomas are the most prevalent cause of endogenous hyperinsulinaemic hypoglycaemia (EHH) in adults and due to their small size difficult to localise. We aimed at prospectively comparing the accuracy and clinical impact of glucagon-like peptide-1 receptor (GLP-1R) positron emission tomography/computed tomography (PET/CT), single-photon emission computed tomography/computed tomography (SPECT/CT), standardised 3-Tesla contrast-enhanced magnetic resonance imaging (study-MRI), and prior performed external computed tomography and/or magnetic resonance imaging (prior-external CT/MRI) in patients with EHH. **Methods:** We prospectively enrolled patients with neuroglycopenic symptoms due to EHH. GLP-1R SPECT/CT, PET/CT and study-MRI were performed in a randomised, crossover order within 3-4 days. The reference standard was surgery with histology and normalisation of blood glucose levels. **Results:** From January 2014 until March 2017, 52 patients were recruited. All imaging and invasive procedures before recruitment identified suspicious lesions in 46.2% of patients. GLP-1R PET/CT, SPECT/CT, and study-MRI detected suspicious lesions in 78.8%, 63.5%, and 63.4% of patients. In 38 patients conclusive histology was available for final analysis. Accuracy (95% confidence interval) for PET/CT, SPECT/CT, study-MRI, and prior-external CT/MRI was 93.9% (87.8-97.5%), 67.5% (58.1-76.0%), 67.6% (58.0-76.1%), and 40.0% (23.9-57.9%), respectively (all P-values<0.01, except comparison of SPECT/CT and study-MRI with a P-value=1.0). Impact on clinical management was 42.3%, 32.7%, and 33.3% for PET/CT, SPECT/CT, and study-MRI. Percentage reading agreement was 89.5%, 75.7% and 71.1% for PET/CT, SPECT/CT and study-MRI. **Conclusion:** PET/CT performed significantly better than SPECT/CT and MRI in the localisation of benign insulinomas and should be considered in patients where localisation fails with CT/MRI.

OP-254

⁶⁸Ga-NODAGA-exendin-4 PET/CT for the localization of insulinomas

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Background: Insulinomas are usually small, single benign tumors. Surgery is the therapy of choice and precise preoperative anatomical localization of the tumor is essential. Imaging techniques like CT, MRI as well as somatostatin receptor (SSTR) imaging have limited sensitivity. The stable glucagon like peptide-1 (GLP-1) analog exendin specifically binds to the GLP-1 receptor (GLP-1R), which is markedly upregulated/overexpressed in insulinomas. ^{68}Ga -DOTA-exendin-4 PET/CT has been shown to be feasible in detecting insulinomas. Replacing the chelator DOTA by NODAGA in the labeling process ensures higher specific activities, allowing imaging with sub-pharmacological peptide doses. We propose ^{68}Ga -NODAGA-exendin-4 PET/CT as a promising new method for improved localization of insulinomas. We here present the first data of a multi center prospective imaging study to evaluate the effectiveness of ^{68}Ga -NODAGA-exendin-4 PET/CT. **Methods:** 33 adults aged 24–65 with biochemically proven hyperinsulinemic hypoglycemia were included. PET/CT images were obtained one and two hours after injection of (5–7 μg) 95–105 MBq ^{68}Ga -NODAGA-exendin-4. Current standard imaging was performed within 8 weeks of ^{68}Ga -NODAGA-exendin-PET in all patients, consisting of CT or MRI and SSTR PET imaging. **Results:** ^{68}Ga -NODAGA-exendin-4 PET imaging confirmed insulinoma, i.e., GLP-1R positive lesions, in 25 of the 33 patients with suspected insulinoma. In 15 of these patients, insulinoma were also confirmed by conventional imaging as well as Sst-receptor PET. In two patients, conventional imaging could not confirm the presence of an insulinoma while Sst-receptor PET as well as ^{68}Ga -NODAGA-exendin-4 PET were positive. In one patient, an insulinoma was found using conventional imaging and ^{68}Ga -NODAGA-exendin-4 PET, while Sst-receptor PET was negative. In 5 patients, all other imaging modalities were negative and an insulinoma could only be visualized by ^{68}Ga -NODAGA-exendin-4 PET. In one MEN1 patient, multiple NETs were visualized by conventional imaging and Sst-receptor PET, but no decisive answer could be given on which of these lesions produced insulin leading to recurrent hypoglycemia. In this patient, ^{68}Ga -NODAGA-exendin-4 PET/CT confirmed only one GLP-1R positive lesion. In all patients, GLP-1R positive lesions were pathologically confirmed to be insulinoma. In 7 patients, insulinoma could not be confirmed despite a positive Whipple's triad with any of the imaging techniques applied, including ^{68}Ga -NODAGA-exendin-4 PET. This result may indicate that false positive results can be excluded following ^{68}Ga -NODAGA-exendin-4 PET. **Conclusion:** In conclusion, ^{68}Ga -NODAGA-exendin-4 PET/CT performed better than standard imaging methods, which indicated it is a promising new technique for non-invasive pre-operative detection of insulinomas.

OP-255

Adjunctive diagnostic value of integrated ^{18}F -Choline-PET/contrast-enhanced-CT in primary hyperparathyroidism

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Purpose: we aimed to evaluate the role of integrated ^{18}F -Choline-PET/contrast-enhanced(Ce)-CT in detecting parathyroid adenomas/hyperplasias in patients with primary hyperparathyroidism (PHPT) and negative conventional imaging (CI) work-up (i.e. neck-ultrasonography plus $^{99\text{m}}\text{Tc}$ -sestamibi-scan). We compared the detection-rate (DR) of ^{18}F -Choline-PET/CeCT with that of ^{18}F -Choline-PET/CT and Dynamic-Computed-Tomography (4DCT). We analysed the correlation between the standard-uptake-value (i.e. SUV-ratio) and Ce-degree of each parathyroid adenoma and the association between SUV-ratio and parathyroid-hormone (PTH) and calcium (Ca) levels. Finally, a multivariate-analysis evaluated the association between clinical parameters (i.e. Ca, PTH, age and gender) and ^{18}F -Choline PET/CeCT results. **Subjects & methods:** we prospectively evaluated 44 consecutive patients with biochemically proven PHPT and negative CI. All patients underwent ^{18}F -Choline-PET/CeCT, ^{18}F -Choline-PET/CT and 4DCT, which were acquired at the same time by using the same dedicated PET/CT-scanner. Experienced readers interpreted the images separately, and the DRs of the three imaging modalities were calculated. SUV-ratio and Ce-degree were registered for each positive finding. Histopathology, laboratory report and multidisciplinary follow-up were used as standard of reference to confirm the presence of parathyroid adenoma or hyperplasia. **Results:** ^{18}F -Choline-PET/CeCT proved positive in 32 of 44 patients, with an overall DR of 72.7%. This was significantly higher ($p<0.05$) than that of ^{18}F -Choline-PET/CT (56.8%) and 4DCT (54.6%). No positive correlation was found between SUVs and the Ce-degree and between SUV-ratio and PTH or Ca levels. In multivariate-analysis, only Ca levels were significantly associated to ^{18}F -Choline-PET/CeCT positive findings. **Conclusion:** in the case of PHPT and negative initial imaging studies, ^{18}F -Choline-PET/CeCT may provide adjunctive diagnostic information in about 70% of patients. Its diagnostic impact is significantly higher than that of ^{18}F -Choline-PET/CT and 4DCT.

OP-256

Primary hyperparathyroidism and negative conventional imaging: value of ^{11}C -Methionine PET/CT and comparison with ^{11}C -Choline PET/CT.

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Aim: We aimed to evaluate the effectiveness of ^{11}C -Methionine PET/CT (MET-PET) for preoperative localization of parathyroid lesions in patients with Primary hyperparathyroidism (PHPT), and

negative or equivocal standard imaging techniques (99mTc-Sestamibi Scintigraphy/SPECT, Ultrasonography). Additionally, we intended to compare ^{11}C -Choline PET/CT (Ch-PET) and MET-PET. **Materials and Methods:** 49 patients with a biochemical diagnosis of PHPT were referred for a MET-PET and retrospectively evaluated. Besides, in 10 out of 49 patients a Ch-PET was also performed. Both PET studies were visual and semi quantitatively analysed (parathyroid SUV_{max} values; parathyroid SUV_{max} to thyroid and liver SUV_{max} and SUV_{mean} ratios). Differences among PET studies, standard imaging, blood tests results and surgical findings (subgroup of 30 patients) were explored. **Results:** MET-PET was positive in 42/49 patients (85%). A typical localization in the neck was found in the vast majority, but in 3 cases an ectopic parathyroid lesion was seen. Among 30 patients who undergone surgery, 26 were histopathologically categorized as adenoma, 2 as hyperplasia, and the remaining 2 as normal glands. MET-PET was positive in 22/26 adenoma, and detected 2/2 cases of hyperplasia. Furthermore, MET correctly identified pathologically confirmed parathyroid lesions in 93% and 89% of cases that presented negative or inconclusive US or 99mTc-MIBI Scintigraphy/SPECT, respectively. The weight of adenomas in positive MET-PET was higher than in negatives (median: 652 mg, 200–3000mg, vs 350mg, 300–400mg; $p=0.14$ Mann-Whitney-U test). PTH values were also higher in positive MET-PET studies (median= 154 vs 122.75 pg/ml; $p=0.058$, Mann Whitney-U test). Thyroid uptake was heterogeneous (SUV_{max} ranging from 1.77 to 7.86), showing multinodular goiter, nodular hyperplasia, lymphocytic thyroiditis among others. Ch-PET seems to be as sensitive as MET PET for the localization of parathyroid adenomas. In contrast, Ch-PET yields significantly higher SUV values (SUV_{max} : 6.37 vs 3.59; $p<0.05$, Wilcoxon-signed-rank test) and clearer lesion to background ratio, with higher values of parathyroid SUV_{max} to thyroid SUV_{max} ratio (2.24 vs 1.19; $p<0.05$, Wilcoxon-signed-rank test), parathyroid SUV_{max} to thyroid SUV_{mean} ratio (2.85 vs 1.43; $p<0.05$, Wilcoxon-signed-rank test), parathyroid SUV_{max} to liver SUV_{max} ratio (0.74 vs 0.34; $p<0.05$, Wilcoxon-signed-rank test), and parathyroid SUV_{max} to liver SUV_{mean} ratio (0.92 vs 0.43; $p<0.05$, Wilcoxon-signed-rank test). **Conclusions:** MET-PET is superior to standard techniques for accurate preoperative localization of parathyroid lesions in patients with PHPT. However, Ch-PET provides higher avidity and better signal to the referenced tissue (thyroid and liver), which may lead to displace not only current conventional studies but also MET-PET.

OP-257

Optimization of ^{11}C -choline positron emission tomography protocol for localization of parathyroid adenomas in patients with primary hyperparathyroidism

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Purpose: To evaluate the optimal tracer uptake time, the minimally amount of radioactivity and the inter-observer agree-

ment for ^{11}C -choline positron emission tomography/computed tomography (PET/CT) in patients with primary hyperparathyroidism (pHPT). **Subjects & methods:** Twenty-one patients with clinically suspected pHPT were retrospectively studied after injection of mean 6.3 ± 1.2 MBq/kg. PET list mode data of the first nine patients, scanned for up to max 60 min, were reconstructed in 10 min frames mimicking varying ^{11}C -choline uptake times from 10 to 60 min postinjection (p.i.) to assess optimal tracer uptake time. Parathyroid adenoma (PTA) to background contrast ratios were calculated, using standardized uptake values (SUVs), and compared. The first time frame in which there were no significant differences compared to later time frames, was considered the optimal uptake time. Also, data was reconstructed with varying durations (1, 2.5 and 5 min) at 20–30 min p.i. (established optimal uptake time), mimicking less administered radioactivity. To establish the minimal radioactivity administered, the variability of SUVs for PTA and thyroid tissue, normalized to 10 min time frame level of the established optimal uptake time (since the individual measurements of SUV per patient varied considerably), was analysed. Furthermore, four observers were asked to analyse the ^{11}C -choline uptake for PET/CT scans in four randomized rounds for all 21 patients, with increasing scan duration per round. P-values of <0.05 were considered statistically significant. **Results:** Most PTA/normal tissue contrast ratios were constant (not significant) at 20–30 min p.i., compared to later timeframes. Variability in SUVs was significantly different for the 1 min versus 2.5 and 5 min scan duration, while there was not a significant difference in SUV variability between the 2.5 min and 5 min scan durations, except for SUV_{mean} thyroid. The inter-observer analysis showed that the Fleiss' kappa and ICC values of the 1 min scan were classified as 'moderate' (values between 0.53 to 0.57). The kappa and ICC values in the scans with 2.5, 5 and 10 min duration classified as 'good' (values between 0.66 to 0.74), although most values were slightly lower in the scan with 2.5 min duration. **Conclusion:** The optimal tracer uptake time for ^{11}C -choline PET/CT for visualizing PTAs in pHPT is 20 minutes. Compared to a scan duration of 10 min using an injected activity of mean 6.3 MBq/kg, the procedure may be shortened (halved) in time, or less radioactivity (half the amount) may be administered, without noticeably losing inter-observer accuracy.

OP-258

The Efficacy of 18F Choline PET/CT in comparison to Tc99m MIBI SPECT/CT in the Localisation of Hyperfunctioning Parathyroid Gland in primary Hyperparathyroidism

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Purpose: To determine the role of 18F-FCH PET/CT in comparison to Tc-99m MIBI SPECT/CT in primary hyperparathyroidism and to investigate if SUVmax may be indicative of disease severity. **Subjects and Method:** Forty-three primary hyperparathyroidism patients (21F,12M, mean age: 56.09) who underwent

Tc-99m MIBI SPECT/CT and 18F-FCH PET/CT and had inconclusive neck USG were involved. Diagnostic power of both modalities and relationship between SUVmax and biochemical (serum PTH, Ca, P, Vit D3 levels, urinary Ca excretion/24 hrs) and clinical (BMD and urinary USG results) parameters were analysed. **Results:** In 34/43 patients, Tc-99m MIBI SPECT/CT and 18F-FCH were concordant ($K=0.58$, $p=0.001$). In 8/43 patients with a negative SPECT/CT, 18F-FCH PET/CT accurately localized parathyroid adenomas. In 1/43 patients, 18F-FCH was false negative and Tc-99m MIBI SPECT/CT showed the lesion. Sensitivity, specificity, PPV, NPV and accuracy of Tc-99m MIBI SPECT/CT and 18F-FCH PET/CT were calculated as 70%, 100%, 100%, 67%, 81% and 96%, 100%, 100%, 93% and 97% respectively. SUVmax was correlated with lumbar T-scores ($p=0.03$). Mean serum PTH levels were significantly higher ($p=0.04$) and lumbar and femur T-scores were significantly lower ($p=0.02$ and $p=0.03$) in patients with SUVmax > 4.59 (that is, mean SUVmax calculated in positive cases). **Conclusion:** 18F-FCH PET/CT has a high diagnostic power in primary hyperparathyroidism and can be used for further evaluation of patients with inconclusive neck USG and Tc-99m MIBI SPECT/CT. SUVmax of the hyperfunctioning parathyroid gland seems to be predictive of disease severity, in terms of serum PTH and BMD results. Studies with larger patient groups are needed to support these data.

OP-259

Dual point imaging using 18F-fluorocholine PET/CT for detection of parathyroid adenoma

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Aim: Evaluation of 18F-fluorocholine (FCH) uptake in primary hyperparathyroidism comparing PET/CT imaging performed 5 and 60 minutes post injection. **Material and Methods:** Dual point imaging was performed in 46 patients with biochemical evidence of primary hyperparathyroidism at predefined 5 and 60 minutes after injection of 3.2 MBq/kg 18F-fluorocholine using a Philips Ingenuity TF (Philips Healthcare, PC Best, The Netherlands) PET/CT scanner. Images were acquired from the base of the skull to the diaphragm and reconstructed using a 3D ordered-subsets iterative TOF (BLOB-OS-TF) algorithm with PSF after correction for scatter and attenuation. Reconstruction matrix was 288x288. Semi-quantitative analysis was performed in both images with Philips IntelliSpace (version 8.0). A circular ROI with at least 4cm diameter in the upper mediastinum was defined for assessing the mean background SUV (BGmean) of 18F-fluorocholine. A threshold-based VOI with a minimum threshold of 2.5 was used to define the maximum SUV (SUVmax) of any focal uptake above BGmean. For calculating the lesion-to-background ratio (LBRmax), the SUVmax was divided by the BGmean. Statistical evaluation was performed using SPSS version 24.0 for Windows (SPSS Inc. and LEAD Technologies). **Results:** Uptake time was 6.9 (± 2.5 , range 4 to 14) and

61.3 (± 9.4 , range 47 to 83) minutes for early and late imaging, respectively, and showed a significant correlation with background SUVmean (Pearson's coefficient of 0.33 and 0.33 with p-values of 0.022 and 0.027, respectively). Analysis of SUV values in all patients, early vs. late imaging ($n=46$): LBRmax: 6.95 (± 2.87) vs. 12.71 (± 5.64), $p<0.001$ SUVmax: 8.27 (± 3.59) vs. 8.39 (± 3.77), $p=0.659$ BGmean: 1.21 (± 0.24) vs. 0.68 (± 0.13), $p<0.001$ Analysis of histologically confirmed parathyroid adenoma, early vs. late imaging ($n=27$): LBRmax: 7.62 (± 3.00) vs. 14.18 (± 5.74), $p<0.001$ SUVmax: 9.31 (± 3.84) vs. 9.64 (± 4.08), $p=0.395$ BGmean: 1.25 (± 0.24) vs. 0.69 (± 0.13), $p<0.001$ **Conclusion:** Early imaging for detection of parathyroid adenoma is feasible. However, lesion-to-background ratio in parathyroid adenoma using FCH is significantly higher in late than in early imaging without changes in maximum SUV.

OP-260

¹⁸F-fluorocholine PET/CT and parathyroid 4D Computed Tomography: First results of an alternative and efficient imaging tool in reoperative patients with primary hyperparathyroidism

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Aim: To evaluate the sensitivity of ¹⁸F-fluorocholine (FCH) PET/CT and parathyroid 4D Computed Tomography (4D-CT scan) for localization of abnormal parathyroid glands in patients with primary hyperparathyroidism (pHPT) and a previous neck surgery. **Materials and methods:** Medical records of all patients referred for a FCH PET/CT in our institution were systematically reviewed. Only patients with pHPT, a history of a neck surgery (for pHPT or another reason) and an indication of reoperation were included. All patients had parathyroid ultrasound (US) and 99mTc-sestaMIBI scintigraphy. 4D-CT scan was performed in 20 patients. Gold standard was defined by pathological findings and/or US-guided fine needle aspiration (FNA) with PTH level in the washing liquid (PTH *in situ*). **Results:** Twenty-nine patients were included in this retrospective study. 18F-FCH PET/CT identified 34 abnormal foci including 19 unusually located. Median size was 8 mm (4.8 to 25 mm). 4D CT scan detected 11 abnormal glands at first reading and 6 additional after 18F-FCH PET/CT guidance. US and 99mTc-sestaMIBI scintigraphy found concordant foci in 8/29 patients. Gold standard was obtained for 31/34 abnormal foci in 26/29 patients. In a per-lesion analysis, sensitivity, specificity, positive predictive value and negative predictive value were respectively 96%, 13%, 76% and 50% for 18F-FCH PET CT, 75%, 40%, 80%, and 33% for 4D-CT scan. In the per-patient analysis sensitivity was 85% for 18F-FCH PET CT and 63% and 4D-CT scan. 18F-FCH PET/CT results enabled to remove successfully 17 abnormal glands in 17 patients, including 11 with a negative or discordance US/99mTc-sestaMIBI scintigraphy result, and allowed healing in 14 of them. **Conclusion:** 18F-FCH PET/CT is a promising tool in the challenging population of reoperative patients with pHPT. Parathyroid 4D-CT scan appears more as a confirmatory imaging modality.

610 Monday, October 15, 2018, 08:00 - 09:00, Hall 28

Cardiovascular: Integrating Models in MPI - From Injection to Interpretation

OP-261

Patient-specific Rubidium-82 activity required for constant image quality in myocardial perfusion imaging with PET

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Aim: Clinical practice shows degrading image quality in heavy patients who undergo myocardial perfusion imaging (MPI) with Rubidium-82 (Rb-82) PET when using a fixed administered activity. Therefore, our aim was to derive a patient-specific activity protocol in order to obtain a more constant image quality in PET MPI. **Materials and methods:** We retrospectively included 132 patients who underwent rubidium-82 PET rest MPI using a fixed Rb-82 tracer activity of 740 MBq. Image quality was indirectly assessed by measuring the number of prompts in the field of view of the PET scanner. This number was correlated with multiple patient-specific parameters: body weight, mass per body length, body mass index, lean body mass and body fat percentage. A power-law model was fitted to the data after which we selected the parameter with a high coefficient of determination that comprises easy implementation in practice. This parameter was used to derive an activity formula providing a constant number of prompts independent on patients' physical characteristics. Subsequently, the derived formula was validated in 38 additional patients. **Results:** A significant decrease in prompts was observed with increasing body weight ($p < 0.001$). The measured prompts typically decreased by a factor 2.4 from patients < 60 kg to patients > 120 kg. All patient-specific parameters correlated with the number of prompts ($p < 0.001$). Body weight was selected as the best parameter ($R^2 = 0.64$) to correct for the decreasing prompts in heavier patients. The derived activity protocol was: $A_{\text{new}} [\text{MBq}] = 8.4 * \text{body weight} [\text{kg}]$. Using this formula, the number of prompts no longer varied with patient's body weight ($p=0.07$). **Conclusion:** Because the observed linear relation between body weight and Rb-82 tracer activity, we recommend the use of a weight-adjusted tracer activity to obtain a constant image quality in Rubidium-82 PET MPI.

OP-262

No Need For Frame-wise Alignment Of CT And Dynamic Rb-82 PET Data For Myocardial Blood Flow Quantification

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Background: Reliable dynamic PET data are needed to calculate the myocardial blood flow (MBF). However, non-returning repositioning of the heart occurs in 52% of patients undergoing regadenoson-induced stress Rubidium-82 (Rb-82) PET. As a result, misalignment of CT and dynamic PET data may occur,

possible affecting CT-based attenuation correction and thereby PET-based MBF quantification. This misalignment could be overcome by matching the CT and PET for each individual time-frame. Our aim was to quantify this non-returning motion and determine the effect of frame-wise instead of general PET-CT alignment on MBF measurements. **Methods:** We retrospectively included ten patients who underwent regadenoson-induced stress Rb-82 PET/CT (D690, GE Healthcare) in whom we observed non-returning motion. For all scans, we applied two types of PET-CT alignment prior to the attenuation correction and image reconstruction of the dynamic PET data: one with general alignment in which PET data acquired between 2:30-7:00 min was aligned with the CT and applied to all PET time-frames and another using frame-wise alignment in which all 26 time-frames (12x5s, 6x10s, 4x20s and 4x40s) were individually registered to the CT. The difference in alignment positions was compared between the general and frame-wise method. We manually corrected the non-returning motion on the reconstructed aligned PET data as standard procedure (Corridor4DM, v2016) before calculating the MBFs for the three vascular territories; RCA, LAD, and LCX and for the whole myocardium. MBFs were calculated using the one-tissue compartment model using a region of interest of Lortie et al. and compared between both alignment methods. A MBF difference $\geq 10\%$ was considered to significantly influence diagnostic assessment. In addition, we determined the correlation between the difference in alignment positions and the difference in MBFs. **Results:** The mean difference in alignment position was 9.9 ± 4.8 mm in caudal-cranial direction, 1.7 ± 1.7 mm in medial-lateral direction and 0.0 ± 1.7 mm in anterior-posterior direction. The resulting mean relative MBF differences was the highest for the RCA: $4.9 \pm 1.9\%$ while the maximal deviation was 8.8% in all territories. Moreover, no correlations were found between the difference in alignment positions and the difference in MBFs ($p \geq 0.58$). **Conclusion:** The mean magnitude of the non-returning motion induced by regadenoson was 9.9 mm in the cranial-caudal direction. Applying frame-wise instead of general PET-CT alignment did not influence the MBF and seems therefore not necessary in Rb-82 PET.

OP-263

Quantitative myocardial perfusion response to adenosine and regadenoson in patients with suspected coronary artery disease measured with ¹⁵O-water PET

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Purpose: Regadenoson is a vasodilator that is increasingly being used in myocardial perfusion imaging, with simpler dosing and better tolerability than adenosine. There are no studies comparing absolute flow response by regadenoson against adenosine in the same patients. The aim of the present work was to directly compare the quantitative flow responses of regadenoson against adenosine using cardiac ¹⁵O-water PET imaging in patients with CAD. **Materials and methods:** Sixteen patients (14 male; mean age 68 y; range 60-79 y) with known or suspected

coronary artery disease underwent two rest/stress PET investigations: at rest and during vasodilator stress with adenosine and at rest and during vasodilator stress with regadenoson. Each PET scan consisted of a 6 min dynamic scan starting simultaneously with bolus injection of 400 MBq ^{15}O -water (5 mL at 1 mL/s followed by a 35 mL saline flush at 2 mL/s). Adenosine (140 $\mu\text{g/kg/min}$) was infused during 8 min starting 2 min prior to ^{15}O -water injection, whereas regadenoson (400 μg in 5 mL saline) was given as a 10 s infusion followed by a 5 mL saline flush during 10 s, starting 30 s prior to ^{15}O -water injection. Data were analysed semi-automatically using aQuant software to calculate segment-based MBF values for three coronary artery territories. Correlation and agreement between adenosine-stress MBF and regadenoson-stress MBF values were assessed using regression analysis and intra-class correlation coefficients (ICC). **Results:** Data from one patient was excluded due to excessive motion artefacts. Global mean ($\pm$ SD) MBF values at rest and adenosine-stress were 0.94 ± 0.27 and 2.45 ± 0.86 mL/g/min and at rest and regadenoson-stress 0.88 ± 0.23 and 2.32 ± 1.15 mL/g/min ($p=0.053$ and $p=0.46$). ICC between adenosine-stress and regadenoson-stress regional MBF was 0.85. **Conclusion:** Regadenoson-stress MBF correlated moderately well with adenosine-stress MBF values.

OP-264

Comparison of Rb-82 PET/CT and Cardiac MRI for Quantification of Left Ventricular Function

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Aim: The aim of this ongoing study is to validate rubidium-82 positron emission tomography and computed tomography (Rb-82 PET/CT) quantification of left ventricular ejection fraction (LVEF) using Corridor 4DM quantitative software (4DM). **Materials:** Amongst patients with known or suspected coronary artery disease referred for routine Rb-82 PET and eligible for cardiac magnetic resonance imaging (cMRI), 10 patients were recruited for additional cMRI for comparison after informed consent. Median age was 62.2 (38.6–78.1) years, 70% male, BMI 27.1 (23.1–31.8). **Methods:** Resting acquisition of rest Rb-82 PET/CT was performed in supine position following intravenous bolus injection of 1100 MBq Rb-82 in the antecubital vein. ECG-gating was performed for 150 sec starting 150 sec after bolus with 8-timebins sampling. Window of acceptance was defined as resting beat-to-beat (R-R) interval $\pm 30\%$. Acquisition was performed at GE Discovery 710 in LIST-mode. Reconstruction was performed iteratively with VUE point FX (2 iterations, 24 subsets) and a standard z-axis filter with 6.4mm cutoff. If necessary PET-overlay was manually fitted to CT before attenuation-correction was performed. Images were analyzed with Corridor 4DM v.2015 to estimate LVEF, end-systolic volume (ESV) and end-diastolic volume (EDV), blinded for the results of the cMRI. Automatic detection of basal plane and left ventricle wall was used for all patients. cMRI was performed according to regular procedure and calculation of LVEF, ESV and EDV was done by an experienced cardiologist. **Results:** Median

and range for cMRI measurements was 116 ml (90–170) for EDV, 38.5 ml (16–113) for ESV and 66.5% (33–87) for LVEF. Median and range for Rb-82 measurements was 88.5 ml (65–158) for EDV, 34 ml (25–106) for ESV and 58% (33–70) for LVEF. EDV was significantly lower ($p < 0.0005$) when determined by Rb-82 than by cMRI (mean difference 24.8 ml, 95% CI 16.3–33.3 ml). There was no significant difference for LVEF ($p = 0.055$). Apart from the significant underestimation of EDV, Bland-Altman analysis did not show any systematic bias for EDV, ESV and LVEF. **Conclusion:** This ongoing study shows good agreement between LVEF obtained by Rb-82 PET/CT and cMRI. However EDV was 24.8 ml lower determined by Rb-PET than by cMRI. The range of examined LVEF in this study is rather small so far. Further studies are needed to validate this method of determining LVEF in patients with a wider range of left ventricular function.

OP-265

Impact of left ventricular mechanical dyssynchrony in patients with long standing diabetes mellitus and normal gated SPECT-MPI

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Purpose: Left ventricular mechanical dyssynchrony (LVMD) indices by phase analysis has been established as a prognostic marker for predicting major adverse cardiac events (MACEs) in ischaemic, non-ischemic cardiomyopathy and end-stage renal disease but not in diabetes mellitus (DM). We sought to test whether the LVMD indices are the predictor of MACEs in diabetic patients with absent perfusion defects and adequate LV ejection fraction ($>55\%$) on gated SPECT-MPI. **Methods:** A total of 136 diabetic patients (age 60.8 ± 11.3 years) with absent perfusion defect and left ventricle ejection fraction (LVEF) $\geq 55\%$ were included in the study. All patients were followed for over a 2-year period for any adverse cardiac event, depending on which patients were divided into two groups. SPECT-MPIs data was reprocessed to derive quantitative parameters such as LVEF, end-diastolic, end-systolic volumes and LVMD indices including phase bandwidth (PBW) and phase standard deviation (PSD). Binary logistic regression analysis and Kaplan-Meier method was used to identify independent predictors of cardiac events. **Result:** During mean follow-up period of a 23.3 ± 10.3 month, thirteen (9.5%) patients experienced MACEs including one cardiac death. Patients who experienced MACEs showed significantly higher PSD and wider PBW ($16.0 \pm 9.4^\circ$ vs $10.3 \pm 6.4^\circ$; $p = 0.004$, and $52.7 \pm 36.4^\circ$ vs $33.1 \pm 16.2^\circ$; $p = 0.001$ respectively) than those who did not. Moreover, both PSD and PBW showed statistically significant correlation ($r = 0.25$; $p = .004$ and $r = 0.27$; $p = .002$, respectively) with duration of DM. Univariate logistic regression analysis revealed a significant association of duration of DM, long-term diabetic complications and LVMD indices (both PSD and PBW) for predicting MACEs. Kaplan-Meier event-free survival analysis revealed a significantly higher rate of MACEs (Log rank = 10.02; $p = 0.001$) in patients with high PSD and wide PBW group than in the low PSD and narrow PBW group. An overall fit model consisting of high PSD and wide PBW group

was improved by the addition of long-term complications ($\chi^2 = 15.9$; $p = 0.03$) of DM and further enhanced by the addition of DM duration of ≥ 15 years ($\chi^2 = 24.7$; $p = 0.007$) as variables.

Conclusion: The LVMD indices by gated SPECT-MPI are novel prognostic marker in patients with DM and absent perfusion defects. Furthermore, the presence of long-term complications and ≥ 15 -year duration of DM provides an incremental advantage for prediction of MACEs.

OP-266

Effects Of Re-training On Neural Network Diagnosis To Detect Ischemia In Myocardial Perfusion Imaging: Comparison Of Two Modes Of Trainings

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Purpose: While artificial neural network (ANN), one of artificial intelligence, was applied to detect ischemia on myocardial perfusion imaging, the effect of training on the diagnostic ability was not evaluated. The aim of this study was to compare the effects of European and Japanese modes of trainings on the diagnostic accuracy of ischemia. **Methods:** ANN was trained on data from 1051 Swedish patients (male 47%, 62 ± 10 years) and experienced Swedish physicians classified perfusion as normal or abnormal (Training E). In the second version re-trained in Japan (Training J), 12 hospitals in Japan collaborated ($n = 1001$, male 75%, 69 ± 10 years) using ^{99m}Tc-MIBI. Definition of localization for candidate regions was refined, and the re-training was performed to identify more number of ischemia and mild degree of abnormality. In the validation study, 106 patients with coronary angiographic findings, comprising multi-vessel disease (≥50% stenosis) (52%) or old myocardial infarction (27%), or who had undergone coronary revascularization (30%) were used. The ANN probabilities of stress defects and induced ischemia were calculated in candidate regions of abnormalities. The diagnostic accuracy was compared using receiver-operating characteristics (ROC) analysis and the area under the ROC curves (AUC). The gold standards were the expert interpretation for all data, and a subgroup of patients with coronary stenosis, from which infarction and coronary revascularization were excluded. **Results:** Although the AUC for stress defects were 0.95 and 0.93 (n. s.) for Trainings J and E, respectively, that for detecting ischemia was significantly improved in Training J ($p = 0.006$): AUC 0.96 (sensitivity 87%, specificity 96%) for Training J vs. 0.89 (sensitivity 78%, specificity 97%) for Training E. The improvement in the AUC was also significant for patients with neither coronary revascularization nor old myocardial infarction ($p = 0.009$). With the gold standard of expert interpretation, AUC was 0.98 (sensitivity 88%, specificity 100%) for Training J and 0.88 (sensitivity 76%, specificity 100%) for Training E. The diagnostic accuracy by Training J was also improved in patients with either single-vessel disease or no stenosis (AUC, 0.81 vs. 0.66, $p = 0.006$) when coronary stenosis was used as the gold standard (AUC by the expert, 0.74, $p = 0.13$ vs. ANN). **Conclusion:** The diagnostic ability of the ANN

was improved by the new training particularly for detecting induced ischemia. The intention of training as a “teacher” could be successfully reflected on the detectability and accuracy of artificial intelligence.

612 Monday, October 15, 2018, 08:00 - 09:30, Meeting Room B
UEMS/EBNM: Clinical Audit Session

OP-267

Introduction

J. Prior; Centre Hospitalier Universitaire Vaudois, Médecine nucléaire, Lausanne, SWITZERLAND.

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QUANUM - An Update

TBA; TBA

OP-269

Clinical Audits - An EURATOM Requirement

TBA; TBA

OP-270

Alternative Pathways to UEMS/EANM Accreditation

S. Mirzaei; Wilhelminenspital der Stadt Wien, Institute of Nuclear Medicine with PET-Center, Vienna, AUSTRIA.

OP-271

Certificate Distribution to Centers Accredited in Since Last EANM Congress

701/704 Monday, October 15, 2018, 10:00 - 11:15, Plenary Hall

Plenary 2: To Do, or Not to Do Dosimetry, that is the Question

OP-272

Personalized Therapies in Oncology: Pro and Cons

S. Gillesen; Division of Cancer Sciences, University of Manchester and The Christie Hospital, Manchester, UNITED KINGDOM and Kantonsspital St. Gallen, Division of Oncology/Haematology and University of Bern, SWITZERLAND.

OP-273

Need of Careful Personalized Dosimetric Evaluation in Radionuclide Therapy

G. Flux; Royal Marsden NHS Trust & Institute of Cancer Research, Sutton, UNITED KINGDOM.

OP-274

Dosimetry in Clinical Radionuclide Therapy: The Devil is in the Detail

L. Bodei; Memorial Sloan Kettering Cancer Center, New York, UNITED STATES OF AMERICA.

801 Monday, October 15, 2018, 11:30 - 13:00, Plenary Hall

CME 6 - Dosimetry: Alpha Particle Dosimetry - When, Why and How

OP-275**Introducing Alpha-Particle Emitter into the Clinic, Does Dosimetry Answer all Questions?***J. Nagaraja; Radboudumc, Radiology and Nuclear Medicine, Nijmegen, NETHERLANDS.***OP-276****Small Scale Dosimetry Models, a Universal Answer for Personalized Alpha-Therapy?***R. Hobbs; Johns Hopkins Medical Institutions, Radiation Oncology, Baltimore, UNITED STATES OF AMERICA.***OP-277****The Significance of Radium - 223 in the Therapy Landscape of Advanced Prostate Cancer***A. Haug; AKH Vienna, Medical University of Vienna, Vienna, AUSTRIA.***OP-278****The Role of Dosimetry to Predict Biological Effect in Patients Treated with Ra233***L. Strigari; IRCCS Regina Elena National Cancer Center, (IRE-IFO), Laboratory of Medical Physics and Expert Systems, Rome, ITALY.***OP-279****The Role of Dosimetry to Predict Biological Effect in Patients Treated with Ra233***R. Sciuto; Istituto Regina Elena, Nuclear Medicine Department, Rome, ITALY.*

802 Monday, October 15, 2018, 11:30 - 13:00, Hall 2

Joint Symposium 11 - Thyroid/ATA / ETA: TBC

Session details not finished as per date of publishing.

803 Monday, October 15, 2018, 11:30 - 13:00, Hall 3

Joint Symposium 12 - Oncology / EORTC: Integrating PET into RECIST

OP-285**Driving (i)RECIST - The EORTC Perspective***S. Litière; EORTC statistician, Brussels, BELGIUM.***OP-286****Methodological Considerations for Integrating PET into RECIST***R. Boellaard; VU University Medical Centre, Radiology and Nuclear Medicine, Amsterdam, NETHERLANDS.***OP-287****How to Integrate PET into RECIST - A Joint EANM/EORTC Project***N. Aide; Service de Médecine Nucléaire, Centre Régional de lutte contre le cancer François Baclesse, Caen, FRANCE.*

806 Monday, October 15, 2018, 11:30 - 12:45, Hall Y

Do.MoRe: Reconstruction

OP-288**Quantitative accuracy of ^{15}O -water cerebral blood flow images based on penalized likelihood reconstruction***J. Sousa¹, L. Appel¹, X. T. Fang¹, M. Engström², M. Khalighi³, H. Ahlström¹, M. Lubberink¹; ¹Department of Surgical Sciences, Uppsala University, Uppsala, SWEDEN, ²GE Healthcare, Stockholm, SWEDEN, ³GE Healthcare, Stanford, CA, UNITED STATES OF AMERICA.*

Objectives: Penalized likelihood reconstruction allows for fully convergent iterative reconstruction that leads to a higher image contrast while limiting noise when compared to ordered subset expectation maximization (OSEM). Use of penalized likelihood reconstruction may have added value in the computation of cerebral blood flow images (CBF) using ^{15}O -water, where noisy PET images due to short frame durations and short radioactive half-life affect quality of parametric images. The aim of the present work was to assess the quantitative accuracy of ^{15}O -water CBF images based on block-sequential regularized estimation maximization (BSREM; Q.Clear) images. **Methods:** Twelve subjects underwent a 10-min dynamic (1x10, 8x5, 4x10, 2x15, 2x20, 2x30, 6x60s) ^{15}O -water PET scan on a 3T time-of-flight (TOF) PET-MR (Signa, GE Healthcare). Arterial blood was sampled continuously and measured using an on-line detector (Swisstrace). PET scans were reconstructed using both OSEM, (4 iterations, 28 subsets, 5 mm Gaussian filter) and BSREM with beta values of 25, 50, 75 and 100, including TOF and resolution recovery, using zero-echo-time attenuation correction. CBF images were computed using a basis function implementation of the standard single tissue compartment model including blood volume parameter. Volumes-of-interest were defined using a probabilistic template on co-registered T1 images and transferred to the CBF images. Correlation (Spearman) and relative difference in CBF values between methods were assessed for whole-brain grey (GM) and white matter (WM) VOIs. Image contrast, defined as GM/WM, was also compared between BSREM and OSEM and image quality was assessed by visual inspection of parametric images. **Results:** High correlation was found between BSREM and OSEM for GM and WM regardless of beta value (r 0.99 and 0.94, respectively). Increase in GM CBF values compared to OSEM ranged from 7.9 (range 5.6-9.3)% (beta 100) to 12.4 (range 8.7-14.0)% (beta 25), with much smaller changes in WM CBF values. Mean GM/WM contrast increased by 6.4 (range 4.3-9.6)% to 7.1 (range 5.9-8.6)% for beta 25 and 100, respectively. Visual inspection of the images showed degraded quality of CBF images for all beta values of 75 or lower. **Conclusion:** A high correlation was found between CBF values based on BSREM and OSEM, with

BSREM images leading to higher GM CBF values and higher GM/WM contrasts. A beta value of 100 resulted in the highest GM/WM contrast and best image quality among the included beta values. Beta values higher than 100 are to be used for dynamic ^{15}O -water PET data if improved CBF image quality is required.

OP-289

Feasibility of Framework to Assess Noisy Data Inconsistency of SPECT Projection Data Prior to Tomographic Reconstruction

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Aims: We propose a framework to assess task dependent SPECT data quality prior to reconstruction, and allowing for decisions to improve or replace the data at the acquisition step. If the task dependent quality is insufficient a re-scan may be the best option, despite the possible correction and compensation methods within the reconstruction. The aim in this work is to test if an image based metric allows assessing noisy SPECT data inconsistency due to motion as compared to a visual observer. **Methods:** We used a computationally efficient center-of-light metric (CLM) on all the frames. In this feasibility work we computed one full FOV CLM and four quarter-FOV CLMs for each projection image. We then performed a local fluctuation analysis on these sets of CLMs, and mapped the local fluctuation quantity in mm to a numerical quality score (1-10), sensitive to both frame-to-frame motion and noise. We used 77 clinical data of different application with a total count median of 7.07Mc. 21 with and 56 without visible motion in the projection data, as well as count reduced the data to 50% and 10% of total counts by binomial subsampling. We performed ROC analysis at these different count levels comparing the CLM to truth established by human observers. **Results:** At 100% standard clinical count level for the respective application the CLM resulted in Area under the ROC curve (AUC) of 97.6% with a standard error (SE) of 0.0169 at $P < 0.0001$, an Associated Criterion of $AC > 6$, a sensitivity of 100% and specificity of 92.86%. At 50% the $AUC = 93.2\%$, $SE = 0.0287$, $AC > 8$, $P < 0.0001$ with sensitivity of 90.48% and specificity of 85.71% and at 10% the $AUC = 54.5\%$, $SE = 0.0713$, $P = 0.53$, $AC > 7$ with sensitivity of 100% and specificity of 8.93%, showing that now noise is excessive, destroying the ability to assess motion with the proposed CLM. A comparison between ROC curves shows no statistical significant difference between the 100% and 50% data, but significant at $P < 0.0001$ when compared to the 10% data. **Conclusion:** We demonstrated the feasibility to assess and characterize quality issues of SPECT data prior to reconstruction using various center-of-light metrics at various noise levels, where at clinical (7 Mc total counts) and 50% reduced count levels the AUC is 98%, 93% respectively dropping to 53% for 10% count reduced data. This also allows establishing a lower noise floor at which subsequent intra reconstruction motion correction methods could fail as noise dominates.

OP-290

Use of the CT Scout View (Topogram) for Accurate Attenuation Correction of Planar Nuclear Medicine Studies

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Introduction: Planar quantitative studies (e.g. renograms) can benefit from the use of geometric mean to correct for organ depth. However geometric mean does not correct for attenuation due to total body thickness. With SPECT-CT systems becoming more common, we have examined the potential for the CT scout view (topogram) to provide an attenuation map for planar studies using the geometric mean. **Method:** We examined the relationship of the topogram pixel values with different depths of water (0-30cm) in a bespoke water tank. The topogram scans were fixed at 20mAs but the tube voltage was varied from 80kVp to 140kVp. A kidney sized phantom with known activity (nominal 100MBq Tc99m) was then imaged at different depths (0-15cm) in the water tank and with variable water levels (15-30cm) which relate to different body thicknesses. The attenuation corrected geometric mean counts were calculated using the derived total thickness from the topogram image and a linear attenuation coefficient of $\mu = 0.12\text{cm}^{-1}$. These values were then divided by the in-air sensitivity factor (cps/MBq) to give a derived activity (MBq). The derived activities of the phantom were compared to the actual activity for the different positions and water depths. **Results:** The relationship of the topogram pixel values with water depth was remarkably linear over the range 0-30cm. The uncertainty for the prediction of 'body thickness' was acceptable at $\pm 4\text{mm}$ (95% CI). All derived measurements of phantom activity using the topogram and geometric mean technique were within $\pm 5\%$ of the actual activity for depths $< 20\text{cm}$ and within $\pm 10\%$ for depths 20-30cm. **Discussion:** We acknowledge that patients are composed of many different substances with varying attenuation coefficients (tissue, fat, blood, bone, etc.). However, the concept is not to use the CT topogram to quantify the different linear attenuation coefficients of these substances (as is the case for SPECT-CT attenuation correction) but rather estimate the equivalent thickness of water that these substances contribute on a pixel by pixel basis. **Conclusion:** The topogram gives a very quick and accurate method to determine total body thickness for attenuation correction of planar studies with minimal additional radiation dose ($< 0.1\text{mSv}$). The corrected organ counts are then directly equivalent to the organ activity in MBq using the in-air sensitivity factor. This method may be a useful technique in quantifying absolute organ activity where SPECT-CT is not possible (e.g. dynamic studies).

OP-291

Joint dual photopeak Lu-177 SPECT image reconstruction with a stacked system model

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Aim: Although Lu-177 has two relatively low intensity gamma-rays, 112.9-keV (6.2%) and 208.4-keV (10.4%), typically only the 208-keV photopeak is used in SPECT imaging. However, including both photopeaks can be beneficial especially in low count-rate situations such as imaging at later time points for

dosimetry following Lu-177 therapies or potentially pre-therapy diagnostic imaging. We propose/evaluate a joint image reconstruction (JIR) method for Lu-177 where a single source distribution is reconstructed from projections acquired from both windows within a unified framework. **Methods:** The JIR approach estimates a single image by concatenating the datasets from the two windows and stacking the corresponding system models that each include the known gamma-ray emission yield, camera detection efficiency, attenuation map and 3D-collimator detector response at each photopeak energy. Because the JIR system model includes gamma-ray yields, the lower-count window is automatically given appropriately lower weight in the Poisson model. To evaluate JIR, we used the following Lu-177 phantom studies with multiple dual energy-window acquisitions/realizations on a Symbia SPECT/CT with medium-energy collimators: 1) measurement with six 'hot' spheres (2,4,8,16,30 and 113 mL) in a 'warm' background, 2) measurement with 'hot' spheres in the 'warm' liver of a torso-phantom at low (typical for pre-therapy) and high count-levels, and 3) XCAT simulations of liver lesions with count-levels typical for patient imaging at 1 and 7 days after Lu-177 DOTATATE. We reconstructed images with single-photopeak (SIR-113, SIR-208) and joint dual photopeaks (JIR) methods, including triple-energy-window scatter, using 50 iterations of in-house EM algorithm. We evaluated each reconstruction with image-ensemble-noise (IEN: variability across multiple acquisitions), contrast-recovery (CR), contrast-recovery-to-noise-ratio (CRNR) and point source calibration-based activity-recovery (AR). **Results:** Visual comparison showed similar quality in both SIR-208 and JIR, while SIR-113 generated noisier image. Quantitatively, JIR improved noise significantly in all studies while keeping AR and CR at similar level, thereby improving CRNR. In sphere phantom measurements, compared to SIR-208, JIR improved IEN by 19.0% and CRNR of each sphere by 20.1–23.2%. In liver-torso phantom measurement, JIR improved IEN by 15.9% (20.9% at lower count-level) and CRNR by 16.7–17.5% (17.3–21.5% at lower count-level). In XCAT simulation, JIR improved IEN by 20.8% (20.9% at lower count-level) and CRNR by 25.4–25.8% (24.9–25.5% at lower count-level). The improvements over SIR-113 were substantially higher. **Conclusion:** In clinically realistic evaluations, joint reconstruction, where the Poisson nature of the multi-window acquisitions is modeled appropriately, significantly improved contrast-recovery-to-noise-ratio compared to single photopeak reconstruction of either photopeak.

OP-292

Evaluation of the accuracy and consistency of a quantitative SPECT reconstruction method for 99mTc Liver MAA images

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Purpose: With the increasing use and diversity of dosimetry applications based on SPECT images, there is a growing need for accurate and consistent quantification of these images. A notable example is the use of 99mTc-MAA scanning for 90Y SIRT pre-planning. In the current work, the accuracy and con-

sistency of 99mTc quantification using an OSEM-based SPECT reconstruction tool (SPECTRA Quant™, MIM Software Inc.) is reported. **Methods:** Five SPECT images of a multi-compartment liver phantom were acquired over a period of 5 hours after injection of 223MBq of 99mTc. The phantom contains a liver compartment with 3 lesion compartments in which known activity concentrations were injected. At each imaging timepoint, primary and lower scatter energy windows were acquired. A CT image of the phantom was acquired for attenuation correction and to define regions, including a large background region in the liver to evaluate the accuracy of a large structure minimally affected by partial volume effect. The first timepoint projections were decay corrected to the injection time before a reconstruction step (8 subsets, 16 iterations), including CT-based attenuation correction, dual energy window (DEW) scatter correction, and resolution recovery. The quantitative conversion factor was defined in counts/second/MBq from the known injected activity and the number of recorded counts within the whole phantom, and was applied to convert the image into units of Bq/ml. Reconstruction of subsequent timepoints followed this same protocol while using the quantitative conversion factor from the first timepoint. **Results:** The average errors between known injected activities and measured activities over each timepoint were: whole phantom, 0.3%; background region, 1.2%; 25mm-diameter sphere, -36.2%; 32mm-diameter sphere, -25.0%; and 48mm x 32mm ovoid, -15.9%. The coefficients of variation (COVs) were: whole phantom, 0.24%; background region, 0.81%; 25mm-diameter sphere, 0.52%; 32mm-diameter sphere, 0.65%; and 48mm x 32mm ovoid, 0.16%. **Discussion:** The quantitative accuracy was very high (<2% error) in larger regions not influenced by partial volume effects, such as the background region, while being lower (15.9–36.2% error) in smaller regions as expected due to the influence of partial volume effects. The algorithm was found to have a high degree of consistency with a COV<1% across the 5 timepoints. The accuracy and consistency of the MIM SPECTRA Quant tool shows promise for use in 90Y treatment planning. *May not be available in all countries. Contact MIM Software for details.

807 Monday, October 15, 2018, 11:30 - 13:00, Hall 1

Pitfalls & Artefacts 4 - Interactive Clinical Cases: Neuroimaging / Physics: Amyloid Imaging

OP-293

Effects of Acquisition and Reconstruction Settings on Image Interpretation and Quantification

B. Sattler, University Hospital Leipzig, Department for Nuclear Medicine, Leipzig, GERMANY.

OP-294

Equivocal and Borderline Amyloid PET Scans - Pitfalls and Challenges of Visual Analysis

S. Morbelli, IRCCS Azienda Ospedaliera Universitaria San Martino, Department of Nuclear Medicine, Genoa, ITALY.

OP-295**Quantifying Amyloid Imaging: SUVR and Centiloids**

W. L. Wong; Mount Vernon hospital, Nuclear Medicine, Middlesex, UNITED KINGDOM.

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Monday, October 15, 2018, 11:30 - 13:00, Hall 4

Clinical Oncology - Rapid Fire Session: GIT up!

OP-297**Metabolic heterogeneity as a PET-biomarker predicts overall survival of pancreatic cancer patients**

E. M. M. Smeets¹, B. Feurecker², J. Teuwen¹, J. A. W. M. van der Laak¹, M. Gotthardt¹, J. Siveke³, R. Braren², F. Ciompi¹, E. H. J. G. Aarntzen¹; ¹Radboudumc, Nijmegen, NETHERLANDS, ²Technical University of Munich, Munich, GERMANY, ³University Hospital Essen, Essen, GERMANY.

Introduction: Pancreatic ductal adenocarcinoma (PDAC) shows a 5-year survival rate of 8% (Siegel et al. 2016), mostly due to the lack of effective treatment options (Ryan et al. 2014). PDAC has a remarkable fibrotic reaction (Neesse et al. 2015) that impacts tumor metabolism, which can be measured on PET/CT images (Heid et al. 2017). To date, standard PET-derived parameters, e.g. SUV_{max} , have not been able to provide prognostic information. In this study, we build a logistic regression model based on [¹⁸F]FDG-PET texture features (TF) that classifies PDAC as heterogeneous or homogeneous. We confirm that our method has a good correlation with overall survival when applied to an independent validation set. **Methods:** Patients with histologically proven PDAC (n=107) who underwent [¹⁸F]FDG PET/CT (Siemens Biograph mCT, Knoxville, US) were selected from the hospital system Nijmegen (The Netherlands). An independent cohort of 37 patients was selected from the hospital system of Munich (Germany). Seventy-one EANM reconstructed scans (Boellaard et al. 2010) from Nijmegen were visually labeled as 'homogenous' (n=32) or 'heterogeneous' (n=39) by two experienced Nuclear Medicine physicians. In order to extract TF, tumors were delineated using 40% threshold of the SUV_{max} with manual correction. TF previously shown to be robust with respect to PET scan variability were extracted using the PyRadiomics toolbox (van Griethuysen et al. 2017). A logistic regression classifier was built and applied to the 73 cases held out, which included the independent cohort of Munich. The training set was classified via leave-one-out cross validation. Prognostic impact was assessed by Kaplan Meier survival analysis and log-rank test. The performance of the classifier was evaluated with a leave-one-out cross-validation. **Results:** We obtained an accuracy of 0.73 and AUC of 0.80 in classifying PDAC as heterogeneous or homogeneous tumors. For the 144 patients the overall survival of PDAC tumors classified as heterogeneous was significantly worse than for homogeneous tumors; median overall survival 34 weeks (95%CI 20 to 49 weeks) versus median 67 weeks (95%CI 46 to 102), p= 0.0285). This is in contrast with single standard PET parameters (SUV_{max} , kurtosis, metabolic tumor volume), single TF (entropy), which had no significant prog-

nostic impact. **Conclusions:** We developed an algorithm that accurately classifies PDAC as heterogeneous or homogeneous, based on a set of [¹⁸F]FDG PET derived texture features. We showed that the classification result has prognostic value improving upon standard PET derived parameters and single texture features and also when applied to an independent cohort.

OP-298**FAPI-PET/CT (Fibroblast Activation Protein Inhibitor) in Staging of Pancreatic Cancer**

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Aim: Preclinical and preliminary clinical results for PET/CT with a ⁶⁸Ga-labeled inhibitor of the fibroblast-activating-protein (FAPI) were promising (1,2). Due to its desmoplastic growth pattern, pancreatic cancer is a promising candidate to especially benefit from this novel tracer. Our aim was to compare the findings of FAPI-PET/CT in patients with pancreatic cancer in comparison to the respective gold-standard. **Methods:** 10 patients suspicious for pancreatic cancer in standard exams received FAPI-PET/CT in advance of a planned surgery. Whipple-pancreatectomy was performed in 6 patients without distant metastases and complete histopathological work up of the pancreas and local lymph-nodes was done. Four patients were suspicious for distant metastases, which were validated by representative biopsies and amended with FDG-PET/CT. **Results:** Primary tumors or histologically proven distant metastasis were detected by FAPI-PET/CT in 10/10 patients; One had a distal cholangiocellular carcinoma, the other nine pancreatic adenocarcinomas. Fibrotic reaction in chronic pancreatitis or pancreatic intra-ductal neoplasia was present in 4/6 resected patients and hampered intra-pancreatic tumor delineation; however, all carcinomas could successfully be allocated as the dominant intra-pancreatic hot-spot. 4 patients had lymph node (LN) metastases, in 2 patients these LN metastases were found remote to the primary tumors and the N+ status was predicted by FAPI-PET/CT (but lesion number was underestimated due to resolution limits), in 2 patients LN metastases were closely adjacent to primary tumors could not be delineated successfully. Out of 4 patients with FAPI-positive distant metastasis, a histological proven lung metastasis was false-negative with FDG, in another patient FAPI detected more (however not histologically proven) lesions than FDG. In two patients with liver metastasis the diagnostic interpretation was identical; however, due to the lower hepatic background the tumor-to-background ratios were higher with FAPI than with FDG-PET. The true-positive FAPI-PET/CT changed the therapeutic concept in the patient with FDG-negative distant metastasis. **Conclusion:** FAPI-PET/CT is of high sensitivity in pancreatic cancer, but specificity for primary tumor detection is limited by uptake in chronic pancreatitis. Preliminary results indicate a possible superiority in comparison to FDG, which has well known limitations in pancreatic cancer. **References:** 1. Loktev A, Lindner T, Mier W, et al. A new method for tumor imaging by targeting cancer associated fibroblasts. J Nucl Med. 2018 Apr 6. doi: 10.2967/jnumed.118.210435. 2. Lindner T, Loktev A, Altmann A, et al. Development of quinoline based theranostic

ligands for the targeting of fibroblast activation protein. *J Nucl Med*. 2018 Apr 6. doi: 10.2967/jnumed.118.210443.

OP-299

Role Of ^{68}Ga -Labelled PSMA PET/CT In Evaluation Of Pancreatic Lesion To Differentiate Benign From Malignant Lesions

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Objective: Recently many reports have shown the PSMA expression in non-prostatic malignancies also. In this study we planned to evaluate the role of ^{68}Ga -labeled PSMA PET/CT in the characterization of pancreatic lesions as benign and malignant and its comparison with ^{18}F FDG PET/CT. **Materials and Methods:** In this pilot study we prospectively included 18 patients (14 male and 4 female, mean age 51.8, Age range 37-67 years) with pancreatic lesions on ultrasound or CT or MRI. All the patients underwent routine FDG PET/CT for evaluation of the pancreatic lesions followed by regional ^{68}Ga PSMA PET/CT. Focal PSMA uptake in the pancreatic lesion was considered as malignancy. Qualitative and semi quantitative (SUVmax values) analysis of the FDG and PSMA uptake were done. The findings of both the PET/CT scans were compared with the reference standard of histopathological or cytological diagnosis. **Results:** Histopathology from the pancreatic lesions revealed neuroendocrine tumors (n=2) which usually show variable FDG uptake and were not further evaluated. Of the remaining 16 patients, histopathology showed adenocarcinoma in 7 and benign lesions in remaining nine patients, which included inflammatory lesions (n=7), serous cystadenoma (n=1) and solid pseudopapillary epithelial neoplasm (n=1). FDG (Mean SUVmax - 9.3, 95% CI 6.1-12.6) and PSMA (Mean SUVmax - 7.5, 95%CI 5.2-9.9) showed focal avidity in all the 7 malignant lesions. Of the 9 benign lesions, FDG (Mean SUVmax - 5.1, 95% CI 3.1-7.0) showed focal avidity in 3 inflammatory lesions while PSMA (Mean SUVmax - 3.7, 95% CI 2.3-5.2) showed focal avidity in 1 lesion (serous cystadenoma). For detection of malignancy, the sensitivity, specificity, PPV and NPV for FDG and PSMA PET/CT was 100%, 66.67%, 70%, 100% and 100%, 88.89%, 87.5%, 100% respectively. PSMA PET/CT was more accurate than FDG PET/CT in defining the nature of the lesion (AUC under the ROC curve was 0.91 for PSMA vs. 0.86 for FDG PET/CT). The SUVmax in the PSMA PET/CT was also seen to be different between the benign and malignant lesions (p=0.003) with malignant lesions showing significantly higher PSMA avidity. **Conclusion:** This prospective pilot study revealed that malignant lesions of pancreas show increased uptake of ^{68}Ga -PSMA with higher SUVmax values compared to the benign lesions. ^{68}Ga PSMA PET/CT is also seen to be a more specific and accurate imaging modality for differentiating malignant pancreatic lesions from the benign lesions like mass forming pancreatitis where the role of FDG is limited.

OP-300

Radiomics analysis in cancer of the gastro-oesophageal junction: ^{18}F -FDG-PET/MRI-derived quantitative features are associated with M-stage

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Aim: To identify quantitative imaging biomarkers from multiparametric ^{18}F -FDG-PET/MRI for predicting distant metastases at staging in patients with gastro-oesophageal junction (GOJ) cancer. **Materials and methods:** Following IRB approval and informed consent, 24 patients with histologically proven GOJ cancer were prospectively recruited; 4 patients were excluded for technical reasons. Finally, 19 male and 1 female (68.3±9.1 years) were included. Patients were injected with 326±28 MBq FDG intravenously. Uptake time was 120 minutes. Two experienced radiologists and nuclear physicians reviewed the images in consensus. All tumours were manually segmented using ImageJ software. Quantitative imaging features were extracted using an in-house software developed in Matlab. First-order and second-order statistical texture features were computed for PET SUV and MRI T1, T2, DWI and ADC images of the whole tumour volume. *k*-means clustering algorithm was used to assess the correlation of feature-pairs with the presence of distant metastases. Multivariate analysis of variance (MANOVA) was performed to assess the statistical separability of the groups identified by feature-pairs. Sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV) and accuracy (ACC) were calculated to quantify the discrimination ability of features in comparison with maximum standardized uptake value (SUVmax) and tumour size. **Results:** Second-order entropy derived from ADC and maximum probability derived from SUV, linked to texture irregularity and homogeneity respectively, were the best feature-pair for discrimination of patients with and without metastatic disease (SE=80%, SP=80%, PPV=80%, NPV=80%, ACC=80%). MANOVA confirmed that the means of these features for the two groups of patients differed significantly, with a *p*-value<0.001. SUVmax (SE=80%, SP=30%, PPV=53%, NPV=60%, ACC=55%) and tumour size (SE=90%, SP=10%, PPV=50%, NPV=50%, ACC=50%) performed worse, particularly for specificity. **Conclusion:** Our preliminary results suggest that greater intra-tumoural heterogeneity in GOJ cancer is associated with metastatic potential. The extraction of quantitative multiparametric features from the primary tumour may facilitate prognostication at staging, identifying patients who will benefit most from more frequent follow-up examinations and consideration of alternative therapies.

OP-301

The correlation between pathological molecular indicators and metabolic parameters of ^{18}F -FDG PET/CT in patients with advanced gastric carcinoma

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Objective: Better understanding of molecular classification of gastric carcinoma (GC) subtype can improve patient selection for therapeutic regimens and prognosis. ^{18}F -fluoro-2-deoxy-D-glucose (FDG) positron emission tomography/ computed tomography (PET/CT) is a sensitive, noninvasive tool for detection of functional malignant lesions and has recently been shown to

predict therapeutic response and outcomes in GC patients. The aim of this study was to evaluate the FDG uptake of local advanced GC by correlating it with the histopathologic features and pathological molecular indicators of the tumors. **Methods:** Data pertaining to patients with a histopathological diagnosis of GC between January 2010 and December 2015 were retrospectively analyzed. A total of 82 patients (60 years, 58.51 ± 13.41 years) with locally advanced GC who were referred for preoperative ^{18}F -FDG PET/CT scans were enrolled in this study (with 32 localized in gastric body and 50 in antrum). The maximum standardized uptake values (SUV_{max}), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of the primary tumor were measured and calculated with the region of interest (ROI) technique. These relationship between metabolic parameters and the status of Ki-67, human epidermal growth factor receptor 2 (HER2), c-Met and epidermal growth factor receptor (EGFR) were investigated in all of patients. **Results:** Significant differences were observed between HER2-positive and HER-2 negative adenocarcinoma in SUV_{max} (8.52 ± 4.11 vs 7.18 ± 7.76 , $P = 0.016$) and SUV_{mean} (4.36 ± 1.04 vs 4.05 ± 2.68 , $P = 0.026$). SUV_{max} , SUV_{mean} and TLG were significantly higher in the high Ki-67 index group (7.93 ± 7.66 vs 3.92 ± 0.67 , $P = 0.015$; 4.27 ± 2.64 vs 2.93 ± 0.46 , $P = 0.033$ and 60.08 cm^3 vs 20.57 cm^3 , $P = 0.026$, respectively). Patients with EGFR mutation has significant lower SUV_{max} and SUV_{mean} ($P = 0.018$, $P = 0.011$) in gastric antral carcinoma. No significant correlation was found between metabolism parameters and the expression of c-Met in GC. Significant differences were observed in the gastric antral carcinoma between diffuse and undiffuse (mixed and intestinal) adenocarcinoma in SUV_{mean} (3.41 ± 1.05 vs 4.53 ± 2.11 , $P = 0.037$). **Conclusion:** Metabolism parameters on ^{18}F -FDG are associated with Ki-67 and HER2 expression in gastric carcinoma, and with EGFR mutation in gastric antral cancer. ^{18}F -FDG PET/CT may be useful for determining the individual therapeutic strategy and predicting the outcome of patients.

OP-302

The Impact of Obesity on ^{18}F -FDG PET-CT tumor metrics in Oesophageal Adenocarcinoma?

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Purpose/Introduction: The purpose of this study was to investigate the impact of obesity on metabolic tumour metrics (SUV_{max} and MTV) in oesophageal AC. Correlations between obesity parameters (BMI, WC) and metabolic tumour metrics were assessed. Associations between obesity parameters (BMI, WC) and CT derived fat measurements were also evaluated. Other factors that may interfere with glucose metabolism, such as diabetes and insulin were evaluated during the study. **Subjects & Methods:** Over a period of five years (2009–2014), 251 patients with locally advanced biopsy-proven AC of the oesophagus or OGJ with the intention to treat with Surgery ($n=101$) or Multimodal (Neo-CRT and Surgery, $n=90$) or Multimodal (Neo-CT and Surgery, $n=60$) were enrolled in the study. All patients underwent a pre-treatment whole body ^{18}F -FDG PET/CT study.

Metabolic tumour metrics (SUV_{max} and MTV), were measured independently by two experienced readers. Measures of obesity including BMI, WC and CT derived fat measurements were obtained. **Results:** The study population consisted of 251 patients (217 men and 34 women), with a mean age of 63.7 ± 10.2 years (range 29 to 86 years). The odds of detecting tumour ^{18}F -FDG uptake as quantified by SUV_{max} and MTV, increased with BMI and WC. However, the expected change in either SUV_{max} or MTV for +1 unit difference in either BMI or WC was not demonstrated. An association between obesity or the metabolic tumour metrics, with treatment response was not observed. It was demonstrated that higher SUV_{max} was associated with worse DFS and OS in Underweight or Normal weight patients in the Surgery group. In comparison, higher SUV_{max} was associated with better DFS and OS in overweight or obese patients in the Surgery group. In comparison, obesity did not affect the relationship between MTV and survival. The SUV_{max} was found to be an independent predictor of overall survival (OS), whereas MTV and obesity were not independent predictors of OS. **Discussion/Conclusion:** Obesity does appear to affect SUV_{max} and MTV measurements in oesophageal AC patients. The odds of detecting tumour tissue as quantified by SUV_{max} and MTV increased with both BMI and WC. The patient's obesity status, along with the tumour tissue itself, appears to contribute to higher metabolic metrics. A potential modifying effect of obesity on the relationship between SUV_{max} and survival in the Surgery group was demonstrated. It is recommended that the patient's obesity status is taken into consideration when interpreting the results of tumour metrics on ^{18}F -FDG PET/CT studies.

OP-303

[^{18}F]-FDG PET/MRI in Locally Advanced Rectal Cancer (LARC) after Preoperative Chemo-Radiotherapy (pCRT): a comparison with conventional imaging

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Purpose: To assess the accuracy of restaging after pCRT with whole body PET/MRI, pelvic T2W plus DWI MRI (pelvic-MRI), pelvic T2W MRI (standard-MRI) and thoraco-abdominal CT when predicting histopathologic TNM stage in LARC. **Material and methods:** 26 patients with LARC underwent PET/MRI and CT before and after pCRT for TNM staging. 21 were treated with total mesorectal excision and 5 with transanal local excision. Histopathologic findings or a follow-up of at least 1-year were the reference standards. One radiologist evaluated pelvic MRI and CT. A second radiologist evaluated standard MRI. A third radiologist and a nuclear medicine physician assessed PET/MRI. T staging results were grouped in T0 and residual disease ($T \geq 1$). N stage was classified on a per-patient basis as positive or negative using MRI dimensional criteria ($\geq 5\text{mm}$ per node), MRI lymph node global size reduction rate criteria (reduction $< 70\%$) and PET/MRI dimensional criteria and/or nodal FDG uptake. **Results:** Sensitivity and specificity for ypT0 were 100%-85.7% for PET/MRI, 94.7%-85.7% for pelvic-MRI and 94.7%-57.1% for standard-MRI. For ypN+ with dimensional criteria, sensitivity and specificity were

100%–88.9% for PET/MRI and 75%–88.89% for pelvic-MRI. The values for pelvic-MRI changed to 87.5% and 72.2% using lymph node global size reduction rate criteria. PET/MRI correctly diagnosed two liver and one distant nodal metastases while missed a lung metastasis. **Conclusion:** PET/MRI improves the accuracy of ycTN staging compared to MRI, but performs worse than CT in ycM staging. Initial results are promising; however, a larger cohort of patients should be examined introducing sequences for lung and gadolinium for liver metastases.

OP-304

PET/MR for staging rectal cancer: a comparison to conventional staging with pelvic MR and thoracoabdominal CT

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Purpose/Introduction: To compare the detection rate of metastatic lesions on PET/MR versus conventional staging (pelvic MR and thoracoabdominal CT) in rectal cancer patients referred for primary staging. **Subjects & Methods:** Ninety-five patients with biopsy proven rectal adenocarcinoma were submitted to whole-body PET/MR for primary staging in addition to conventional staging with pelvic MR and thoracoabdominal contrast-enhanced CT (ceCT). One reader analyzed the MR (blinded to PET findings) regarding locoregional staging. Another reader (also blinded to the high-resolution part of pelvic MR) analyzed the PET/MR about T-, N- and M-stage. A third blinded reader assessed the M-stage by ceCT. Standard of reference was biopsy when feasible or imaging follow-up. Lesions were categorized as positive, negative or indeterminate. **Results:** On a lesion-based analysis, PET/MR detected 24.5% more positive metastatic lesions than conventional imaging (305 vs. 254 lesions). The higher detection rate on PET/MR was observed for non-regional lymph nodes (73 vs. 37 lesions). On a patient-based, PET/MR was positive in 38 out of 95 patients (40%), while conventional staging in 24 out of 95 patients (25.3%). PET/MR was indeterminate in 7 patients (7.4%), which 1 was positive on CT (non-regional lymph nodes, later confirmed to be sarcoidosis), while conventional imaging was in 30 patients (31.6%), which 10 were positive on PET/MR, mainly for non-regional lymph nodes and liver. **Discussion/Conclusion:** For rectal cancer staging, PET/MR presents not only a higher detection rate of metastatic lesions than conventional imaging (pelvic MR and thoracoabdominal ceCT), but also clarifies the etiology indeterminate lesions. Thus, PET/MR might be preferred for whole-body staging of rectal cancer patients, with a higher detection rate and potential clinical impact.

OP-305

Impact Of PET-PCI Using FDG PET CT For Predicting Tumour Grade And Recurrence In Pseudomyxoma Peritonei

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Introduction: Pseudomyxoma peritonei (PMP) is a rare condition where gelatinous ascites disseminate in the peritoneum after the rupture of a mucinous tumour. The Peritoneal Cancer Index (PCI), widely used for quantitative assessment in PMP, is calculated based on surgical findings of tumour distribution and implant size throughout the abdomen and the pelvis. We hypothesized that modified PCI (PET-PCI) obtained by FDG-PET/CT could be a suitable marker to reflect tumour burden and viability. The aim of this study was to evaluate the utility of PET-PCI for predicting progression free survival (PFS) in patients with PMP. **Subjects & methods:** We enrolled PMP patients who underwent FDG-PET/CT before cytoreductive surgery (CRS) ± hyperthermic intraperitoneal chemotherapy (HIPEC). PET-PCI were obtained by summing up the visually scored FDG-uptake of the PMP lesions in 13 specific abdominal-pelvic regions that were used when evaluating PCI at surgery. The uptake score was defined as follows: 0 (no lesion or no uptake into the lesion), 1 (uptake equivalent to blood pool), 2 (uptake equivalent to liver), and 3 (higher uptake than liver). The SUVmax of the lesion that showed the highest uptake amongst the 13 regions was also evaluated. Recurrence of the disease was determined by the combination of followed CT features and elevation of tumour markers. **Results:** Thirty-five patients (male:female = 12:23, 56.7±13.7 years) with a mean follow-up time of 18.3 months were included. Pathological diagnosis indicated 19 patients with low-grade PMP and 16 patients with high-grade PMP. Patients with high-grade PMP showed statistically higher PET-PCI and SUVmax than the patients with low-grade PMP (PET-PCI: 14.8 vs. 8.7, p=0.003; SUVmax: 3.6 vs. 2.6, p=0.012). Using a cut-off PET-PCI of 12.0, Kaplan-Meier analyses showed a statistically significant difference in PFS in patients with a high vs. low PET-PCI (p<0.001), with a hazard ratio (HR) of 12.4 (95%CI: 2.9–54.0). For SUVmax, the best cut-off value was 2.7 and the correlation with PFS was also statistically significant (p=0.008) with a HR of 4.7 (95%CI: 1.4–16.6). In multivariate Cox proportional-hazards regression, PET-PCI was independently and significantly correlated with PFS, whereas SUVmax was not statistically significant. **Conclusion:** PET-PCI obtained from FDG-PET/CT is useful for predicting recurrence in patients with PMP. PET-PCI can reflect histopathologic features and is likely to show a strong correlation with tumour burden.

OP-306

Reliability of 18F-FCH-PET/CT compared to CT in the early response evaluation of 90Y-Trans-Arterial-Radioembolization in HCC patients

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Aim: Hepatocellular carcinoma (HCC) is a common cause of cancer related mortality. Among the therapeutic procedures, Trans-Arterial-Radioembolization (TARE) with 90Yttrium-micro-

spheres has demonstrated high efficacy across the whole spectrum of HCC from early to advanced stages. Diagnosis and treatment response evaluation in HCC patients is mainly performed with contrast-enhanced Computed Tomography (ceCT), based on RECIST criteria. However, morphological changes on CECT could be not detected before 3 months. The aim of this study was to assess the reliability of 18F-FCH-PET/CT in the early response evaluation to TARE compared to ceCT, in well-differentiated HCC patients. **Materials and methods:** 20 patients (mean age 72.4 years, range 53–84) affected by unresectable well-differentiated HCC and treated with TARE, performed 18F-FCH-PET/CT and ceCT before and after 1 month from treatment. Radiologic response assessment was performed according to RECIST criteria as: Complete Response (CR), Partial Response (PR), Stable Disease (SD), and Progressive Disease (PD). The semiquantitative analysis, by using SUVmax variation (%), was evaluated to establish PET/CT response assessment as following: CR (absence of lesions), PR (SUVmax reduction >25%), PD (SUVmax increase >30%) and SD (no PR or PD). CR+PR patients were considered responders, while SD+PD were no responders. The agreement between the two imaging methods was calculated by using Cohen's K. **Results:** 13/20 (65%) patients had multifocal HCC at baseline CT and 18F-FCH-PET/CT, while 7/20 (35%) had a single lesion (mean diameter 46 mm, range: 35–80). According to RECIST: 3/20 (15%) patients were classified as CR, 5/20 (25%) PR, 9/20 (45%) SD, 3/20 (25%) PD. According to semiquantitative 18F-FCH-PET/CT analysis: 8/20 (40%) patients were considered CR, 7/20 (35%) PR, 2/20 (10%) SD, 3/20 (15%) PD. In particular, in 7/20 (35%) patients 18F-FCH-PET/CT and ceCT showed discordant response: CR vs SD in 3/7 (42%) patients (single lesion), PR vs SD in 4/7 (57%) patients (3 multifocal and 1 single lesion). PD was detected in both imaging modalities. The agreement between the two imaging methods was fair ($k = 0.364$, 95%CI: 0.070–0.657). **Conclusion:** Our preliminary results demonstrated that 18F-FCH-PET/CT is a reliable method to the early evaluation of patients with unresectable well-differentiated HCC who underwent to TARE. This allows a better management of HCC patients, avoiding an over-treatment in patients in complete response or conversely early treat those, particularly with multifocal disease, that need to complete the treatment in the other lobe.

809 Monday, October 15, 2018, 11:30 - 12:45, Hall 6

Special Session: Tomorrow's Experts Session - Best-Ranked Papers from the Under-30s

OP-307

Increased P2X7 receptor binding is associated with neuroinflammation in acute but not chronic models for Parkinson's disease

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Introduction: The purinergic P2X7 receptor (P2X7R) is a key mediator in (neuro)inflammation. In Parkinson's disease (PD), the inflammatory process has long been associated with ongoing neurodegeneration and excitotoxicity. Recently, P2X7R imaging has become possible with novel PET radioligands, including [¹¹C]JNJ-54173717. We investigated P2X7R availability, in comparison with availability of the 18 kDa translocator protein (TSPO), in two well-characterized rat models of PD using *in vitro* autoradiography at multiple time points throughout the course of the disease. **Subjects and Methods:** Rats received either a unilateral injection with 6-hydroxydopamine (6-OHDA) in the striatum (STR), or with recombinant adeno-associated viral vector overexpressing human A53T alpha-synuclein (α -SYN) in the substantia nigra (SN). Respective saline/eGFP controls were included. Rats were sacrificed at following time points throughout the neurodegenerative process: 6-OHDA at 4, 7, 14, 21, and 28 days; α -SYN at 4 days and 14, 28, and 42 days ($n=3-6$ rats/time point). Transverse brain cryosections were incubated with tracer for either P2X7R ([¹¹C]JNJ-54173717, 2.4 μ Ci/slice) or TSPO ([¹⁸F]DPA-714, 16 μ Ci/slice). Blocking studies with A-740003 (10 μ M) for P2X7R and PK-11195 (20 μ M) for TSPO were performed to evaluate nonspecific binding. Statistical analysis was done using ipsi- to contralateral (I/CL) binding ratios. The limb-use asymmetry test was included to evaluate motor symptom development. **Results:** [¹¹C]JNJ-54173717 binding ratios were transiently elevated in the STR of 6-OHDA rats at day 14, 21, and 28 post-injection, with peak P2X7R binding at day 14 ($p \leq 0.01$). This largely coincided with the time course of STR [¹⁸F]DPA-714 binding which was elevated at 7, 14, and 21 days, with peak TSPO binding earlier at day 7 ($p \leq 0.001$). In the chronic α -SYN model, no significant differences were found in P2X7R binding, but TSPO binding in the SN was significantly elevated between day 28 and 42 ($p \leq 0.01$), as compared to controls. Behavioral analysis showed unilaterally impaired forepaw use beginning at 4 days in the 6-OHDA model and beginning at 28 days in the α -SYN model, compared to controls ($p \leq 0.001$). **Conclusion:** This study showed for the first time an increased P2X7R availability in acute (6-OHDA), but not chronic (α -SYN), PD models in a time window corresponding with elevated TSPO binding and motor behavior changes. Since P2X7R are activated by high ATP concentrations, this might explain the differences we found between acute versus chronic conditions. These results may indicate a potential for P2X7R-targeted therapy and *in vivo* monitoring of neuroinflammation using [¹¹C]JNJ-54173717 in an acute neuroinflammatory setting.

OP-308

P2X7 as a novel target for neuroinflammation: a first-in-human biodistribution and kinetic modelling study using [¹¹C]-JNJ54173717

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Introduction: The P2X7 receptor is an ATP-gated ion-channel which is predominantly expressed on activated microglia. Activated microglia reflect neuroinflammation, which is important in many neurodegenerative diseases such as Parkinson disease (PD). [^{11}C]JNJ54173717 ([^{11}C]JNJ717) is a selective P2X7 receptor tracer with nanomolar affinity (1.6 nM). In this first-in-human study we report the biodistribution and dosimetry, kinetic modelling and short-term test-retest variability in healthy volunteers (HV). **Subjects and methods:** First, a biodistribution and dosimetry study was performed in 3 HV (30.4 ± 2.4 , 2F/1M) by consecutive whole body PET/CT scanning covering the tracer biodistribution for 3h post injection. Next, the normalized cumulative activity was determined in appropriate source organs and effective Dose was calculated using OLINDA v1.1. Secondly, 90-min dynamic scans on an integrated PET/MR (GE Signa) were performed in 6 HV (60.9 ± 12 , 3F/3M) to determine the most appropriate kinetic model. Additionally, 4 subjects (55.8 ± 13 , 1F/3M) (interscan interval 20 ± 12 days, range 0–28) underwent test-retest scans. The average injected dose was 242 ± 67 MBq. PET reconstruction included resolution modelling and time of flight information while attenuation correction was performed using an in-house validated ZTE based approach. Tissue volume of distribution (V_T) was calculated using a 1- and 2-tissue compartment model (1-2TCM) and Logan graphical analysis (LGA) (Pmod v3.7). **Results:** An effective dose of 4.47 ± 0.32 $\mu\text{Sv}/\text{MBq}$ was determined for [^{11}C]JNJ717. Highest organ absorbed doses were observed in the gallbladder (25 $\mu\text{Sv}/\text{MBq}$), liver (22 $\mu\text{Sv}/\text{MBq}$) and small intestine (20 $\mu\text{Sv}/\text{MBq}$). No adverse events occurred. Reversible 2TCM with a sigmoidal metabolite curve fit was identified as the appropriate kinetic model. LGA showed similar V_T values. Highest V_T values were observed in the thalamus, brainstem and striatum with relatively homogeneous uptake in grey matter. Inter-subject variability in HV was relatively low (20–30% difference between highest and lowest V_T). The average regional test-retest variability was $12.5 \pm 13\%$ for 2TCM and $14.1 \pm 12\%$ for LGA. **Conclusion:** [^{11}C]JNJ717 is a suitable and safe PET ligand for quantification of P2X7R expression in the human brain with acceptable test-retest variability. Therefore, dynamic [^{11}C]JNJ717 PET can be a valuable tool to study the role of P2X7 receptors in healthy and diseased brain. The study was sponsored by a Michael J Fox Foundation Grant nr. “PRI-PD” #12062. The precursor for the study was kindly donated by Janssen Pharmaceuticals.

OP-309

Effects of tau-pathology on glucose metabolism mitigated by level of education

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GERMANY, ⁶Department of Neurodegenerative Diseases and Geriatric Psychiatry, University Hospital Bonn, Bonn, GERMANY, ⁷Nuclear Chemistry, Institute of Neuroscience and Medicine (INM-5), Research Center Jülich, Jülich, GERMANY, ⁸Institute of Radiochemistry and Experimental Molecular Imaging, University Hospital Cologne, Cologne, GERMANY, ⁹Department of Medical Psychology – Neuropsychology and Gender Studies, University Hospital Cologne, Cologne, GERMANY.

Introduction: Recently, we showed that higher educated (HE) patients with Alzheimer’s disease (AD) presented greater tau-pathology burden than lower educated (LE) AD patients with similar cognitive impairment (Hoenig et al. 2017). This finding likely underlies reserve-related mechanisms such as neural resistance capacity. Since PET imaging studies have consistently demonstrated a close relationship between tau-pathology and changes in glucose metabolism (i.e. neuronal dysfunction), we investigated whether this relationship is influenced by the level of education, a proxy for neural resistance level. **Subjects & Methods:** We included 38 patients with mild-to-moderate AD ($M(\text{Age})=67.05$ years, $M(\text{MMSE})=23.89$ points, $M(\text{Education})=13.72$ years), for whom a [18F]AV-1451 and [18F]FDG scan was available. The PET scans were co-registered, normalized to a common template in MNI space, and intensity standardized to the cerebellum. Next, we z-transformed the pre-processed scans using a [18F]AV-1451 and [18F]FDG template of a healthy control sample, which was age-matched to our patient sample. Afterwards, the z-transformed images were thresholded at a z-score of $z \geq 3.0$ representing a one-tailed p-value of $p=0.001$. We then extracted three distinct volumes: the tau-specific, the FDG-specific, and the overlap volume for each patient. The tau-specific volume comprised regions characterized by significant tau-pathology in absence of neuronal dysfunction. Likewise, the FDG-specific volume consisted of regions with significant neuronal dysfunction in absence of tau-pathology. The overlap volume comprised the regions with significant neuronal dysfunction and tau-pathology. Mean z-scores and volume sizes were extracted respectively, and used as dependent variables in regression analyses with education as predictor. All models were corrected for age and MMSE. **Results:** Years of education were positively associated with the tau-specific volume size ($\beta=.390$, $t(34)=2.454$, $p=.019$) meaning that HE patients presented a more extended tau-pathology pattern in absence of regional neuronal dysfunction. Concomitantly, education was positively related with tau-pathology load in the overlap region ($\beta=.328$, $t(34)=2.187$, $p=.036$) suggesting that more tau-pathology is necessary to induce neuronal dysfunction at higher levels of education. Moreover, we observed a negative trend between education and the FDG-specific volume ($\beta=-.247$, $t(34)=1.429$, $p=.162$). **Conclusion:** At higher levels of education tau-pathology is less paralleled by regional and remote neuronal metabolic decline. This may explain why HE patients can maintain cognitive function despite a greater tau-pathology burden compared to LE patients. Presumably, early lifetime factors such as education may facilitate neural resistance mechanisms, which potentially mitigate disease-related neurotoxic effects late in life.

OP-310

Non-invasive prediction of IDH-genotype in newly diagnosed gliomas using dynamic ^{18}F -FET-PET

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According to the updated World Health Organization (WHO) classification of gliomas with its emphasis on molecular parameters, tumours with an isocitrate dehydrogenase (*IDH*) wildtype status have a dismal prognosis. ^{18}F -FET PET has shown to be an important diagnostic tool for glioma management in the past, delivering both prognostic and therapy response information. The aim of the study was to assess the value of dynamic ^{18}F -FET-PET for non-invasive prediction of *IDH*-wildtype status prior to further therapies. Newly diagnosed WHO grade II-IV glioma patients, in whom *IDH*-mutation status, dynamic ^{18}F -FET-PET scans and contrast-enhanced MRI were available at initial diagnosis prior to any therapies were included. Analyses of dynamic ^{18}F -FET-PET include evaluation of the maximal tumour to background ratio (TBR_{max}) and minimal time-to-peak (TTP_{min}). These were tested for their diagnostic power (sensitivity, specificity, accuracy, positive and negative predictive values) for non-invasive prediction of *IDH*-wildtype genotype in the overall study group and, additionally, in the subgroup of non-contrast enhancing gliomas. In sum, 341 patients were included. Molecular analyses revealed 178 *IDH*-mutant and 163 *IDH*-wildtype tumours. 270/341 gliomas were classified as FET-positive ($\text{TBR}_{\text{max}} > 1.6$); 90.2% of *IDH*-wildtype and 69.1% of *IDH*-mutant gliomas. Although the median TBR_{max} in *IDH*-wildtype gliomas was significantly higher compared to *IDH*-mutant gliomas (2.9 vs. 2.3, $p < 0.001$), ROC-analyses revealed no reliable cut-off for TBR_{max} due to high overlap (range 1.0–7.1 vs. 1.1–7.9). Dynamic analysis revealed a significantly shorter TTP_{min} in *IDH*-wildtype gliomas; using $\text{TTP}_{\text{min}} \leq 12.5$ minutes as an indicator for *IDH*-wildtype gliomas ($\text{AUC} = 0.796$, $p = < 0.001$) a high positive predictive value and a high specificity was reached (sensitivity: 72%, specificity: 87%, accuracy: 79%, positive predictive value: 87%; negative predictive value: 72%). 161/341 gliomas did not show contrast enhancement in MRI; even in this subgroup, $\text{TTP}_{\text{min}} \leq 12.5$ minutes remained a good predictor of *IDH*-wildtype gliomas ($\text{AUC} = 0.868$, $p < 0.001$) with an even higher diagnostic power (sensitivity: 74%, specificity: 94%, accuracy: 89%, positive predictive value: 83%; negative predictive value: 90%). TTP_{min} analysis in dynamic ^{18}F -FET-PET provides a diagnostic tool for the non-invasive detection of gliomas with a highly aggressive *IDH*-wildtype genotype. In particular, a high diagnostic power was observed in the subgroup of non-contrast enhancing gliomas. These findings can optimize the identification of patients with potentially worse prognosis, especially in gliomas without contrast enhancement in MRI.

OP-311

Clinical outcome of 121 patients after PSMA-targeted radioguided surgery for early biochemical recurrent prostate cancer

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Aim: To facilitate intraoperative detection of prostate cancer (PC) lesions in salvage surgery, we recently introduced PSMA-targeted radioguided surgery (PSMA-RGS) using gamma-emitting PSMA-ligands for intraoperative detection of metastatic lesions. In this retrospective analysis we present follow-up data of the first 121 patients and tried to shed light on preoperative parameters for optimal patient selection. **Materials and Methods:** 121 consecutive patients with recurrent oligometastatic PC on PSMA-targeted PET (PSA median: 1.13 ng/ml, range: 0.0 - 13.90 ng/ml) after primary treatment with radical prostatectomy underwent ^{111}In - or $^{99\text{m}}\text{Tc}$ -based PSMA-RGS from April 2014 to May 2017. PSA response without additional treatment was determined 6–16 weeks following PSMA-RGS. Complete biochemical response (cBR; PSA < 0.2 ng/ml), biochemical recurrence-free survival (bRFS) and PC-specific treatment-free survival were evaluated and correlated with preoperatively available PSA and unifocality/multifocality on PET imaging. **Results:** In almost all patients (120/121, 99.2 %) PC metastases were removed. One patient died six days postoperatively, five patients were lost to follow-up. Eleven patients suffered from grade III complications according to Clavien-Dindo. cBR was achieved in 75 out of 114 patients (65.8 %). The frequency of cBR was higher in patients with a pre-RGS PSA level below the median of 1.13 ng/ml (77.6 %) compared to patients with higher PSA values (53.6 %). cBR was higher in patients with a single anatomical location of recurrence (71.4 %) compared to patients with multiple locations (58.8 %). Median follow-up was 12 months. Median bRFS was 6.4 months in the whole patient cohort and 19.8 months for patients with a complete biochemical response. Patients with a preoperative PSA < 1.13 ng/ml (median) had a significantly longer bRFS than pts with higher PSA values (median 14.9 vs 3.2 months, $p = 0.007$). Patients with a single location of recurrence had a longer bRFS than patients with multifocal recurrence (14.9 months vs. 4.2 months, $p = 0.009$). After one year of follow-up, 61.6 % of the patients did not receive any further PC-directed treatment, 19 patients exhibit an ongoing cBR and 8 patients for at least 18 months. **Conclusions:** PSMA-RGS facilitates the intraoperative detection of metastatic lesions during salvage surgery with an acceptable rate of high grade complications. It leads to a remarkable interval of bRFS and treatment-free survival in a subset of patients. Our data indicates that patient selection for PSMA-RGS is crucial as bRFS was highest in patients with a low preoperative PSA and a single anatomical site of recurrence on PSMA-targeted PET.

OP-312

Re-challenge Radioligand Therapy In Patients With Advanced Prostate Cancer: Outcome And Safety

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Purpose: There is a sparse data regarding the feasibility of radioligand therapy (RLT) with [^{177}Lu]Lu-PSMA-617 as a retreatment. We aimed to assess the outcome and safety of re-challenge RLT in patients with progressive prostatic cancer who previously benefited from the therapy. **Subjects and methods:** Assessed were patients who received re-challenge therapy at our department from January 2015 to December 2017. Nonhematological and hematological adverse events were evaluated from laboratory data and clinical reports and were graded according to the Common Terminology Criteria for Adverse Events (CTCAE v. 4.02). Time to prostate-specific-antigen (PSA) progression and overall survival of the study patients were calculated from the date of the first re-challenge cycle. The response data was determined using [^{68}Ga]Ga-PSMA-PET/CT and measurements of the tumor marker PSA. **Results:** Included in this retrospective study were 30 patients, who were initially treated with a median of 3 cycles (range 1-5) RLT and were eventually retreated after a median of 6 months (range 2 - 26). Each patient received a median of 2 (range 1-6) re-challenge cycles. None of the patients experienced a disabling or life-threatening adverse event (CTC-4). Grade 3 toxicity occurred in 7 patients (23%). Serious adverse events included leucopenia (n=2), anemia (n=3), thrombopenia (n=3) and elevated renal parameters (n=1). According to PSA-measurements at least 4 weeks after the RLT-application between re-challenge-cycle 1 to 5 at least 75% of patients showed a response (PSA-decrease $\geq$ 25%) or stable PSA-levels (change < 25%). Sixteen patients (53%) are alive; the median overall survival is still not reached. **Conclusion:** Re-challenge PSMA therapy is with an acceptable safety profile. The majority of the re-treated patients showed a benefit.

OP-313

Development of a PET Imaging Approach for Selection of Patients for Affibody-Based PNA-Mediated Pretargeted Radionuclide Therapy

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Aim: Clinical PET/CT imaging using ^{68}Ga -labeled ABY-025 provides non-invasive whole-body quantification of HER2 expression in patients with metastatic breast cancer. We have recently demonstrated that affibody-based peptide nucleic acid (PNA)-mediated pretargeted radionuclide therapy with lutetium-177 successfully delayed tumor growth and doubled median survival of mice bearing SKOV3 xenografts, with no acute toxicity or kidney damage. These promising results and clinical applicability of affibody molecules prompted us to develop a theranostic methodology, where PET/CT imaging would guide the selection of patients for therapy. The goal of this study was

to compare two imaging approaches, when either the primary targeting agent $Z_{\text{HER2:342}}\text{-SR-HP1}$ or the secondary targeting agent HP2 were labeled with gallium-68, and to evaluate their efficiency for discrimination between high and low HER2 expression in a corresponding mouse model. **Methods:** $Z_{\text{HER2:342}}\text{-SR-HP1}$ and HP2, carrying a DOTA chelator, were labeled with gallium-68. *In vitro* binding specificity of [^{68}Ga]Ga- $Z_{\text{HER2:342}}\text{-SR-HP1}$ to HER2-expressing cells was tested by HER2 saturation. The specificity of ^{68}Ga -HP2 pretargeting to cells pretreated with the primary agent was tested in the presence of parental affibody, unlabeled HP2 or [^{68}Ga]Ga-HP2 only. Cellular retention of ^{68}Ga -labeled primary agent and pretargeted complex by cells was studied. Biodistribution of [^{68}Ga]Ga-HP2 was compared to [^{177}Lu]Lu-HP2 in NMRI mice. The biodistribution of ^{68}Ga -labeled primary and secondary agents was evaluated in BALB/C nu/nu mice bearing SKOV3 (high HER2 expression) and DU145 (low HER2 expression) xenografts. PET/CT imaging was used to confirm the results of biodistribution studies. **Results:** Labeling of both agents with gallium-68 was performed with good yields and high specific activities. Binding of [^{68}Ga]Ga- $Z_{\text{HER2:342}}\text{-SR-HP1}$ to cells with high (SKOV3, BT474) and low (DU145) HER2-expression was HER2-specific. Pretargeting of [^{68}Ga]Ga-HP2 to $Z_{\text{HER2:342}}\text{-SR-HP1}$ -pretreated cells was PNA-mediated. Retention of ^{68}Ga -labeled primary agent and pretargeted complex was higher in SKOV3 cells than in DU145 cells. Retention of [^{68}Ga]Ga-HP2 in blood and normal organs was higher than of [^{177}Lu]Lu-HP2. Direct targeting using [^{68}Ga]Ga- $Z_{\text{HER2:342}}\text{-SR-HP1}$ provided 3.3-fold difference between uptake in SKOV3 and DU145 xenografts, while pretargeting using [^{68}Ga]Ga-HP2 provided 11.8-fold difference. Pretargeting improved tumor-to-organ ratios (e.g. 54-fold higher tumor-to-kidney ratio), compared to direct targeting in mice bearing SKOV3 xenografts. **Conclusion:** Side-by-side comparison of direct targeting and pretargeting showed that both approaches allowed discrimination between tumors with high and low HER2 expression. However, pretargeting provided better discrimination, higher tumor-to-organ ratios and better correlation with the uptake of the therapeutic [^{177}Lu]Lu-HP2. Therefore, this pretargeting method could be considered as the most promising for clinical translation.

OP-314

PET/CT imaging of angiogenesis with ^{68}Ga -DOTA-(RGD)₂ in patients with arterio-venous malformations

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Purpose: Angiogenesis, where normally quiescent endothelium switches to an activated state, is key in the progression of arterio-venous malformations (AVM). This results in the breakdown of vessel walls and subsequent enlargement of the AVM.

Currently, new treatments of AVM lesions using angiogenesis inhibitors are being implemented. To non-invasively image angiogenesis, we have developed a gallium-68-labeled RGD peptide targeting activated $\alpha_v\beta_3$ integrins on endothelial cells of newly formed blood vessels. This tracer can be used to characterize AVM lesions and may assess treatment response using PET/CT imaging. The aim of this study was to show the feasibility of [^{68}Ga]Ga-DOTA-(RGD) $_2$ PET/CT imaging in patients with an AVM lesion. **Methods:** Tracer uptake was determined in 8 patients diagnosed with a peripheral AVM who were scheduled for embolization treatment. PET/CT images were acquired 60 minutes after intravenous injection of [^{68}Ga]Ga-DOTA-(RGD) $_2$ (70 μg , 200 MBq). Tracer uptake in AVM lesions was quantified as peak Standardized Uptake Values (SUV_{peak}). Surgically removed AVM tissue was analyzed by immunohistology with monoclonal anti- $\alpha_v\beta_3$ LM609 to assess $\alpha_v\beta_3$ integrin expression. This study is actively recruiting more patients (study target $n=10$) and further analysis of data will be presented. **Results:** To date, eight patients (4 male, 4 female) with an AVM classified as Yakes AVM type II (6 patients), type IIIa (1 patient), and type IIIb (1 patient), mean age 42 years (26–64 years), were enrolled. Seven patients received multiple embolizations before [^{68}Ga]Ga-DOTA-(RGD) $_2$ PET/CT imaging; one patient has not received any treatment yet. [^{68}Ga]Ga-DOTA-(RGD) $_2$ PET/CT imaging was feasible in all patients, with significantly higher tracer uptake in AVM tissue compared to (surrounding) normal tissue. Volume-of-interest measurements showed a mean SUV_{peak} of 2.1 ± 0.8 in the AVM lesions. Immunohistochemistry of AVM tissue showed $\alpha_v\beta_3$ integrin expression in all samples. **Conclusion:** These results suggest that [^{68}Ga]Ga-DOTA-(RGD) $_2$ PET/CT imaging of $\alpha_v\beta_3$ integrin expression in AVM patients is feasible. The tracer uptake is increased in AVM compared to normal tissue, suggesting locally increased $\alpha_v\beta_3$ integrin expression in AVM. Our preliminary findings show that [^{68}Ga]Ga-DOTA-(RGD) $_2$ PET/CT imaging might be used to stratify patients prior to anti-angiogenic therapies or as a response-monitoring tool. Further studies will be conducted to explore these potential applications.

901 Monday, October 15, 2018, 14:30 - 16:00, Plenary Hall

CME 7 - Radiation Protection / Paediatrics:
Optimization of Diagnostic Reference Levels in Hybrid Imaging in Paediatric Nuclear Medicine

OP-315

Dose Reduction Techniques in Hybrid Imaging

D. de Palma; ASST-settelaghi, Nuclear Medicine, Varese, ITALY.

OP-316

Practical Implementation of Dose Reduction Techniques

A. I. Santos; Hospital Garcia de Orta, E.P.E., Nuclear Medicine Department, Almada, PORTUGAL.

OP-317

Harmonization Between European and North American Administered Activities

M. Lassmann; University Hospital Würzburg, Department of Nuclear Medicine, Würzburg, GERMANY.

902 Monday, October 15, 2018, 14:30 - 16:00, Hall 2

Joint Symposium 13 - Neuroimaging / Drug Development / ECNP: Imaging Phosphodiesterases (PDEs) in the CNS: Targets for Drug Development

OP-318

Novel Radioligands for Cyclic Nucleotide Phosphodiesterase Imaging with Positron Emission Tomography - The Latest Developments

W. Deuther-Conrad; Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden-Rossendorf, Leipzig, GERMANY.

OP-319

Preclinical Imaging of PDE10A - Its Role in Energy Homeostasis

M. K. Hankir; University of Würzburg, Würzburg, GERMANY.

OP-320

Imaging of PDE10A in the Basal Ganglia - Age-Related Changes and Results from Studies in Huntington's Disease

A. Varrone; Karolinska Institutet, Stockholm, SWEDEN.

903 Monday, October 15, 2018, 14:30 - 16:00, Hall 3

Joint Symposium 14 - Oncology / EHA: PET/CT Guided Treatment in Hodgkin Lymphoma

OP-322

PET Guided Treatment Strategies in Hodgkin Lymphoma

M. Hutchings; Department of Haematology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, DENMARK.

OP-323

Risks and Benefits of PET in Hodgkin Lymphoma

P. Borchmann; German Hodgkin Study Group, University Hospital of Cologne, Cologne, GERMANY.

OP-324

Metabolic Tumour Volume to Predict Survival in Hodgkin Lymphoma

S. Kanoun; The University Cancer Institute Toulouse Oncopole, Toulouse, FRANCE.

904 Monday, October 15, 2018, 14:30 - 16:00, Hall 5

CTE 3 - Technologists / Neuroimaging: Nuclear Medicine Imaging in Dementia

OP-325

Consolidated Practice in Nuclear Medicine Imaging for Dementia

K. van Laere; KU Leuven, Nuclear Medicine Department, Leuven, BELGIUM.

OP-326

State of the Art of Dementia Treatment

P. Schoenknecht; Leipzig University & Academic Hospital Arnsdorf, Arnsdorf, GERMANY.

OP-327

Future Trends in Nuclear Medicine Imaging for Dementia

H. Barthel; University of Leipzig, Department of Nuclear Medicine, Leipzig, GERMANY.

905 Monday, October 15, 2018, 14:30 - 16:00, Hall X

M2M: Antibodies & Peptides: Let's Modify!

OP-328

Site-specific modification of antibody fragments by combining chemoenzymatic bioconjugation and click chemistry

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Introduction: A wealth of preclinical experiments has clearly demonstrated that site-specific protein modification results in a more homogenous product population with defined and tunable properties compared to traditional bioconjugation techniques (1, 2). This is of particular importance for antibodies and their fragments as random conjugation strategies can compromise their functionality and interfere with or abolish their immunoreactivity (3). That specifically applies to small-sized antibody formats such as single chain variable fragments and single-domain antibody-fragments due to their compact structure and limited number of available functional reactive residues outside the antigen-binding site (4-6). Here, we describe a versatile two-step approach for site-specific introduction of bifunctional radiometal-chelating agents into antibody-de-

rived fragments for the generation of highly defined radioimmunotracers. **Methods:** The first step of this approach uses enzyme-mediated bioconjugation for regioselective incorporation of an azide-containing linker into an antibody fragment. The second step of this modular approach involves the modification of the azide-tagged antibody fragment with dibenzocyclooctyne (DBCO)-containing fluorescent dyes or DBCO-modified bispidine via Cu-free strain-promoted alkyne-azide cycloaddition. **Results:** In an exemplary way, we demonstrate the versatility of this two-step approach by the site-specific incorporation of fluorescent dyes or radiometal chelators for fluorescence or positron emission tomographic imaging at physiological conditions. In vitro binding studies on different human cancer cell lines using dye- or ⁶⁴Cu-labeled antibody fragments showed high specificity, co-localization and a receptor-mediated cellular uptake of the EGFR-specific probes. Noteworthy, we did not observe any detrimental effect to the functionality of the antibody fragments. **Discussion and Conclusion:** The site-specific insertion of a bioorthogonal handle into the targeting moiety allows the subsequent convenient and straightforward incorporation of a variety of complementary probes. In addition, the heterogeneity of the conjugate population is substantially reduced as the conjugation site is defined and maximally one probe is attached per antibody fragment. **References:** 1. Agarwal P, Bertozzi CR. *Bioconjug Chem.* 2015;26(2):176-92. 2. Sletten EM, Bertozzi CR. *Angew Chem Int Ed Engl.* 2009;48(38):6974-98. 3. Schumacher D, Hackenberger CP, Leonhardt H, Helma J. *J Clin Immunol.* 2016;36 Suppl 1:100-7. 4. Meyer JP, Adumeau P, Lewis JS, Zeglis BM. *Bioconjug Chem.* 2016;27(12):2791-807. 5. Massa S, Xavier C, Muyldermans S, Devoogdt N. *Expert Opin Drug Deliv.* 2016;13(8):1149-63. 6. Schumacher D, Helma J, Schneider AFL, Leonhardt H, Hackenberger CPR. *Angew Chem Int Ed Engl.* 2018;57(9):2314-33.

OP-329

Synthesis of *trans*-cyclooctene derivatives with restricted isomerization rate for optimal *in vitro* and *in vivo* pretargeting strategiesJ. B. Bequignat¹, A. Rondon^{1,2}, A. Baufond¹, M. Quintana¹, C. Boucheix³, J. P. Pouget², E. Miot-Noirault¹, J. M. Chezal¹, I. Navarro-Teulon², F. Degoul¹, E. Moreau¹, N. TY¹; ¹Clermont Université, Université d'Auvergne, U1240 Imagerie Moléculaire et Stratégies Théranostiques, Clermont-Ferrand, FRANCE, ²IRCM INSERM U1194, Montpellier, FRANCE, ³Université Paris Sud, U935, Villejuif, FRANCE.

Purpose: Pretargeting strategy relies on the dissociation of a vector (mAb) from a radionuclide carried by a probe. This specific recognition between a mAb and a probe can be performed using an inverse electron demand Diels-Alder cycloaddition (IEDDA) with *trans*-cyclooctene (TCO) and tetrazine (Tz) as bio-orthogonal groups. Despite good results obtained both *in vitro* and *in vivo*, some obstacles to improve this approach still remain such as i) the control over the isomerization of TCO into its unreactive *cis*-cyclooctene (CCO) isomer, yet poorly documented in papers, and ii) the controversial role of PEGylated linkers between TCO and mAb (Rossin *et al.* 2013; Rahim *et al.* 2015). We wished to prove the importance of the control of the isom-

erization rate on mAb-PEG_nTCO+Tz ligation efficiency *in vitro*, before considering further *in vivo* studies. **Methods:** PEGylated aminoacid spacers were readily obtained by introduction of a carboxylic acid moiety from a primary alcohol, and converted to the corresponding TCOPEG_nNHS with restricted *trans*-isomerization (100% for n=0 and ≥ 90% for n=4, 8, 12). Then, Ts29.2, a non-internalizing mAb targeting TSPAN8 overexpressed in colorectal cancers, was functionalized with mixtures of TCOPEG_nNHS containing more or less CCO (10, 50 and 90%). Ts29.2-PEG_nTCO±CCO conjugates were 1) evaluated by fluorescence imaging on HT29 cells and 2) subjected to stability studies in PBS and plasma at 37°C with gel electrophoresis monitoring, to study both the impact of isomerization rate and PEGylation on the reactivity and stability of Ts29.2-PEG_nTCO conjugates towards fluorescent Tz probes. **Results:** As the proportion of CCO increased in Ts29.2-PEG_nTCO±CCO conjugates, the mean fluorescence intensity decreased as expected on HT29 cell assay. Moreover, PEGylated mAb conjugates tend to isomerize faster than the non-PEGylated mAb-PEG₀TCO at 37°C in both PBS and plasma, whatever was the starting isomerization rate, indicating that the further TCO were from the mAb, the more isomerized they would be. We were able to prove that efficient TCO-Tz ligation required strict control of TCOPEG_nNHS isomerization before coupling to mAb to minimize false negative results when undertaking *in vitro* and *in vivo* assays. **Conclusion:** We were able to develop efficient syntheses of PEGylated aminoacid spacers and TCOPEG_nNHS while limiting their isomerization rate to 10%. This work clearly demonstrated the consequences of isomerization rate and PEGylation on the TCO-Tz ligation efficiency, thus confirming that Ts29.2-PEG₀TCO was the best candidate for further *in vivo* experiments with radiolabeled Tz probes as previously described (Rondon *et al.*, 2017).

OP-330

Silencing the background signal associated with local tracer administration

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Introduction: The over-shining effect, which occurs in close proximity to the site of local tracer administration, can limit imaging-based identification of structures of interest, e.g. sentinel nodes or nerves. In an attempt to control this phenomenon for fluorescent tracers, a novel pre-targeting and “click” chemistry-based de-activatable fluorescence quenching concept was applied. The efficacy of this approach was evaluated *in vivo* in mice using a fluorescence-based neuronal tracing set-up. **Methods:** Pre-targeting was achieved using a previously published neuronal tracer that consisted out of a Cy5-labeled wheat germ agglutinin (WGA) lectin.¹ For this study WGA was functionalized with a Cy5 dye that contained a chemo-selective azide handle (N₃-Cy5-WGA; 29 μM, 20 μL). Chemical reaction with a Cy7 quencher dye (Cy7-DBCO; 1330 μM), yielded Cy7-[“click”]-Cy5-WGA; a compound wherein Forster resonance energy transfer quenches the Cy5 emission. The photophysical properties and activation kinetics of these compounds were evaluated *in situ*. Quenching kinetics were quantitatively evaluated *in vitro* using

fluorescence confocal imaging of a Schwannoma cell culture. The potential of *in vivo* injection site background quenching was evaluated during imaging of the Nervous Ischiadicus in THY-1 YFP mice (24 hours p.i.). **Results:** *In situ*, conjugation of Cy7-DBCO to N₃-Cy5-WGA resulted in >80% reduction of the signal intensity of Cy5 fluorescence. In cells, pre-targeting with the N₃-Cy5-WGA lectin resulted in membranous staining. Over the course of 30 minutes Cy7-DBCO yielded signal de-activation until only nuclear and lysosomal reference stainings could be identified. *In vivo*, initially Cy5-based visualization of the Nervus Ischiadicus was limited by an intense background signal emitted at the injection site. Administration of Cy7-DBCO at the location of the injection site effectively quenched this background signal, while the fluorescence signal present in the Nervous Ischiadicus remained intact. Increasing the volume of Cy7-DBCO (5–20 μL; 6.6–26.6 nmol) resulted in an increase of the diameter of the quenched portion of the initial injection site. **Discussion/Conclusion:** The presented quenching technology allowed fast and effective reduction of the background signal at the injection site, while preserving *in vivo* nerve visualization. While this proof-of-principle study was focused on fluorescence imaging of nerves, this concept could also be expanded to other local tracer applications where background signal present and issue. **References:** 1. KleinJan *et al.*, Molecules, 2014; 19, 9876–9892

OP-331

Fast Radiofluorination And Characterization Of A Novel Hybrid Peptide Analogs Based On Mucin And Folic Acid: Potential Breast/ovarian Cancers Pet Imaging Agent

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Epithelial mucin (MUC1) and folic acid (FA) are overexpressed by most epithelial cancers hence attracting increasing interest as potential targets for imaging and therapy. The high expression of MUC1 and FA on breast and ovarian cancers and low expression on normal tissues makes them potential targets for diagnosis and therapy of cancers. To develop an efficient ¹⁸F-labeled radiopharmaceutical with enhanced breast/ovarian cancer targeting capacity we have designed and synthesized a novel MUC1-derived peptide and also conjugated MUC1 to FA in order to formulate MUC1-FA hybrid peptide conjugate for targeting MUC1/FA receptors. MUC1 and hybrid MUC1-FA were prepared by solid-phase synthesis following Fmoc/HBTU method. FA was attached to MUC1 via terminal Lys by manual conjugation. The synthetic approaches for radiofluorination of MUC1 and MUC1-FA entailed a one-step reaction through the primary amine of the Lys residues. The key precursors 4-N,N,N-trimethylammonium benzoate-MUC1 and MUC1-FA triflates were treated using catalyzed nucleophilic no-carrier-added ¹⁸F in ACN at 80°C for 5 min. The radiofluorinated conjugates were purified by C18 Sep-Pak column. *In vitro* receptor binding was performed on T47D as well as MCF7 cell lines and biological evaluation was done in normal and mice bearing MCF7 cells xenografts. The structure and purity of conjugates were confirmed by mass spectrometry and HPLC. As determined by HPLC, the radioflu-

oration efficiency of these radioconjugates were >70% and radiochemical purities always >95% in less than 30 min. These synthetic approaches hold considerable promise as a rapid and efficient method amenable for automation for the radiofluorination of peptides with high radiochemical yield and short synthesis time. **In vitro** tests have shown that significant amount of the [^{18}F]-MUC1 and [^{18}F]-MUC1-FA associated with cancer cell fractions. **In vivo** characterization in normal mice revealed rapid blood clearance of hybrid [^{18}F]-MUC1-FA with excretion by both urinary and hepatobiliary pathways. Biodistribution of [^{18}F]-MUC1 and hybrid [^{18}F]-MUC1-FA in mice bearing MCF7 xenografts demonstrated significant tumor uptakes (3% and 12%, respectively). These uptakes were blocked by excess co-injection of FA and MUC1 suggesting receptor-mediated process. **In vivo** imaging using animal PET/CT is in progress and will be reported. These results demonstrate that [^{18}F]-MUC1 and [^{18}F]-MUC1-FA may be useful as molecular probes for detecting and staging of breast and ovarian cancers and their metastasis as well as monitoring tumor response to treatment and deserves further evaluation.

OP-332

Triazole-Based Radiopeptidomimetics: Novel Minigastrin Analogues for Improved Tumour Targeting

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Introduction: The systematic replacement of amide bonds in the amino acid sequence of peptides by stable 1,4-disubstituted 1,2,3-triazoles, termed a triazole-scan, has previously been shown to yield peptidomimetics with improved proteolytic stability and tumour targeting properties.^{1,2} To prove the general utility of this new methodology, a triazole-scan was performed with DOTA[Nle¹⁵]-MG11. This truncated analogue of gastrin has a high affinity and specificity towards the cholecystokinin 2 receptor (CCK2R) but a low stability against metabolic degradation.³ The goal of this project is to identify an analogue of DOTA[Nle¹⁵]-MG11 with improved targeting of CCK2R positive tumours including medullary thyroid or small cell lung cancer. **Methods:** A library of triazolominigastrins (TZMGs) with single or multiple insertions of triazoles was prepared by a combination of standard solid-phase peptide synthesis and the Copper(I)-catalysed azide-alkyne cycloaddition (CuAAC). The novel conjugates were radiolabelled with [^{177}Lu]LuCl₃ for evaluation of their physiochemical properties in vitro (receptor affinity, cell internalisation, plasma stability) and in vivo biodistribution studies in xenografted mice. **Results:** We present the successful synthesis of the TZMG library in high yields and purities. The compounds were radiolabelled with [^{177}Lu]LuCl₃ in radiochemical yields >95%. In vitro, the majority of the tested compounds displayed maintained or improved biological activity. For example, one TZMG showed remarkably increased receptor affinity (IC₅₀), whereas other analogues exhibited improved plasma half-lives (t_{1/2} >24 h). First results of in vivo stud-

ies in mice showed a 2.5-fold improved tumour uptake of a lead candidate compared to the all-amide reference peptide. The triazole-scan of DOTA[Nle¹⁵]-MG11 is the first example of the amide-to-triazole switch leading to a peptidomimetic with improved receptor affinity. **Conclusion:** The triazole-scan is an efficient and straight forward methodology for the identification of radiolabelled peptide analogues with improved biological characteristics. The approach is applicable to many tumour-targeting peptides that may benefit from metabolic stabilisation. (1) Valverde, I. E.; Bauman, A.; Kluba, C. A.; Vomstein, S.; Walter, M. A.; Mindt, T. L. *Angewandte Chemie International Edition* 2013, **52**, 8957. (2) Mascarin, A.; Valverde, I. E.; Vomstein, S.; Mindt, T. L. *Bioconjugate Chemistry* 2015, **26**, 2143. (3) Grob, N. M.; Behe, M.; von Guggenberg, E.; Schibli, R.; Mindt, T. L. *Journal of Peptide Science* 2017, **23**, 38.

OP-333

^{18}F -Fluorination of Leucine-Containing Peptides via TheDT PhotoFluor Platform

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Purpose: ^{18}F -Fluorodeoxyglucose ([^{18}F]FDG) is the most widely used Positron Emission Tomography (PET) radiotracer for cancer imaging today, but [^{18}F]FDG is not a target-specific tracer and only provides information on tumor glucose metabolism. Thus, development of new ^{18}F -PET tracers that are able to target specific biomarkers is an important pursuit. Peptide-based tracers are often preferred for receptor imaging owing to their ease of synthesis, tuneable targeting properties and favourable pharmacokinetics. However, it is a long-standing challenge to label a peptide with ^{18}F and the use of prosthetic groups can negatively impact target affinity, target specificity and pharmacokinetics. We have recently reported a unique fluorination strategy that enables the insertion of ^{18}F directly into the tertiary C-H bond of branched amino acids (e.g., leucine and its analogues) with no protecting groups in aqueous solution, using sodium decatungstate (NaDT) catalyzed photofluorination (DT PhotoFluor) chemistry¹. Here we demonstrate that the DT PhotoFluor platform can also successfully radiolabel leucine residues in an array of peptides. **Subjects & Methods:** [^{18}F]NFSI was synthesized from [^{18}F]F₂ using a reported method². Then [^{18}F]NFSI was reacted with leucine containing peptides in the presence of sodium decatungstate and UV light. The reaction was carried out using either a micro-fluidic chip or borosilicate NMR tubes immersed in 8-lamp reactor or PTFE tubes wrapped around a black-light-bulb lamp. The ^{18}F -fluorinated peptides were purified by cation exchange column or HPLC. The compatibility of this chemistry with other amino acids was studied, and several ^{18}F -fluorinated biologically relevant, small peptides were synthesized. **Results:** Several ^{18}F -fluorinated leucine containing peptides have been synthesized using this method, including dipeptides (NL and KL), tetrapeptides (AELG and ELAF), FALGEA and PSMA KL (decay corrected radiochem-

ical yield ranged from 8% to 40%). **Conclusion:** Using the DT PhotoFluor platform, we have successfully realized the direct radiofluorination of unprotected leucine containing peptides under mild aqueous reaction conditions. The DT photoFluor platform is amenable to automation which will increase the specific activity to meet and facilitate the clinical use. Overall, decatungstate-mediated fluorination of peptides represents a convenient and facile method to rapidly accelerate the discovery process for radiolabelled peptides as imaging agents and the discovery of peptide-based drugs. **References:** 1. M. Nodwell, H Yang, M. Čolović, Z. Yuan, H. Merckens, W. Fu, R. E. Martin, F. Bénard, P. Schaffer, R. Britton, *J. Am. Chem. Soc.*, 2017, **139**, 3595. 2. H. Teare, E. G. Robins, E. Årstad, S. K. Luthra, V. Gouverneur, *Chem. Commun.* 2007, 2330.

OP-334

Optimization of molecular design of ^{68}Ga -labeled affibody molecule for PET imaging of HER3 expression

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Aim: The human epidermal growth factor receptor type 3 (HER3) is a central contributor to cancer development, progression and resistance to HER-targeted therapy. Development of anti-HER3 therapeutic agents is advancing. However, reliable methods for selection of patients with an elevated receptor expression level are necessary for efficient treatment. Achieving high contrast imaging of HER3 continues to be challenging because of generally low expression levels of HER3 in the target and considerable natural expression in normal organs, particularly liver. We have previously demonstrated that gallium-68 labeled HER3-targeting affibody molecules are able to visualize HER3 expression in a pre-clinical model. Aim of this study was to optimize the molecular design of HER3-targeting affibody molecule Z_{08698} for PET imaging using gallium-68. We investigate the influence of two different gallium-68/chelator-complexes at C-terminus of Z_{08698} in presence or absence of a hydrophilic N-terminal (HE)₃-tag on imaging contrast. **Methods:** Affibody molecules (HE)₃- Z_{08698} -X and Z_{08698} -X (X=NOTA, NODAGA) were labeled with gallium-68. Stability was tested in PBS and human serum. Binding specificity and cellular processing were studied in HER3-expressing human cancer cell lines BxPC-3 and DU145. Biodistribution of the conjugates was studied 3 h pi in Balb/c nu/nu mice bearing BxPC-3 xenografts. To confirm results of the biodistribution studies mice were imaged 3 h pi using PET/CT. **Results:** All conjugates formed stable complexes with gallium-68. Specific binding to HER3 was preserved after labeling. In vitro, binding was rapid and internalization rate was slow for all variants in both cell lines. In vivo, all variants demonstrated specific uptake to HER3 in tumors and mErbB3 in normal organs. For (HE)₃-tag containing variants blood clearance was quicker and tissue activity uptake was lower, including the tumors. The chelators influenced activity distribution in tissue. Presence of the neutral ^{68}Ga -NODAGA complex lead to lower hepatic uptake compared to variants with positively charged ^{68}Ga -NOTA complex, especially for vari-

ants without (HE)₃-tag. Among tested variants ^{68}Ga -(HE)₃- Z_{08698} -NODAGA provided the lowest blood and hepatic activity uptake and the best tumor-to-organ ratio 3 h pi (tumor-to-blood 15±2). Biodistribution results were confirmed by PET/CT. **Conclusion:** Presence of the hydrophilic (HE)₃-tag facilitated blood clearance and decreased hepatic uptake of HER3-targeting affibody molecules. Hepatic uptake was also lower for variants containing a neutral ^{68}Ga -NODAGA complex than for variants with positively charged ^{68}Ga -NOTA complex. Combination of hydrophilic (HE)₃-tag at N-terminus and neutrally charged radiometal/chelator-complex at C-terminus provided the most favorable properties for imaging of HER3 expression using gallium-68 labeled affibody molecules.

OP-335

Dual-isotope Imaging Reveals Inter-Individual Differences in Passive Uptake of Radiolabelled Antibodies in Tumours

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Aim: Radiolabelled antibodies have found great utility as PET and SPECT imaging agents in oncology. However, a notable shortcoming of antibody-based imaging agents is their tendency to accumulate non-specifically within tumour tissue. The degree of this non-specific contribution to overall tumour uptake is highly variable - in some cases, substantial - and is influenced by several tumour-specific factors. This can ultimately lead to false-positive indications, resulting in patients undergoing unnecessary or incorrect treatment regimens. Therefore, the aim of this study has been to develop an imaging technique which provides a reliable measure of inter-individual differences in non-specific tumour uptake, thus improving the accuracy of antibody-based nuclear imaging techniques. **Methods and Materials:** Dual-isotope imaging and *ex vivo* biodistribution experiments were performed using BALB/c nude mice bearing xenograft tumours established from three human breast cancer cell lines with differing expression levels of the cancer biomarker HER2 (MDA-MB-468 [HER2-negative], MDA-MB-231 [low-HER2], and MDA-MB-231/H2N [high-HER2]). These experiments involved co-administration of the anti-HER2 antibody Trastuzumab and an isotype-matched non-specific control IgG antibody, each radiolabelled with either the PET radiometal zirconium-89 (^{89}Zr) or the SPECT radiometal indium-111 (^{111}In). Each of the two possible radioisotope combinations was evaluated, *i.e.* ^{89}Zr Trastuzumab/ ^{111}In IgG, and ^{111}In Trastuzumab/ ^{89}Zr IgG. Immunohistochemical analysis of harvested tumour allograft tissue and *in vitro* saturation binding assays were also performed to further scrutinize the influence of HER2 expression (and lack thereof) on uptake and distribution of the radiolabelled antibodies. **Results:** As expected, *ex vivo* biodistribution analysis revealed that uptake of ^{89}Zr Trastuzumab in the HER2-negative MDA-MB-468 tumours was identical to the ^{111}In -IgG, resulting in a ^{89}Zr Trastuzumab/ ^{111}In IgG ratio of 1.0±0.1. While similar uptake values of ^{89}Zr Trastuzumab were measured in MDA-MB-231 (low-HER2) and MDA-MB-231/H2N (high-HER2) tumours (ranging between 12-19 %ID/g), the amount of non-specific uptake as indicated by the ^{111}In

IgG uptake value was greater in the MDA-MB-231 tumours. Consequently, [^{89}Zr]Trastuzumab/[^{111}In]IgG ratios of 1.8 ± 0.1 and 2.3 ± 0.2 were determined for the low- and high-HER2 tumour types, respectively. These values were reflected in the corresponding SPECT images in which intra-tumoural regions of non-specific uptake were clearly highlighted. **Conclusions:** The dual-isotope imaging method which has been developed allows determination of inter-individual (and voxel-per-voxel) values of non-specific uptake for radiolabelled Trastuzumab. This approach can be readily adapted to any radiolabelled antibody of interest and offers the ability to more accurately quantify receptor expression levels.

906 Monday, October 15, 2018, 14:30 - 16:00, Hall Y

Do.MoRe: Dosimetry in PSMA Therapy - What is the Benefit?

OP-336

First Clinical and Dosimetry Results of Tandem Alpha-Beta PSMA Radioligand Therapy (TABPRLT) Using a Combination of Ac-225 and Lu-177 Labelled PSMA-617 for Progressive End-Stage Metastatic Prostate Cancer

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Purpose: Prostate specific membrane antigen (PSMA) targeted radioligand therapy (PRLT) using alpha emitter Ac-225 PSMA-617 has demonstrated promising results in progressive end-stage metastatic prostate cancer (PC). We present the first clinical and dosimetry results of tandem alpha-beta PRLT (TABPRLT), concurrently administering both Lu-177 PSMA-617 and Ac-225 PSMA-617. **Methods:** Six PC patients with widespread metastases, having progressed after multiple previous therapies including Lu-177 PSMA, received Ac-225 PSMA-617. TABPRLT using 5 MBq of Ac-225 PSMA-617 concurrently applying 6 - 7.5 GBq Lu-177 PSMA-617 was performed in 4 patients (P1, P2, P4, P5). Two patients (P3, P6) received 8 and 10 MBq Ac-225 PSMA-617, respectively. For preliminary safety evaluation, renal dose estimations were made for Ac-225 PSMA-617 in 2 patients (P1 and P4) using OLINDA. The time-activity curves derived from serial Lu-177 PSMA whole-body scans and quantitative SPECT/CT were extrapolated to the physical half-life of Ac-225. The assumptions in the estimation regarding Ac-225 were: instantaneous decay of unstable daughter radionuclides, relative biological effectiveness of 5 and biodistribution similar to Lu-177 PSMA-617. At the time of analysis, follow-up with Ga-68 PSMA PET/CT, PSA and laboratory evaluation at 8 weeks after therapy was available in 2 patients (P1, P2) undergoing TABPRLT, and one (P3) receiving only Ac-225 PSMA. **Results:** Excellent response with nearly complete remission was observed on Ga-68 PSMA PET/CT in 2 patients (P1, P2) after TABPRLT. PSA reduced by more than 99 % from 153 to 0.9 ng/ml and from 186 to 0.1 ng/ml, respectively.

Patient 3 receiving Ac-225 PSMA-617 experienced partial remission with significant PSA-decline from 1080 to 173 ng/ml. In P1 and P4, mean absorbed renal dose with Ac-225 PSMA were 0.5 Sv(RBE5)/MBq and 1.7 Sv(RBE5)/MBq, respectively; with Lu-177 PSMA were 0.6 and 1.52 mSv/MBq, respectively. The higher renal dose in P4 was due to a single functioning kidney. No xerostomia was reported by any patient. There was no fall in hemoglobin or blood counts despite disseminated bone marrow metastases. No organ toxicity was noted. **Conclusions:** TABPRLT administering Ac-225 PSMA-617 and Lu-177 PSMA-617 in combination enables dose estimations, and appears to be feasible, safe and effective in end-stage metastatic prostate cancer refractory to Lu-177 PSMA. The lower administered activity of Ac-225 PSMA-617 could possibly minimize the risk of dose-limiting toxicity like xerostomia. There might be a potential synergistic effect employing together two radionuclides with different emission characteristics.

OP-337

Dosimetry in Radioligand Therapy of Metastatic Castration-resistant Prostate Cancer using Lu-177 Labelled PSMA Small Molecules I&T and 617

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Aim: The aim of our study was to determine the kinetics and dosimetry of Lu-177 labelled prostate specific membrane antigen (PSMA) small molecules -I&T and -617 in patients undergoing PSMA radioligand therapy (PRLT) of metastatic castration-resistant prostate cancer (mCRPC). **Methods:** PSMA expression was verified previously by Ga-68 PSMA PET/CT in 138 patients of progressive mCRPC undergoing PRLT and included in the analysis - 51 patients received 3.4 - 7.6 GBq Lu-177 PSMA I&T and 87 patients were treated with 4.9 - 8 GBq Lu-177 PSMA-617. The biodistribution was determined based on planar whole-body scans & SPECT/CT and dosimetric calculations were performed using OLINDA software (MIRD Scheme). The kinetics were represented in terms of median effective half-life (hours) and median uptake (%IA, fraction of injected activity), which were calculated using the fit of the time-dependent activity curve to a mono- or bi-exponential function. **Results:** All patients demonstrated an intense uptake of the radiolabelled PSMA molecule in the metastases and significant uptake in the kidneys, parotid and lacrimal glands. Lu-177 PSMA-617 revealed a higher uptake in whole-body as well as in parotid and lacrimal glands. The renal uptake was higher for Lu-177 PSMA-I&T. Despite the longer half-life of PSMA-617 in kidneys and parotid glands, the renal dose was slightly higher for PSMA I&T (PSMA I&T 0.92Gy/GBq, PSMA-617 0.77Gy/GBq). Both PSMA small molecules demonstrated a comparable dose to parotid glands (0.5Gy/GBq). All metastases exhibited a higher initial uptake when using PSMA I&T, the longer half-life of which was consistent with PSMA-617. Bone metastases demonstrated the longest half-life when using PSMA-617 (PSMA-617 60h, PSMA I&T 44h). On the other hand, lymph node metastases revealed the highest tumour dose, also in case of PSMA-617 (PSMA I&T 6.9Gy/GBq, PSMA-617 7.1Gy/GBq). The

tumour-to-kidney mean absorbed dose ratio was slightly higher for PSMA-617 (7.6) as compared to PSMA I&T (6.3). **Conclusions:** PRLT of mCRPC using Lu-177 PSMA I&T and Lu-177 PSMA-617 is safe due to the rapid clearance from blood, predominantly renal elimination and the resulting low mean absorbed doses delivered to whole body and moderate dose to the kidneys. Highest absorbed dose amongst healthy organs were observed in the lacrimal and parotid glands, however, not resulting in any significant clinical sequel on long-term follow-up. There was a large inter-patient variability of the dosimetric parameters. Therefore, individual patient-based dosimetry is important for a personalised PRLT.

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First-in-Human Study of ^{177}Lu -EB-PSMA-617 in patients with MetastaticCastration-Resistant Prostate Cancer and Comparison with ^{177}Lu -PSMA-617

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Purpose: In prior studies, we synthesized ^{177}Lu -EB-PSMA-617 by conjugating a truncated Evans Blue (EB) molecule and DOTA chelator onto PSMA-617 and labeled it with ^{177}Lu to increase the tumor accumulation and retention for radioligand therapy. This study aims to evaluate the dosimetry of ^{177}Lu -EB-PSMA-617 and response to single low-dose treatment in patients with metastatic castration-resistant prostate cancer (mCRPC). **Methods:** With institutional review board approval and informed consent, 9 patients with mCRPC were recruited. Four patients accepted intravenous injection of 0.80–1.1 GBq (21.5–30 mCi) of ^{177}Lu -EB-PSMA-617, then underwent serial whole body planar and SPECT/CT imaging at 2, 24, 72, 120 and 168 h. The other 5 patients accepted intravenous injection of 1.30–1.42 GBq (35–38.4 mCi) ^{177}Lu -PSMA-617, then underwent the same imaging procedures at 0.5, 2, 24, 48, and 72 h. All patients were evaluated by ^{68}Ga -PSMA-617 PET/CT before and one month after the treatment. Dosimetric evaluation was carried out using the OLINDA/EXM 1.0 software. **Results:** When the bone metastasis tumors with comparable baseline SUV_{max} from 10.0–15.0 were selected from the two groups for comparison, the accumulated radioactivity of ^{177}Lu -EB-PSMA-617 was about 3.02-fold higher to that of ^{177}Lu -PSMA-617 ($0.0575 \pm 0.0214 \text{ MBq}\cdot\text{h}/\text{MBq}/\text{g}$ vs. $0.0190 \pm 0.0116 \text{ MBq}\cdot\text{h}/\text{MBq}/\text{g}$, $P < 0.001$). The ^{177}Lu -EB-PSMA-617 treatment showed significant more decrease of ^{68}Ga -PSMA uptake than that of the ^{177}Lu -PSMA-617 therapy (SUV change: $-32.43 \pm 0.14\%$ vs. $0.21 \pm 0.37\%$; $P = 0.002$). ^{177}Lu -EB-PSMA-617 also had higher absorbed dose in the red bone marrow and kidneys than that of ^{177}Lu -PSMA-617 (0.0547 ± 0.0062 vs. $0.0084 \pm 0.0057 \text{ mSv}/\text{MBq}$ for red bone marrow, $P < 0.01$; 2.39 ± 0.69 vs. $0.39 \pm 0.06 \text{ mSv}/\text{MBq}$ for kidneys, $P < 0.01$). However, only reversible minor leucocyte reduction were observed in 2/4 patients accepted ^{177}Lu -EB-PSMA-617. **Conclusion:** This first-in-human study

demonstrates that ^{177}Lu -EB-PSMA-617 had higher accumulation in mCRPC and a single low dose appears to be effective to the high-uptake tumors. The ^{177}Lu -EB-PSMA-617 uptake in kidneys and red bone marrow also increased but well tolerated in low dose. Further investigations with increased dose and frequency of administration are needed.

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Relevance of kidneys and bone marrow as dose-limiting organs during Lu-177-PSMA-DKFZ-617 therapy for patients with high bone tumor burden

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Aim: Both, the kidneys and the bone marrow, are considered as organs at risk in Lu-177-PSMA therapy of metastasized castration-resistant prostate cancer (mCRPC). mCRPC patients often present with a high tumor load, which may affect the risk of kidney or bone marrow toxicities via tumor sink effects. The aim of this work was to assess kidney and bone marrow absorbed doses in correlation to the patient-specific tumor load.

Methods: The study is based on the first cycle of 14 patients, treated with 3.7 or 6 GBq Lu-177-PSMA-DKFZ-617. Each patient received a pre-therapeutic Ga-68-HBED-CC-PSMA PET/CT, abdominal SPECT acquisitions 24 (+CT), 48, and 72 h p. i. and a whole-body planar scan 24 h post administration. For 10 patients, blood samples were drawn 20 and 80 min p. i. and before each image acquisition session. Kidney dosimetry was performed for all patients, based on the abdominal sequential SPECT, CT-delineated kidney volumes, a mono-exponential fit and mass-scaled S-values. The bone marrow absorbed dose was estimated for 10 patients via mass-scaled S-values, with consideration of blood, remainder of the body (ROB) and kidneys as source regions. The ROB contribution was assessed via the mono-exponential time-activity-curve from the abdominal sequential SPECT, scaled via the whole-body activity 24 h post administration. The blood contribution was derived from a bi-exponential fit of the blood time-activity-measurements. The patient-specific tumor volume was determined from the pre-therapeutic PET/CT scan via manual thresholding. **Results:** Kidney and bone marrow absorbed doses were found to be 0.33 Gy/GBq (range: 0.03–0.59 Gy/GBq) and 15 mGy/GBq (range: 6–36 mGy/GBq), respectively. The mean tumor volume was determined to be 1524 ml (range: 8–3108 ml). Significant strong negative correlation of the kidney absorbed dose with the tumor volume was verified (Pearson's $r = -0.80$, $p < 0.05$). For the bone marrow absorbed dose and the tumor volume significant strong positive correlation was found (Pearson's $r = 0.75$, $p < 0.05$). **Conclusion:** Our data indicates a significant and strong correlation of the patient-specific tumor volume and the absorbed dose to risk organs. The relevance of the kidneys as dose-limiting organs decreases with increasing tumor volume, while the risk of marrow toxicities may become more severe due to an increasing bone marrow absorbed dose.

OP-340**Voxel based dosimetry of ^{177}Lu -PSMA-617 within a prospective clinical trial: Whole body tumour dosimetry and correlations with pre-therapeutic imaging and biochemical outcomes**

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Aim: Determine the radiation dosimetry of ^{177}Lu -PSMA-617 using a voxel-based technique and analyse relationships to pre-therapeutic imaging and clinical outcomes. **Materials and methods:** 30 patients with advanced prostate cancer receiving ^{177}Lu -PSMA-617 within a prospective clinical trial (AC-TRN12615000912583) were studied. All patients underwent pre-therapeutic ^{68}Ga -PSMA-11 PET-CT to confirm high PSMA expression (SUVmax of tumour at least 1.5 times SUV of liver). Following therapy patients underwent quantitative SPECT-CT at 4, 24 and 96 hours. Pharmacokinetic uptake and clearance at a voxel level was calculated and cumulated activity translated into absorbed dose using Monte Carlo determined voxel S values. Volumes-of-interest were drawn on normal tissues and tumour bearing regions to determine dose. 'Whole-body' tumour dose was also defined by threshold of all tumour that received doses greater than 2 and 5 Gy. Correlations between PSMA PET-CT parameters, dosimetry and therapeutic response were analysed for spearman's r -values. Difference in absorbed doses to tumour in patients that achieved a PSA-response greater than 50% was evaluated by Wilcoxon-Mann-Whitney test. **Results:** Mean 'whole body' tumour absorbed doses (above 2 Gy) was 7.7 Gy and (above 5 Gy) 12.55 Gy. 'Whole body' tumour dose was associated with PSA response at 12 weeks with a mean dose of 14.67 Gy in patients who achieved PSA $\geq$ 50% decline vs. 10.42 Gy for those achieving a PSA<50% decline ($p<0.01$). Of 11 patients receiving a tumour dose less than 10 Gy, only one achieved PSA fall $\geq$ 50% Mean absorbed dose to kidneys, submandibular and parotid glands, liver, spleen and bone marrow were 0.39, 0.44, 0.58, 0.1, 0.06 and 0.11 Gy/MBq, respectively. Tumour volume SUVmean on PSMA PET correlated with "whole body" mean absorbed dose ($r=0.62$). SUVmax of the parotid glands also correlated with absorbed dose ($r=0.67$). Absorbed dose in salivary glands was 0.65 and 0.43 Gy/MBq for the eight patients with the highest and lowest tumour burdens respectively. **Conclusions:** Significant correlation between "whole body" voxel-based tumour dose and PSA response at 12 weeks was observed that could assist in identifying patients who are likely to respond based on post-treatment imaging. Patients receiving a dose less than 10 Gy were unlikely to achieve a fall in PSA $\geq$ 50%. Significant correlations between aspects of screening ^{68}Ga -PET-CT and tumour and normal tissue absorbed dose were observed that might allow a priori prediction of response and toxicity. A reduction in salivary absorbed dose was observed in patients with higher tumour burdens providing a rationale for future patient-specific dosing.

OP-341**Shortened acquisition times for the dosimetry In ^{177}Lu -PSMA Treatments: a comparison of different dosimetry scenarios**

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Introduction: Dosimetry in radionuclide treatments is expected to be accurate for full 3D (SPECT/CT) imaging. An axial scanning range of 3 field of views ("FOV") in [^{177}Lu]-PSMA treatments covers the patient's body from the salivary glands to the pelvis and is necessary for full organ- and tumor dosimetry. However, this procedure is time consuming and therefore not tolerable for many patients. Aim of this study was to investigate the accuracy of alternative scenarios with shorter acquisition times compared to SPECT/CT as a gold standard. **Material and methods:** 16 patients underwent [^{177}Lu]-PSMA treatments. The post treatment radionuclide distribution was scanned on 4 consecutive days using a DiscoveryNM/CT670pro SPECT/CT (GE Healthcare). Both a 3 FOV-SPECT/CT and a whole-body planar scan ("WB") were acquired for each patient with mean administered activity of 6166 ± 295 MBq [^{177}Lu]-PSMA. A commercially available software toolkit (Dosimetrix®, GE Healthcare) was used to analyze the data for three scenarios: (1) Multi-SPECT/CT ("MS") using 3D-data only, (2) Multi-WB ("MB") for planar data only and (3) Hybrid ("MH") as a combination of multiple WB scans and one SPECT/CT. Absorbed doses were calculated for salivary glands, kidneys, liver, lung and reference tumor regions for each scenario. **Results:** Mean tumor dose from Multi-SPECT/CT was 51 ± 23 Sv and could not be reproduced in the other scenarios because of insufficient delineation of tumor boundaries in the planar scans. Liver and lung doses were overestimated in MB (1.1 ± 0.9 Sv (liver) / 0.8 ± 0.6 Sv (lung)) vs. 0.6 ± 0.2 Sv (liver) / 0.6 ± 0.5 Sv (lung) in the MS scenario whereas doses to the salivary glands were underestimated: 0.8 ± 0.5 Sv (MB) vs. 1.6 ± 0.6 (MS). Significantly increased kidney doses were observed in the MB scenario 2.7 ± 1.3 Sv vs. 1.2 ± 0.7 Sv in the MS scenario. The organ doses from the MH scenario did not differ significantly from the MS doses with individual variations of $\pm 20\%$. Scan times were 4x30min (MS), 4x10min (MB) and 4x10min + 1x30min (MH) and could thus be reduced by approx. 50% for MB and MH scenarios. **Conclusions/Discussion:** The hybrid scenario seems to be a good trade-off between patient convenience and accurate dosimetry for organs. However, the tumor doses can be approximated from the SPECT/CT in the MH scenario using the physical half live and/or known average values for the effective half live.

OP-342**Comparison of absorbed dose to kidneys using quantitative SPECT/CT and whole body planar images for ^{177}Lu -PSMA I&T in prostate cancer therapy**

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Purpose: Dosimetric calculations can be based on calibrated planar images of whole body or quantitative SPECT/CT images. Overlapping activity distributions are expected to affect the dose value based on planar images. Thus, the aim of this study was to quantify the difference of calculated absorbed dose to kidneys for ¹⁷⁷Lu-PSMA I&T therapy in prostate cancer patients.

Subjects & methods: Patient images were acquired with a SPECT/CT (Symbia T6, Siemens) and reconstructed by Flash 3D software provided by the vendor. Six patients were measured at 2, 24, 48, 72 and 168 hrs post injection. The mean administrated activity of ¹⁷⁷Lu-PSMA I&T was 6.9 ± 0.3 GBq. At each time point, data sets of a whole body planar and an abdominal SPECT/CT (one bed position) were acquired. SPECT/CT data were calibrated using a mean calibration factor derived by using a NEMA IEC phantom and two vials of different volumes: 25 and 180 ml representing a lesion and a kidney, respectively. For planar whole body data, the conjugate view method including background subtraction was applied. The kidney organ absorbed dose was calculated using OLINDA/EMX software and the individual kidney volume was derived from pre-therapeutic PET/CT. **Results:** Kidney dose using SPECT/CT and planar data ranged from 0.42 Gy/GBq to 0.88 Gy/GBq and from 0.39 Gy/GBq to 0.92 Gy/GBq, respectively. The average kidney dose based on planar images was 23% higher than the dose calculated from SPECT/CT data (0.69 ± 0.24 Gy/GBq vs 0.53 ± 0.21 Gy/GBq). **Conclusion:** In this limited patient cohort, the difference in dose values based on planar and SPECT/CT data is less than the inter-individual variation. Special care needs to be taken in organ delineation, if planar images are used for dose calculation. For a precision dose assessment of main critical organs such as kidneys, salivary gland, and liver, time efficient SPECT/CT whole body scan protocols need to be developed.

OP-343

Investigation of the effect of patient motion onto 3D dose estimates in Lu-177-PSMA therapy using Siemens xSPECT Quant reconstruction with integrated motion correction and Dosimetry Research Tool

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Introduction: In radionuclide therapy of metastasized castration resistant prostate cancer (mCRPC) the post-therapeutic estimation of the induced radiation dose to tumours and organs-at-risk is important for the evaluation of therapy effects and for therapy planning. Dose estimation techniques in 3D are employed for detailed analysis of tissue dose. Since patients expressing mCRPC often suffer from pain, which hinders a motion-free SPECT acquisition, we investigated the effect of small pain-induced patient movements during SPECT acquisitions onto dose

estimates computed from quantitative reconstructions which employ an integrated reprojection-based motion correction algorithm. **Subjects & Methods:** We selected a patient with SPECT scans at 24, 43 and 67 h post administration of 6 GBq of Lu-177-PSMA. SPECT data were acquired with a Siemens Symbia T2 in 120 projections (15 s, 256x256, 2.4 mm/pixel). Four distinct patient movements were simulated by shifting 8 projections (every 45 degree) of the scan at 24 h transaxially by 1, 2, 3, 5 and 10 pixels. These movements simulate patient's aims to release pain by changing position for the duration of a few seconds (one projection). Data were reconstructed with a prototype Siemens xSPECT Quant reconstruction using high resolution CT from the pre-therapy PET/CT scan. Organs' VOIs were created by Siemens CT segmentation prototype, lesion VOIs were segmented by a 70 % threshold on the motion-free reconstruction of the 67 h SPECT. 3D dose maps were computed using Siemens Dosimetry Research Tool (DRT). A baseline dose map was computed from the original SPECT scans. **Results:** Applying motion correction to the original data changed dose estimates of the kidneys by 1 % and of a spinal tumour (30 ml) by 4 %. Before motion correction, the differences of dose estimates for 1, 2, 3, and 5 pixels motion compared to the baseline were 1, 1, 1 and 2 % for the kidneys and 1, 2, -3 and -40 % for the tumour. For 10 pixel shift, the error in the kidneys raised to 22 %, whereas the voxel-wise fitting in the tumour failed in the majority of the contained voxels. After motion correction all differences for all shifts including the 10 pixel shift were reduced to less than +/-5 % in the kidneys and the tumour. **Conclusion:** We demonstrate the potential for dose estimation error due to patient motion, as well as the potential to correct for motion to improve quantitation.

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Monday, October 15, 2018, 14:30- 16:00, Hall 1

Teaching Session 3 - Interactive Clinical Cases: ESMIT - Modern Insight in Medical Education

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Flipping the Classroom: Making the most of your time with the learner

R. M. Schwartzstein; Harvard Medical School, Boston, UNITED STATES OF AMERICA.

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Principles of Workplace Learning - The Art and Science of Becoming a Nuclear Medicine Clinical Educator

P. Brand; Groningen University, Groningen, NETHERLANDS.

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Monday, October 15, 2018, 14:30 - 16:00, Hall 6

Thyroid: Radioiodine Therapy of Benign Thyroid Diseases

OP-346

The influence of radioiodine therapy in 2800 patients with nodular goiter in subclinical hyperthyroidism

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Subclinical hyperthyroidism (SHT) is a state of increased thyroid function with few or no clinical definitive signs or symptoms of hyperthyroidism, characterized by low serum thyrotropin (TSH) level, and normal serum free thyroxine (FT4) and triiodothyronine (FT3) levels. The incidence ranges between 0.7% and 10%. The risk of progression to overt hyperthyroidism varies between studies 1–15% / year. The main related adverse effects of SHT include cardiovascular disease, with increase risk of atrial fibrillation, and cardiovascular death, but also all-cause mortality. The indications for treatment of SHT are matter of discussion, and there is no high quality evidence to guide treatment recommendations. The aim of our study was to assess the influence of radioiodine therapy (RAIT) on the achievement of euthyroidism, prevention of adverse effects on the cardiovascular and prevent progression to overt hyperthyroidism. **Materials:** We treated 2800 patients with nodular goiter in subclinical hyperthyroidism referred to our department during the last 12 years, aged 19–87 years; 88% of them were females and 12% males; 908 patients with multinodular goitre (MNG), and 1892 patients with autonomous nodule (ATN). Qualification of these patients were based on: clinical features, normal levels of serum FT3 and FT4, low levels of serum TSH and characteristic appearance on thyroid scans. Malignant changes were excluded in all nodules by fine-needle aspiration biopsy. All the patients had serum TSH levels less than 0.1 mU/l before RAIT, thyroid volumes were ranged between 15–145 ml, and effective half-life was more than 3 days at the time of treatment. The activity dose was calculated by the use of Marinelli's formula and ranged between 200 and 800 MBq. The absorbed dose (Gy) ranged between 180 and 300. Follow-up control was done every 6 weeks. **Results:** Euthyroidism achieved in 99% of patients with ATN and 92% of MNG; 1% of patients with ATN and 7% of patients with MNG develop hypothyroidism. Second dose of RAIT used for 1% of patients with MNG due to failure of treatment. In all of the patients, the symptoms and signs of SHT disappeared (palpitation, tachycardia, atrial fibrillation, exercise tolerance improved, and the blood pressure normalized. **Conclusions:** The achievement of euthyroidism and the remission of the symptoms and signs of SHT, were due to good diagnosis and accurate measurement of administered activity. We advocate RAIT to be the first-line treatment in majority of patients suffering from subclinical thyrotoxicosis due to multinodular toxic goitre and solitary toxic adenoma.

OP-347

Clinical outcome after treatment with ^{131}I correlates with radiation sensitivity in hyperthyroidism patients

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Aim: Therapy of hyperthyroidism with ^{131}I is still mostly performed on an empirical basis. The role of the genes controlling

radiation sensitivity(GCRS) played in the ^{131}I -therapy is undefined yet. The present study was undertaken to find GCRS markers indicating individual radiosensitivity and predict the hypothyroidism in hyperthyroidism patients treated by ^{131}I in a prospective randomized trial. **Methods:** 59 patients diagnosed with hyperthyroidism in our hospital were randomly selected for the present study between May and October 2013. The GCRS (including Bcl-2, NF- κ B, Survivin, Ku70, Tob1, EGFR, Egr-1, p53, BRCA-1 and ATM) mRNA levels of the tissue sample were analyzed with quantitative polymerase chain reaction (qPCR). With a follow-up period of at least 2 years after the ^{131}I treatment, the patients divided into two groups by the clinical outcome. The expression of the GCRS defined as high and low groups by the median value. The relationship between clinical outcome and the expression of GCRS were analyzed using Chi-square test. Quantitative variables were analyzed with the Student's t-test or Mann-Whitney U test. In addition, logistic regression analysis was also used to evaluate the impact to which particular parameters contributed to the occurrence of hypothyroidism after ^{131}I treatment. A p-value <0.05 was considered statistically significant. **Results:** 44 patients enrolled with a clinical outcome after at least 2 years' follow up, while 14 patients were lost. There were 11 men and 33 women whose average age was 44.79 ± 12.94 years. The clinical outcome: 59% (26/44) patients were hypothyroidism (59%), while 41%(18/44) patients were non-hypothyroidism, including 18%(8/44) sustained hyperthyroidism. A significant correlation between the mRNA level of Ku-70 and the clinical outcome was found. The mRNA levels of other GCRS did not associate with the clinical outcome. The hypothyroidism group(1.24(0.84,3.54))showed significantly lower Ku-70 mRNA expression than non-hypothyroidism group(3.24(1.25,6.43)) (P<0.05), while no significance was detected in another GCRS mRNA expression(All p>0.1). The logistic regression analysis showed that the Ku-70 were significantly correlated with the hypothyroidism after ^{131}I treatment(P<0.05). **Conclusions:** The correlation between Ku-70 and the clinical outcome of ^{131}I treatment suggests its important role in radiosensitivity of the hyperthyroidism patients who received this ^{131}I therapy. And it could be a prognostic factor of the ^{131}I treatment in the hyperthyroidism patients.

OP-348

The Outcome of Radioiodine Therapy for Graves' Hyperthyroidism: a Single Institution Experience with Calculated Dose Regimen

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The aim of the study was to evaluate the effectiveness of I-131 therapy (RAIT) calculated dose regimen on the outcome of Graves' hyperthyroidism (GH) patients (pts). Secondary aim was to assess the effect of RAIT on thyroid gland weight (TGW). **Patients and methods:** We retrospectively reviewed 101 GH pts aged 28–83 years (y) (88 females with median age 50y and 13

males with median age 46y) treated with I-131. Most of the pts were treated with antithyroid drugs prior to RAIT, underwent thyroid function tests (TFTs), thyroid ultrasound (US) with estimate of thyroid gland weight (TGW), and 24h-I-131 uptake test. The administered I-131 activity was calculated to deliver 3,33–4,44 MBq I-131/g thyroid x TGW (g)/ 24-h-I-131 uptake. After RAIT, pts had been followed-up with serum TSH, FT3 and FT4. Median follow-up period was 24 months (range 12–80 months). The outcome of RAIT was recorded according to TFTs results after 3, 6, 12 months, and overall outcome after 24 months following RAIT. Post-treatment US was performed 1y following RAIT. The evaluate the effect of RAIT on TGW, pts were divided in three groups: <20 (average 18g), 20–40 (average 30g), >40 (average 60g). **Results:** Overall 71 pts (70.3%) required a single RAIT, 23 pts (22.8%) received 2 RAIT and 7 pts (6.9%) 3 RAIT. Median pre-treatment US TGW was 33 g (14–124g), 24h¹³¹I uptake 60% (25–82%), median I-131 dose 259 MBq (7 mCi) (3–30 mCi), and overall median applied dose 296 MBq (8 mCi) (3–45 mCi). Overall outcome of RAIT after 2y was 94,4% pts cured with 50% hypothyroid, 44,4% euthyroid and 5,6% hyperthyroid. Overall average applied dose according to TGW was: 185 MBq, 296 MBq and 629 MBq. The cure rate after 2y was 100% (85% hypothyroid), 92% (46% hypothyroid), and 89% (54% hypothyroid). Average TGW decrease was 53%, 52% and 53% respectively. In group 20–40g, 20% pts required 2 RAIT and 1% 3 RAIT. In group >40g, 35% pts required 2 RAIT and 14% 3 RAIT. **Conclusions:** Iodine-131 therapy is effective treatment of GH. In pts with lower TGW (<20g), with this calculated dose approach, 100% cure rate was achieved with one RAIT. However, for larger glands, more than one RAIT was necessary to cure hyperthyroidism, especially for TGW>40g. Therefore, for large glands, ablative approach with 5,92–7,4 MBq I-131/g of TGW should be advocated. No difference in median TGW decrease was observed between groups probably due to calculated approach.

OP-349

Individualized post-therapy dosimetry of kidney in patients undergoing I-131 treatment for differentiated thyroid cancer (DTC): how feasible is it?

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Purpose: I-131 therapy of differentiated thyroid cancer (DTC) delivers high absorbed doses to kidneys, therefore patient-specific dosimetry of these organs at risk is important, especially for patients undergoing subsequent I-131 therapies. This study aims to assess the feasibility of individualized kidney post-therapy dosimetry in patients treated for DTC in clinical routine.

Subjects and methods: 15 patients treated for DTC with I-131 were included. Administered activity ranged from 50 to 150 mCi. Conjugate view whole body (WB) images were acquired 1,2,3,4 and 18 hours after oral I-131 administration on dual

head γ-camera (SOPHA DST-Xli). SPECT acquisition over the abdomen was performed on the same system, at 18 hours post administration. Low dose CT images were acquired on Siemens Somatom Emotion system. CT images were used only for the determination of each kidney's volume and body thickness, d. Image processing and analysis were performed on Xeleris 3.1 workstation and ImageJ. WB anterior (I_A) and posterior (I_P) images were fused to form the geometric mean image which was then attenuation corrected based on the following formula: $I_0 = (I_A * I_P)^{1/2} * e^{ud/2}$ where, I_0 is the attenuation corrected image. Region of interest were drawn around each kidney, on I_0 image and measured counts were converted to activity by multiplying them with system's sensitivity. Time-Activity Curves (TACs) obtained by WB images were rescaled by the ratio of the activity derived from SPECT image and the activity from the kidney region in the WB image at 18 h post administration. Origin software was used for SPECT derived TAC-fitting and integral calculation in order to determine cumulative activity, $\bar{A}$, in each kidney. Kidney absorbed dose was determined according to MIRD equation: $D = \bar{A} * S * m_{reference} / m_{kidney\ tissue}$ ($m_{reference}$ equals to 288 g for unit density tissue). **Results:** System's WB planar sensitivity was 127 counts/μCi and SPECTs Cross-calibrator factor was 1.8 KBq/cps. Average attenuation coefficient was measured equal to 0.0095 cm⁻¹. Patients' kidney mass ranged from 148 to 245 g and kidney mean absorbed dose ranged from 92.2 to 199.6 cGy. **Conclusion:** Patient specific dosimetry, based on molecular imaging is continuously becoming important in nuclear medicine therapies. The above described method is an efficient and quite accurate tool to estimate kidney mean absorbed dose for patients undergoing I-131 therapy for DTC. It can be easily applied in routine clinical practice of any department performing molecular radiotherapy.

OP-350

Radioiodine therapy of goiter with low radioiodine uptake after endogenous TSH stimulation by antithyroid drugs.

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Introduction: Relatively low radioiodine uptake (RAIU) represents a limitation for ¹³¹I therapy, especially in patients with goiter. Pretreatment with low-dose recombinant human TSH was shown to ameliorate thyroid dosimetry but its use remains rather complex with limited tolerance. In this study, we evaluated the alternative use of antithyroid drugs (ATD) therapy on TSH levels, RAIU, regional distribution of radioiodine and estimated absorbed dose (in Grays). This is a control study, each patient being his own control. Then, we prospectively evaluated the efficiency of ¹³¹I therapy on thyroid volume (TV) and function.

Methods: Forty-five patients (mean age: 75 years) with significant goiter (mean 92 ml), underwent two ¹²³I thyroid scan, at baseline (TS0) and after a 1-to-4 months administration of ATD

(TS1), when a low ^{123}I concentration ($< 0.4\%$ at 120') was first measured (TS0), in absence of known iodine overload. TSH was monthly checked till necessary and ATD withdrawn 3 days before TS1. The patients finally received a calculated ^{131}I activity limited to 740 MBq (ambulatory administration). Thyroid volume was estimated by ultrasound, before and after ^{131}I therapy. **Results:** Patients received a mean 37 mg of carbimazole for 2.6 months. The mean TSH increased from 0.45 ± 0.45 to 2.7 ± 4.0 mU/L ($p < 0.0001$), corresponding to serum free T4 and free T3 concentrations decreases by 28% and 9.4%, respectively. This small TSH variation yielded nevertheless great mean 120 minutes-RAIU from $5.7 \pm 3.5\%$ to $20.5 \pm 13.5\%$ ($p < 0.0001$). Regional distribution of radioiodine was not changed by the procedure, as IT in 50% and 80% of the volume did not differ significantly ($p = 0.86$ and $p = 0.051$ respectively). There was a 134% increase in the predicted median absorbed dose ($p < 0.0001$) from 47 ± 23 Gy to 110 ± 80 Gy. At the end of follow-up (average of 30 months), thyroid volume decreased by $46 \pm 20\%$ ($n = 36$, $p < 0.001$). The rate of hypothyroidism was of only 31%; **Conclusion:** Pretreatment with ATD proved to be effective to improve thyroid dosimetry in patients with intermediate-to-big goiters and relatively low RAI uptake at baseline. A small TSH increase and a three days withdrawal of ATD is enough to allow both a large increase of the mean RAIU and of the estimated median absorbed dose. ATD's preparation is therefore a safe, cheap, easily accessible way to improve ^{131}I therapy, with excellent tolerance, good reduction of TV and limited occurrence of hypothyroidism.

OP-351

Serum Level of Thyroperoxidase Antibodies in Patients with Graves-Basedow Disease One Year After Radioiodine Treatment

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Background: Graves-Basedow disease (GBD) is one of the most common thyroid autoimmune disorders. Elevated anti-TSH receptor antibodies (TRAb) and thyroperoxidase antibodies (aTPO) serum levels are usually observed. Radioiodine therapy ^{131}I is one of recommended treatment options. The aim was to evaluate the correlation between aTPO concentration before and after the ^{131}I treatment and its outcome like thyroid volume and function in patients with GBD. **Material and methods:** Retrospective evaluation of medical records in one-year observation of total 46 patients - 38 (82.6%) women and 8 (7.4%) men aged 47.4 ± 13 years with clinical and laboratory features of hyperthyroidism in the course of GBD who received therapeutical dose of ^{131}I was performed. The serum level of TSH, FT4, aTPO, TRAb, iodine uptake and the thyroids volume by ultrasound were done before treatment and one year after ^{131}I therapy. To prevent radioiodine treatment associated exacerbation of GBD orbitopathy, the daily oral dose of 30 mg prednisone was given with gradual reduction by 8 weeks in 8 (17.4%) patients. Patients were treated with 178–969 MBq (av. 463.5 ± 55.9) with absorbed dose (250 Gy) in all patients. **Results:** Successful treatment results like normal thyroid func-

tion or hypothyroidism was obtained in 42 (91.3%) patients. Persistent hyperthyroidism was observed in 4 (8.7%) patients. No significant differences in aTPO serum levels before and one year after ^{131}I treatment ($p = 0.67$) were observed. There were no significant correlation in aTPO level and age in total group of patients, except of statistically significant higher level of aTPO observed in the men group compared to women group after therapy ($p < 0.025$). The steroid prophylaxis had no influence on the results of therapy ($p = 1.0$). The average volume of the thyroid gland significantly decreased after radioiodine treatment ($p < 0.00001$). There were no significant associations between thyroid volume and aTPO serum levels after treatment ($p = 0.49$). No significant differences in aTPO serum level and the outcome of radioiodine treatment as well as 24 hours ^{131}I uptake to 48 hours ^{131}I were found ($p = 0.85$ and $p = 0.38$, respectively). **Conclusion:** In one year follow-up despite of thyroid volume reduction and more than 90% success rate of radioiodine treatment aTPO remained high.

OP-352

The feasibility of relying on dose calculation for more successive therapy in Graves and Toxic adenoma guided by one year follow up.

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Aim: the goal of the current study was to show the efficacy of dose calculation on the treatment outcome and to analyse the impact of different rationales on the dose estimation through evaluating the treatment response in Graves and Toxic Adenoma. **Material and Methods:** the involved patients ($n = 25$) were suffering from Graves ($n = 15$) and Toxic Adenoma ($n = 10$). The eligibility was determined by experienced nuclear medicine physician according to blood tests, $^{99\text{m}}\text{Tc}$ -pertechnetate scintigraphy and ultrasound scans (US). A properly calibrated thyroid uptake probe equipped with sodium iodide crystal NaI(Tl) was used to measure the uptake values at 2, 24, 48, 72, and 96 hours following administration of 0.5–1 MBq iodine tracer. Neck and femur quantification was made up to 1 minute and repeated 3 times to reduce the deviation error. Three models were employed to calculate the absorbed dose involving OLINDA, EANM, and ellipsoidal thyroid model. The treatment response was evaluated across one-year after therapy and subdivided into euthyroid, minimum hypothyroidism, excessive hypothyroidism, hyperthyroidism. **Results:** the mean effective half-life was 125.8 h (range: 73.7–180.1 h) and mean residence time was 110.1 h (range: 38.4–210.2 h). The calculated activity that would deliver 200 Gy for Graves patients ($n = 15$) according to OLINDA was 359 ± 246 MBq where the mean deviation of EANM and the ellipsoidal model was - 4% and 15%, respectively. The activity required to impart 300 Gy for toxic adenoma was determined as 672 ± 348 MBq based on OLINDA, where the mean deviation of EANM and ellipsoidal thyroid model was 41% and 65% respectively. TA patients were evaluated as euthyroid during follow up visits in which the absorbed dose was 360 ± 99 Gy. For Graves patients, 10 out of 15 patients received 240 ± 55 Gy and showed euthyroid status, while the patients who received ≥ 385 Gy was

deemed excessive hypothyroidism. **Conclusion:** mean dose of 350 Gy seems adequate for treating toxic adenoma that verify euthyroid status while the desired dose due to graves should not be less than 200 Gy to ascertain euthyroid. EANM method which is based on 3 measures seems more practical and cost effective to be applied for Graves patients, while unite density sphere model is indispensable and more feasible to be applied in toxic adenoma. On the basis of the current study, considering elliptical shape of thyroid gland / or nodule during treatment planning is apparently irrelevant as seen in the presented outcome after treatment.

OP-353

The occurrence of Graves' disease after radioiodine treatment of benign thyroid disorders

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Aim: The occurrence of Graves' disease (GD) after the radioiodine (I-131) treatment of toxic nodular goiter has been described in approximately 5% of treated patients. Since less data is available on the etiology of this phenomenon, our aim was to evaluate the incidence and risk factors of I-131-induced GD in patients with benign thyroid disorders of different etiologies living in an iodine sufficient area. **Material and Methods:** In this retrospective study we included consecutive patients with the benign thyroid disease that were treated with I-131 in the period between January and June 2014 at our department. Before treatment, we measured the uptake of iodine 123 (I-123) at 20-hours or the uptake of technetium-99m-pertechnetate (Tc-99m). During the follow-up, in all patients without GD, "de novo" occurrence of GD during 12 months after I-131 application was evaluated on the basis of thyroid function evaluation, thyrotropin receptor antibodies (antiTSH-R) measurement and thyroid scintigraphy. Mann-Whitney analysis was applied, p value <0.05 was considered statistically significant. **Results:** In the observed period, 298 patients (249 women and 49 men; mean age, 62.83±17.01 years) were treated with I-131. Among them, 97 (32.6%) were treated for GD, 98 (32.9%) for solitary toxic adenoma, 93 (31.2%) for toxic multinodular goiter, 6 (2.0%) had Hashimoto's thyroiditis and 4 (1.3%) patients had euthyroid nodular goiter. Compared with other causes of hyperthyroidism, GD patients showed significantly higher uptake of I-123 (median, 76% and 31%, respectively, p<0.01) or Tc-99m (median, 3.0% and 1.1%, respectively, p<0.01). The treatment activity in GD patients was significantly lower than in other patients (median, 727 MBq and 745 MBq, respectively, p<0.01). Among 201 patients without previous GD, GD occurred after I-131 therapy in only 4 (2.0%) patients (3 women, 1 man); 2 patients received I-131 for toxic multinodular goiter, 1 patient for solitary toxic adenoma and 1 patient for hyperthyroidism due to Hashimoto's thyroiditis. Patients with I-131-induced GD were significantly younger than those without GD after I-131 therapy (mean, 45.0±18.2 and 68.8±14 years, respectively, p=0.01), whereas the received activity of I-131 (median, 573 MBq and 745 MBq, respectively, p=0.06),

and Tc-99m uptake before therapy did differ significantly (median, 1.1% and 1.1%, respectively, p=0.90). **Conclusion:** I-131-induced GD occurs rarely in I-131-treated patients with benign thyroid disorders without previously known GD. According to our preliminary data, possible risk factor represents a younger age of I-131-treated patients.

910 Monday, October 15, 2018, 14:30 - 16:00, Hall 28

Joint Symposium 29 - Radiopharmacy / Dosimetry / Radiation Protection / EMA: Title TBC

Details to be announced

1001 Monday, October 15, 2018, 16:30 - 18:00, Plenary Hall

CME 8 - Oncology: Different Strategies in the Management of Hepatic Metastases in NEN

OP-358

Nuclear Medicine Physicians' View (PRRT; SIRT)

S. Ezziddin; University Clinic Homburg / Saarland, Department of Nuclear Medicine, Homburg, GERMANY.

OP-359

Oncologists' View

N. Fazio; European Institute of oncology, IEO, Division of Gastrointestinal Medical Oncology and Neuroendocrine Tumors, Milan, ITALY.

OP-360

Surgeons' View

A. Frilling; Imperial Collage London / Hammersmith Campus, Department of Surgery and Cancer, London, UNITED KINGDOM.

1002 Monday, October 15, 2018, 16:30 - 18:00, Hall 2

Joint Symposium 15 - Cardiovascular / ASNC: Detecting Cardiac Microvascular Disease with PET

OP-361

CAD and Diabetes

W. Acampa; Institute of Biostructures and Bioimaging, Naples, ITALY.

OP-362

Women

P. Cremer; Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, UNITED STATES OF AMERICA.

OP-363

Cardiomyopathy

F. Bengel; Hannover Medical School, Department of Nuclear Medicine, Hanover, GERMANY.

OP-364**Role in Guiding and Assessing Treatments?**

V. Taqueti; Brigham and Women's Hospital, Boston, UNITED STATES OF AMERICA.

1003

Monday, October 15, 2018, 16:30 - 18:00, Hall 3

Joint Symposium 16 - Physics / EFOMP / ESR:
Dedicated and Low Dose Molecular Imaging

OP-365**Imaging for Radioembolisation**

S. Walrand; Université Catholique de Louvain, Nuclear Medicine, Brussels, BELGIUM.

OP-366**Dedicated PET Technology and Systems**

A. Gonzalez; Institute for Instrumentation in Molecular Imaging, i3M, Valencia, SPAIN.

OP-367**Total Body PET**

S. Vandenberghe; Ghent University, MEDISIP, Ghent, BELGIUM.

OP-368**Intra-Operative Molecular Imaging with Cerenkov Light**

J. Grimm; Memorial Sloan Kettering Cancer center, Molecular Pharmacology, New York, UNITED STATES OF AMERICA.

1004

Monday, October 15, 2018, 16:30 - 18:00, Hall 5

CTE 4 - Technologists: Latest Development in PET/MR

OP-369**The Physicist's View on PET/MR Developments**

A. Barnes; UCL Hospitals NHS Foundation Trust, London, UNITED KINGDOM.

OP-370**Clinical Applications of Cardiac PET/MR**

C. Rischpler; Klinik für Nuklearmedizin, Universitätsklinikum Essen, Universität Duisburg-Essen, Essen, GERMANY.

OP-371**PET/MR in Brain Applications – A Technologist's Tale**

V. Lupson; University of Cambridge, Wolfson Brain Imaging Centre, Cambridge, UNITED KINGDOM.

1005

Monday, October 15, 2018, 16:30 - 18:00, Hall X

M2M: Antibodies and their Fragments

OP-372**Pharmacokinetics of ^{111}In -anti-mPD-L1 in immune challenged tumor-bearing mice**

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Introduction: Immune checkpoint inhibitors have shown impressive efficacy in cancer patients. However, only a subgroup of patients benefits from this treatment and serious immune related adverse effects call for predictive biomarkers. Preclinical studies have shown that microSPECT/CT using radiolabeled anti-programmed death-ligand 1 (PD-L1) antibodies can be used to detect and quantify PD-L1 expression *in vivo*. However, the presence of PD-L1 positive immune cells may alter the pharmacokinetics of anti-PD-L1 antibodies. As oncological patients may suffer from local or systemic infections during the course of immune therapy, it is important to know whether this affects the biodistribution and tumor uptake of anti-PD-L1 antibodies. Therefore, we investigated the effects of lipopolysaccharide-mediated (LPS) immune activation on the pharmacokinetics and tumor-targeting of ^{111}In -anti-PD-L1. **Methods:** The effect of immune activation on anti-PD-L1 *in vivo* biodistributions was evaluated in three conditions; healthy BALB/c mice, Renca tumor-bearing BALB/c mice, and LPS-challenged (0.6 mg/kg body weight) Renca tumor-bearing BALB/c mice. All mice were intravenously injected with 30 μg ^{111}In -labeled anti-mPD-L1 (optimal dose as assessed previously in tumor-bearing BALB/c mice). In addition, subgroups of mice were injected with 100 μg of ^{111}In -anti-mPD-L1. Pharmacokinetics was assessed by taking blood samples and biodistribution was quantified by microSPECT/CT and *ex vivo* biodistribution studies 72 h after tracer injection. PD-L1 expression in organs of interest was evaluated immunohistochemically. **Results:** There were no statistically significant differences in the *in vivo* biodistribution of ^{111}In -anti-PD-L1 between tumor-bearing and non-tumor-bearing mice. However, in immune-challenged mice, splenic tracer uptake significantly increased compared with non-LPS challenged tumor-bearing mice (65.0 ± 10.3 %ID/g vs. 35.2 ± 4.9 %ID/g; $p < 0.001$), resulting in accelerated blood clearance and reduced tumor targeting (blood 24 hours pi: 4.2 ± 0.3 %ID/g vs. 9.3 ± 3.1 %ID/g; $p < 0.05$, tumor: 7.9 ± 5.3 %ID/g vs. 25.9 ± 11.6 %ID/g; $p < 0.05$). Increasing the tracer dosage to 100 μg resulted in reduced splenic uptake (27.3 ± 4.9 %ID/g vs. 12.1 ± 3.5 %ID/g; $p < 0.05$) and slower blood clearance (blood 24 hours pi: 12.2 ± 2.5 %ID/g vs. 14.3 ± 2.6 %ID/g; ns), thereby restoring tumor targeting (18.1 ± 1.7 %ID/g vs. 15.3 ± 4.3 %ID/g; ns). **Discussion:** These results show that severe inflammatory responses can significantly alter pharmacokinetics and tumor targeting of radiolabeled anti-PD-L1 antibodies.

By increasing the anti-PD-L1 antibody dose, splenic uptake was saturated and efficient tumor targeting restored. This information is essential to accurately interpret PD-L1 scans in the clinical setting, as oncological patients may suffer from systemic infections which could lead to an underestimation of anti-PD-L1 antibody tumor uptake in case of suboptimal antibody-dosing.

OP-373

Cytotoxicity In Vitro and Anti-Tumour Effects In Vivo of Trastuzumab-DM1 (T-DM1) are Correlated with HER2 Expression Level and Tumour Uptake of ^{89}Zr -DFO-Trastuzumab-DM1 Assessed by PET

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Objective: The antibody-drug conjugate trastuzumab-DM1 (T-DM1; Kadcyla) is approved for treatment of HER2-positive breast cancer (BC). HER2 overexpression criteria used for trastuzumab are also used for T-DM1 but it is not known if T-DM1 is effective for treatment of BC with lower HER2 expression. Our objective was to determine the correlation between HER2 levels and cytotoxicity of T-DM1 in vitro and between the tumour uptake of ^{89}Zr -DFO-T-DM1 by PET and response to treatment with T-DM1.

Methods: Tumour cells with HER2 ranging from HER2 0 to 3+ were exposed in vitro to T-DM1 or trastuzumab (0–100 $\mu\text{g}/\text{mL}$) for 72 h and cytotoxicity determined in clonogenic survival (CS) assays. To study tumour delivery of T-DM1 by PET, T-DM1 was conjugated to desferrioxamine (DFO) and labeled with ^{89}Zr . MicroPET/CT was performed in mice bearing subcutaneous BT-474 (HER2 3+), MDA-MB-361 (HER2 2+), MDA-MB-231 (HER2 1+), or trastuzumab-resistant TrR1 (HER2 2+) BC xenografts, injected with a therapeutic dose of T-DM1 incorporating ^{89}Zr -DFO-T-DM1 (10 μg , $6 \pm 1.2 \text{ MBq}$). Mice were imaged at 96 h post-injection. Tumour and normal tissue biodistribution were determined. Mice with these same BC xenografts were treated with T-DM1 (3.6 mg/kg) every 3 weeks for 7 weeks to determine tumour response. **Results:** Clonogenic assays revealed greater potency of T-DM1 than trastuzumab on HER2 positive tumour cells sensitive or resistant to trastuzumab. The CS of BT-474 cells (HER2 3+) exposed to 10 $\mu\text{g}/\text{mL}$ of T-DM1 or trastuzumab was 0.0% vs. $46.4 \pm 7.5\%$, respectively ($P < 0.001$) while the CS of MDA-MB-361 cells was $0.6 \pm 0.2\%$ vs. $62.7 \pm 16.4\%$, respectively ($P < 0.001$). T-DM1 was significantly more potent towards trastuzumab-resistant TrR1 BC cells and SK-OV3 ovarian cancer cells at 10 $\mu\text{g}/\text{mL}$ (CS = $3.5 \pm 0.0\%$ vs. $84.1 \pm 16.5\%$ and 0.0% vs. $55.4 \pm 11.7\%$, respectively; $P < 0.001$). Tumour uptake of ^{89}Zr -DFO-T-DM1 was directly correlated with HER2 expression ranging from 2.4% ID/g for MDA-MB-231 (HER2 1+) to 9.8% ID/g for BT-474 (HER2 3+) BC xenografts. Tumours were visualized by microPET/CT. Tumour uptake was also correlated with in vitro cytotoxicity of T-DM1. A direct correlation was found between tumour uptake of ^{89}Zr -DFO-T-DM1 and response to T-DM1 (doubling time). **Conclusion:** The cytotoxicity of T-DM1 in vitro is directly correlated with HER2 expression but T-DM1 was more potent than trastuzumab. The direct correlation between tumour uptake of ^{89}Zr -DFO-T-DM1 in vivo and response to T-DM1 suggests that PET could predict response to treatment in patients with HER2-positive BC.

OP-374

Diagnostic evaluation of a novel ^{89}Zr -labeled monoclonal antibody against tumor-associated mucin 1 in a preclinical breast cancer model

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Introduction: There is still a great “unmet medical need” concerning diagnosis and treatment of breast cancer which can be addressed by utilizing molecular targets for more specific diagnosis and therapy. Tumor-associated mucin 1 is expressed on over 90 % of all breast cancer entities and differs strongly from its physiological form on epithelial cells, therefore presenting a unique target for breast cancer diagnosis and antibody-mediated immune therapy. We generated a monoclonal antibody (GGSK-1/30) selectively recognizing the human tumor-associated mucin 1 by means of a synthetically prepared anti-tumor vaccine. This antibody is highly specific against tumor-associated mucin 1 and shows stronger binding to breast cancer cells than several commercially available monoclonal antibodies against mucin 1. **Subjects & Methods:** In this study a desferrioxamine (Df’)-conjugated GGSK-1/30 monoclonal antibody was labelled with ^{89}Zr and evaluated as a potential PET tracer. Self-generated primary murine breast cancer cells expressing human tumor-associated mucin 1 were transplanted subcutaneously in wild type and human mucin 1-transgenic mice. Binding and pharmacokinetic properties of [^{89}Zr]Zr-Df’-GGSK-1/30 were measured *in vitro* in tumor-associated mucin 1-expressing human and murine cell lines and in breast tumor-bearing mice by *in vivo* PET/MRT imaging as well as by *ex vivo* organ biodistribution analyses. **Results:** [^{89}Zr]Zr-Df’-GGSK-1/30 was radiolabeled with a radiochemical yield of >60 %, a radiochemical purity of >95 % and an apparent specific activity of 6.1 GBq/ μmol . After 7 d, stabilities >80 % in human serum and >90 % in saline were observed. *In vitro* cell studies showed strong binding to human and murine cell lines expressing the human tumor-associated mucin 1. The breast tumor-bearing mice showed an *in vivo* tumor uptake of >50 %ID/g and clearly visible specific enrichment of the radio-conjugate *via* PET/MRT. **Conclusion:** A novel radioimmunoconjugate based on a new monoclonal antibody GGSK-1/30 against tumor-associated mucin 1 was successfully generated and identified as a promising candidate selectively targeting breast cancer cells. It was further studied as a diagnostic PET-tracer for breast cancer imaging.

OP-375

Biodistribution, Imaging and Metabolism Studies of 64-Copper Radiolabelled Monoclonal Antibody: Comparison of DOTA and TE1PA Chelating Agents in a Murine Model of Multiple Myeloma

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Purpose: TE1PA is a C-functionalized monopicolinate cyclam designed for 64-copper chelation. It was proven to have excellent Cu(II) and Cu(I) chelation properties, with fast kinetics, high thermodynamic stability and resistance to transchelation *in vitro*, and a usefulness for phenotypic imagery when coupled to antibodies. This work presents *in vivo* studies (biodistribution, metabolism and imaging) of TE1PA in a syngenic multiple myeloma model on mice, compared to DOTA, its main competitor. **Materials and methods:** p-SCN-Bn-TE1PA and DOTA-NHS ester were grafted on 9E7.4 rat IgG_{2a} antibody, targeting murine CD-138. Immunoconjugates were then radiolabelled with ⁶⁴Cu. Both ⁶⁴Cu-9E7.4-p-SCN-Bn-TE1PA and ⁶⁴Cu-9E7.4-NHS-DOTA were injected in 12 mice previously grafted with 5T33 cells, allowing the development of subcutaneous tumors expressing CD-138. Each mouse was injected with 100 µg of radioimmunoconjugates corresponding to 10 MBq of ⁶⁴Cu. For each time studied (2h, 24h and 48h post-injection), a biodistribution and a liver metabolism studies were conducted on mice for both radiolabelled antibodies. Additionally, a micro-PET scan was performed on 4 mice injected with ⁶⁴Cu-9E7.4-p-SCN-Bn-TE1PA at those 3 times. **Results:** Biodistribution study shows an excellent hepatic clearance of the ⁶⁴Cu-9E7.4-p-SCN-Bn-TE1PA over time. Significantly higher radioactivity was found in blood, lungs and heart at 48h PI for ⁶⁴Cu-9E7.4-NHS-DOTA, which suggests a release of ⁶⁴Cu from antibody, in parallel with a higher intestinal elimination. This was correlated by the liver metabolism study, which shows a better *in vivo* resistance to transchelation for ⁶⁴Cu-9E7.4-p-SCN-Bn-TE1PA. The imaging study of ⁶⁴Cu-9E7.4-p-SCN-Bn-TE1PA shows an increasing targeting of the tumors over time and confirms the hepatic clearance at 24h and 48h PI. **Conclusion:** ⁶⁴Cu-9E7.4-p-NCS-Bn-TE1PA has shown a very high tumor targeting, associated to an increasing of tumor-to-tissues ratio over time that suggests an overall clearance from healthy tissues. Compared to DOTA, TE1PA displays an *in vivo* stability and resistance to transchelation significantly superior. This confirms the previous results obtained *in vitro* and ⁶⁴Cu-labelled TE1PA proved once again its usefulness for immuno-PET imaging in a preclinical model.

OP-376

Development and *in vivo* characterization of a chimeric anti-Gal-3 Fab for immuno-PET imaging of thyroid cancer

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Purpose: Galectin-3 (Gal-3) is a promising target for imaging of thyroid nodules because of its well documented expression in

thyroid cancer, but not in benign thyroid nodules. To take advantage of the better tissue penetration compared with full-size antibodies, we have developed a chimeric rat/human Fab-fragment directed against Gal-3 that has optimized clearance characteristics. This novel protein tracer was subjected to *in vitro* characterization and *in vivo* validation in a thyroid orthotopic murine model. **Methods:** The variable light and heavy chain gene segments of an anti-Gal-3 mAb were amplified from the hybridoma M3/38. The corresponding Fab-fragment carrying human IgG1/κ constant genes was subsequently produced in the periplasm of *E. coli* and purified to homogeneity in a functional state. The resulting chimeric rat/human Fab-fragment was furthermore fused with a long disordered amino acid chain comprising Pro, Ala and Ser residues (PASylation) to tune the plasma half-life and increase tumor uptake. The anti-Gal3 PAS₂₀₀-Fab was conjugated with Dfo and labeled with ⁸⁹Zr under mild conditions. After purification by gel filtration the tracer was analyzed by radio-HPLC, TLC and SDS-PAGE for integrity, followed by testing for immunoreactivity on TC cell lines. Finally, athymic nude mice were inoculated with TC cells into the left thyroid lobe and tumor growth was monitored via US and fluorescence molecular tomography (FMT). After i.v. injection with ~3.0 MBq of ⁸⁹Zr-DFO-PAS₂₀₀-Fab the mice underwent PET/CT imaging followed by biodistribution and immunoistochemical analysis. **Results:** The recombinant anti-Gal-3 Fab showed high affinity toward recombinant human Gal-3 (K_D ≈ 1 nM) as measured by real-time plasmon resonance spectroscopy (Biacore), both in the PASylated and the plain format. The anti-Gal3 ⁸⁹Zr-DFO-PAS₂₀₀-Fab tracer was produced with high radiolabeling yield (83±5%) and radiochemical purity (>98%). The stability in 50mM DTPA solution and serum was >80% and >98% over 24 hours. In vitro studies on TC cells showed an immunoreactivity of 48±5%. *In vivo* PET/CT imaging showed excellent image contrast already 12 h p.i., with maximal accumulation 24h p.i., and signal associated to the orthotopic-implanted tumors but no uptake in the tumor-free thyroid lobe. Biodistribution studies further confirmed the accumulation in orthotopic tumors. **Conclusions:** Our novel anti-Gal3 ⁸⁹Zr-DFO-PAS₂₀₀-Fab tracer demonstrated selective and strong accumulation in the TC-positive thyroid left lobe. The *in vivo* validation of the chimeric rat/human Fab directed against Gal-3 opens the possibility of fast translation into clinical application of immunoPET imaging of thyroid cancer, supporting the personalized management of patients bearing thyroid nodules.

OP-377

MicroSPECT/CT Imaging of Patient-Derived EGFR-Positive Tumour Xenografts with Technetium-99m Labeled Panitumumab Fab Fragments

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Aim: Patient-derived tumour xenografts (PDXs) in mice more reproducibly recapitulate the heterogeneity of human tumours, and are more strongly predictive of the effectiveness of new cancer therapies than cell line based xenografts (CTX). We previously developed ^{99m}Tc -labeled panitumumab Fab (^{99m}Tc -PmFab-SMCC-His₆) which retained binding to EGFR ($K_d = 59.7 \pm 4.2$ nM) and localized in EGFR-positive MDA-MB-468 human breast cancer (BC) xenografts in mice [tumour uptake = 14.9 ± 1.8 %ID/g at 24 h p.i. and tumour/blood (T/B) ratio = 11.6]. Tumours were visualized by microSPECT/CT at 4 h p.i. of ^{99m}Tc -PmFab-SMCC-His₆. Our aim in this study was to further examine the imaging properties of ^{99m}Tc -PmFab-SMCC-His₆ using more clinically relevant PDX mouse models that are EGFR-positive. **Methods:** PDX were established in NOD/SCID mice by engrafting surgical specimens from patients with BC, head and neck squamous cell carcinoma (HNSCC) or pancreatic cancer (PnCa). Each PDX model represented a different patient specimen. Mice (n=2-4) were injected i.v. with 30-40 MBq (70 µg) of ^{99m}Tc -PmFab-SMCC-His₆ and microSPECT/CT studies were carried out at 4 and 24 h p.i. Biodistribution studies were performed following imaging. The EGFR positivity of excised tumors from different PBX was confirmed by immunohistochemical (IHC) staining. **Results:** Tumors were imaged by microSPECT/CT at 4 h p.i. of ^{99m}Tc -PmFab-SMCC-His₆ and remained modestly visible at 24 h p.i. in all PDX models. Biodistribution studies revealed that tumor uptake ranged from 3.8-11.4 %ID/g with a T/B of 1.8 – 17.5 in BC models and 6.9 – 14.5 %ID/g with a T/B ratio of 7.1-7.6 in HNSCC models. Tumour uptake in PnCa models ranged from 3.8 - 4.6 %ID/g with a T/B of 2.4 - 5 for primary tumours and 3.1 - 3.8 %ID/g with a T/B ratio of 2.1 - 3.6 for metastatic lesions on the abdominal wall. IHC staining revealed strong EGFR-positivity in all excised tumours. **Conclusion:** ^{99m}Tc -PmFab-SMCC-His₆ strongly localized in PDX in mice derived from patient tumours from three different EGFR-positive cancer types enabling imaging by microSPECT/CT. Tumor uptake is explained by EGFR expression that was confirmed by IHC and variability may be explained by a heterogeneous expression of EGFR. PDX mouse models may be very informative for predicting the utility of new molecular imaging probes for visualizing tumours in different patients and different cancer types. **Research Support:** Supported by the Canadian Cancer Society Research Institute.

OP-378

Development of ^{99m}Tc -Labeled Pertuzumab Fab as a Molecular Imaging Agent for HER2 Positive Tumour Xenografts Using MicroSPECT/CT

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Purpose: In the treatment of HER2-positive breast cancer (BC), diagnostic tools that can quantitatively assess individual lesion HER2 expression are needed to better predict response to HER2-targeted therapies. Our aim was to develop a targeted molecular imaging agent comprised of pertuzumab Fab modified with a histidine-containing peptide for labeling with ^{99m}Tc (^{99m}Tc -His₆-SMCC-Fab) and study its potential for imaging HER2-positive tumours in mice by microSPECT/CT. **Methods:**

^{99m}Tc -His₆-SMCC-Fab was obtained by papain digestion of pertuzumab. The Fab fragments were then conjugated to a histidine-containing peptide (CGYGGHHHHHH) through a sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (sulfo-SMCC) linker. The His₆-modified Fab was radiolabeled with a ^{99m}Tc -tricarbonyl complex. The purity of the Fab was assessed by SDS-PAGE. Incorporation of radioiodinated His₆-peptides into the conjugation reaction was used to quantify the number of His₆-peptides per Fab. ^{99m}Tc -labeling efficiency of the Fab was assessed by ITLC-SG in 0.1M sodium citrate buffer, and stability of the ^{99m}Tc -His₆-SMCC-Fab was studied in PBS and human serum for 24h at 37°C. Cell binding assays were conducted to determine the binding affinity (K_d) of ^{99m}Tc -His₆-SMCC-Fab in SK-BR-3 (HER2+) BC cells. Tumour and normal organ uptake was studied in NOD/SCID mice bearing HER2+ SK-OV-3 human ovarian cancer xenografts. Organ uptake was assessed by biodistribution studies at 24h and microSPECT/CT at 4h and 24h post-injection of either ^{99m}Tc -His₆-SMCC-Fab or a nonspecific control Fab with an endogenous histidine motif for radiolabeling. **Results:** ^{99m}Tc -His₆-SMCC-Fab was synthesized as a pure product with an average of 2.2 ± 0.8 His₆-peptides conjugated per Fab. His₆-SMCC-Fab were labeled with ^{99m}Tc to high efficiency (94-97%). ^{99m}Tc -His₆-SMCC-Fab was stable in PBS and human serum (>93% bound). Cell binding assays indicated specific high affinity binding of ^{99m}Tc -His₆-SMCC-Fab to HER2 with a K_d of 24.5 ± 1.8 nM. Biodistribution studies indicated that ^{99m}Tc -His₆-SMCC-Fab specifically localized in HER2-expressing SK-OV-3 human ovarian cancer tumours (tumour uptake = 3.5 ± 0.3 % ID/g and tumour/muscle ratio = 7.0 ± 0.7) and demonstrated a significantly higher tumour uptake than the nonspecific control Fab ($P < 0.01$, tumour uptake = 0.32 ± 0.02 % ID/g). Tumours were visualized by microSPECT/CT. **Conclusions:** ^{99m}Tc -His₆-SMCC-Fab was produced in high radiochemical purity and retained high affinity binding to HER2. ^{99m}Tc -His₆-SMCC-Fab localized specifically in HER2-expressing tumours in mice allowing imaging by microSPECT/CT. **Supported by a grant from the Ontario Institute for Cancer Research.**

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Monday, October 15, 2018, 16:30 - 18:00, Hall Y

Do.MoRe: Alpha-Particle Emitter Dosimetry

OP-379

Absorbed dose-dependent DNA damage in leukocytes after internal irradiation of blood with Ra-224 compared to Ra-223

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Introduction: Irradiation with α-emitters creates densely packed damage tracks along particle trajectories in exposed cells, including complex DNA damage and closely spaced double-strand breaks (DSBs) in hit nuclei. These damage tracks (α-tracks) can be visualized by immunofluorescent (IF) staining

with γ -H2AX and 53BP1 antibodies and be used as a biomarker for α -particle exposure. The aim of this study was to correlate the number of α -tracks in blood leukocytes after internal **ex-vivo** irradiation with Ra-224 to the absorbed dose to the blood and to compare the results to a previous study using the radium isotope Ra-223. **Subjects & Methods:** Blood samples from three healthy volunteers were split into aliquots and irradiated by adding Ra-224 solution of different activity concentrations, followed by 1 h incubation at 37°C. The activity in each sample was determined using a calibrated, high purity germanium detector. Additionally, corresponding non-irradiated baseline samples were prepared. After leukocyte separation, fixation in ethanol and two-color IF staining, the number of α -tracks and the number of small γ -H2AX and 53BP1 foci were enumerated manually in 100 cells per sample using a red/green double band pass filter of a fluorescence microscope. Absorbed dose coefficients were calculated separately for the α - and the β -contribution to the absorbed dose to the blood, assuming that the energy of all α - and β -particle emissions of Ra-224 and its progeny is deposited locally. **Results:** The absorbed doses to the blood in the samples ranged from 0 to 127 mGy, with an α -particle contribution of 96.8%. A linear fit showed a good correlation between the number of α -tracks and the absorbed dose to the blood and revealed a slope value of $(0.220 \pm 0.024) \text{ mGy}^{-1}$, which is similar to the slope value obtained after irradiation with Ra-223 (Schumann et al., Sci Rep, 2018). The frequency of small γ -H2AX + 53BP1 DSB foci indicative of β -irradiation was similar to baseline values, which is also in agreement with the Ra-223 results. **Conclusion:** Since the α -emitter-induced DNA damage in **ex-vivo** Ra-224 and Ra-223 exposed blood leukocytes was similar, it can be assumed that radiation-induced DNA damage-related effects in the peripheral blood after **in-vivo** application of either radium isotope will be similar for a comparable absorbed dose to the blood.

OP-380

Lesion dosimetry and follow-up for a large group of castration-resistant prostate cancer (CRPC) patients and bone metastases treated with 223Ra therapy

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Aim: A personalized approach could be fundamental in mCRPC patients treated with 223Ra therapy and many studies are aimed to identifying dosimetry in these patients. The purpose of the study is to evaluate the absorbed dose (AD) to lesions on a large patient group, assessing variability ranges for AD and effective half-life (T1/2eff). Correlation studies among AD, or T1/2eff, overall survival (OS), or other clinical indicators are also ongoing. **Materials and Methods:** 49 patients were included, and the AD to the lesion with highest uptake (not overlapping gastrointestinal tract, or other bones/lesions) was assessed after the first 223Ra-dichloride injection, with a methodology previously published [1]. The AD contributions of 223Ra decay-daughters were considered. Recovery coefficients (RCs) for partial volume correction were obtained using test-objects with a cross-sectional

area varying between (118–5800) mm². Patient follow-up (FU) includes monitoring of alkaline phosphatase (ALP), hemoglobin, prostate-specific antigen, ECOG status and OS. The correlation between FU data and dosimetry was preliminarily investigated by mono-variable statistical analysis for 18 patients, as resulting after excluding 9 patients who died before completing the 6 injections (due to rapid disease progression or other not disease-related causes), 4 patients with ongoing treatments, and 18 surviving patients. **Results:** The test-objects yielded a minimum RC of 0.62, whereas for lesions the minimum estimated RC was 0.72. The mean T1/2eff and AD (mean[range]) were 175[62–270] h and 3.8[0.8–15.2] Gy. The total AD for a complete treatment can be estimated multiplying the AD by the injection number (6). Median OS was 17 mo. (6 cases) vs 8 mo. (12 cases), for total AD higher or lower than 25 Gy, ($p=0.048$). T1/2eff also showed significant differences considering an ALP threshold of 226 ($p=0.011$). **Conclusion:** The wide AD and T1/2eff ranges confirm the need of patient-specific dosimetry. A correlation between OS and total AD to the lesion with highest uptake was preliminarily observed.

OP-381

Evaluation of iterative reconstruction compensated by Monte Carlo simulation for quantitative radium-223 SPECT

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Purpose: Radionuclide Therapy (RNT) using Radium-223 (Ra-223) improves patients' outcome in castration-resistant prostate cancer with bone metastases. However, accurate determination of radionuclide concentration in patients by SPECT remains a major challenge because standard iterative reconstruction usually provides qualitative images but not adequately quantitative images. At EANM'17 meeting, we suggested a Monte Carlo simulation built-in iterative reconstruction method which improved quantification for diagnostic radionuclides such as technetium-99m without using cross-calibration. The purpose of this study was to apply our method to quantitative Ra-223 SPECT and to evaluate its accuracy. **Materials and Methods:** The SIMIND Monte Carlo code, widely used for simulation of scintillation camera imaging, can output list-mode data in which emission point, detection point in the crystal, photon weight, etc. are recorded. Since this list-mode data can be used as a probability density matrix in forward projection, we designed a maximum likelihood-expectation maximization algorithm in which the list-mode data was incorporated into the forward projection using CUDA-C language. To evaluate the accuracy of our method, a NEMA body phantom filled with Ra-223 solution (spheres of 37, 28, 22, 17, 13, and 10mm in diameter: 2382.90[Bq/ml], background: 600.47[Bq/ml]) was measured using a SPECT/CT

(Symbia-T6, Siemens) with LMEGP collimator. Quantitative performance was compared between our method and a standard cross-calibration method. Since SIMIND does not have a default code for the LMEGP collimator, we coded the collimator by conducting sensitivity measurement with Ra-223 as the source and by acquiring gamma-ray images with an imaging plate which is used for standard radiography. **Results:** For LMEGP collimator, the length was 3.939[cm] by sensitivity measurement, and the diameter and septa were 0.270 and 0.060[cm] by gamma-ray imaging. We incorporated these values into our reconstruction, and the voxel values of 37 and 28mm spheres, background, and air were calculated as 2303.36, 1023.12, 548.57, and 117.00[Bq/ml], respectively. The voxel values of spheres of less than 28mm were equivalent to that of background. In the cross-calibration method, the voxel values of 37 and 28mm spheres, background, and air were measured as 1294.29, 1196.84, 661.02, and 293.71[Bq/ml], respectively. Our method showed a better agreement with known radioactivity concentration. In our simulation calculation, the breakdown of photons detected by the scanner was about 25% each for photons from Ra-223, penetration, scatter by collimator, and characteristic X-ray from collimator. **Conclusions:** Our method without using cross-calibration could quantify concentration of Ra-223 on SPECT with a higher accuracy, and opens up new possibilities for dosimetry in RNT.

OP-382

Improving Accuracy Of Quantitative ^{223}Ra -Dichloride Planar Imaging Using Compartmental Models

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Aim: In a previous study, we developed a compartmental model for ^{223}Ra in patients with metastatic bone disease from castration-resistant prostate cancer [1] using γ -camera, blood sample assay and whole-body (WB) counting data. The shape of the activity retention curve of the skeleton and GI tract was found to be well described by the model. Nevertheless, model predictions of bone uptake were systematically lower (up to 50%) than activity retention measured in patients at any time point. Furthermore, the sum of all activity from all organs was in many cases found to be higher (up to 30%) than the total injected activity. Systematic errors in the determination of sensitivity calibration factors and the attenuation correction applied are possible reasons for this deviation. The aim of this work was to improve the accuracy of quantitative ^{223}Ra -Dichloride planar imaging using those compartmental models to better match the predicted output. Systematic adjustments to the γ -camera data are potentially possible using compartmental models which could provide a relationship between the three independent sets of measurements (γ -camera, blood samples and WB). **Material and Methods:** Compartmental models of 6 patients, each given 2 administrations of 110 kBq/kg ^{223}Ra , were built in SAAM II v2.3. Compartmental models and initial rate constants were based on results of a previous study [1]. Input data from γ -camera imaging were scaled by a correction factor equal to the mean ratio of the measured skeletal activity to the modelled

skeletal activity. Model rate constants were re-evaluated and a new set of modelled activity data produced. These steps were repeated until no further changes ($< 0.1\%$) in the correction factor and rate constants were achieved. **Results:** The iterative determination of calibration factors for individual patients and treatments was found to converge in all cases after 5 or 6 iterations. Correction factors varied in between patients. Correction factors from 0.6 to 0.7 were determined. After applying the correction factor, total activity in the body was calculated to be less than or equal to the injected activity at all time points. **Conclusion:** Improving the accuracy of quantification from planar ^{223}Ra imaging using the proposed methods is feasible. Systematic errors are likely to vary between patients due to differences in patient attenuation and biodistribution which may explain the variation of calibration factors between patients. [1] Taprogge, J., et al., Eur J Nucl Med Mol Imaging (2017) 44 (Suppl 2):S807-S808.

OP-383

Accurate activity measurements for ^{223}Ra

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Aim: ^{223}Ra -dichloride is a calcium analogue that targets the hydroxyapatite in areas of increased bone turnover and has been shown to improve survival in patients with castration-resistant prostate cancer. It decays via 5 alpha emitting and 2 beta emitting radionuclides which delivers high linear energy transfer radiation, increasing the probability of cell kill whilst minimising the damage to healthy tissue. The widespread adoption of ^{223}Ra necessitated the development and dissemination of traceable activity measurement standards to allow accurate patient administrations. The aim of this study was to generate calibration factors for accurate ^{223}Ra activity measurements for a range of commercially available radionuclide calibrators. **Materials and Methods:** Two of NPL's well-characterised secondary standard ionisation chambers (Fidelis and PA782) and two commercially available ionisation chamber systems (Capintec CRC-25R and an Atomlab-500) were used to determine the calibration factors required for accurate activity measurements. These instruments allow comparative measurements using devices commonly found in clinical sites. Standardised solutions of $^{223}\text{RaCl}_2$ were measured in a range of clinically relevant geometries and volumes to determine dial settings or calibration factors along with correction factors for volume dependency. **Results:** Dial settings and calibrations factors for commonly used vials, syringes and ampoules at specific volumes are presented along with robust uncertainty estimates (dependent on the type of calibrator in use). The effect of volume in each geometry is also presented along with realistic correction factors that may be used in lieu of independent dial factors for each volume. **Conclusion:** Accurate measurements of ^{223}Ra can be made in a clinical setting using commercially available detectors in a variety of geometries. This will ensure the correct prescribed activity is administered to patients and in turn will improve the accuracy of whole-body and tumour uptake and absorbed dose calculations.

OP-384

A novel method for accurate activity measurements of emerging ^{227}Th -labelled conjugates

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Aims: Activity measurements for radiopharmaceuticals using commercially available radionuclide calibrators are commonplace and in the majority of cases the procedure used is widely known and simple to implement. Recent interest in the use of ^{227}Th -labelled conjugates has led to a demand for knowledge of the measurement characteristics of this radionuclide. Unlike conventional radionuclides, ^{227}Th is measured at intervals following separation from its decay progeny (T_0) which means that careful thought must be given to the equilibrium status of the solution at the measurement time. The response of conventional calibrators depends on the relative ratios of the decay progeny, therefore the aim of this study was to develop a method to determine a suitable dial setting and time dependent correction factor. **Materials and Methods:** The Bateman equations account for the temporal dependence of the number of radioactive atoms in a decay chain and are required to model the decay series of ^{227}Th and ^{223}Ra . ^{227}Th decays to ^{223}Ra , which in turn decays into a series of 7 different radionuclides. In the case of ^{223}Ra , the system equilibrates within about 7 hours. From this point, the total activity is approximately 6.0072 times the ^{223}Ra activity and decaying with the half-life of ^{223}Ra . A similar series of calculations on the decay series of “pure” ^{227}Th leads to a more complex situation whereby the total activity of the system increases to more than 3.2 times the initial starting activity of ^{227}Th . After approximately 20 days, the system contains more of the decay progeny than ^{227}Th . In order to determine dial settings for individual calibrators a series of readings was taken of a ^{227}Th source as a function of time. Using some fundamental information such as the activity of the ^{227}Th in the geometry of interest at T_0 , the dial setting for the calibrator for ^{223}Ra in the same geometry, and predicted dial settings for each of the ^{227}Th decay progeny, a dial setting may be determined. **Results and Conclusion:** Two methods to obtain accurate activity measurements for ^{227}Th activities were developed for a range of commercially available radionuclide calibrators. This method requires prior knowledge of the calibrator dial factor for ^{223}Ra , as well as a standardised source of ^{227}Th , at an accurately known chemical separation time of the ^{227}Th from its progeny. This methodology will provide clinical sites with accurate measurements of activity for patients with cancer treated with ^{227}Th -labelled conjugates.

OP-385

Pharmacokinetics and dosimetry of BAY 1862864, an alpha-emitting targeted thorium conjugate (CD22-TTC) in the Cynomolgus monkey

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Aim: The aim of this study was to evaluate the pharmacokinetics of the alpha-particle emitting anti-CD22 TTC (BAY1862864) in Cynomolgus monkeys and, based on tissue distribution, to estimate dosimetry in the indicated patient group, i.e. those with non-Hodgkin's Lymphoma. **Materials and Methods:** BAY1862864 comprises a monoclonal antibody targeting CD22 (epratuzumab) conjugated to a chelator that contains the alpha-particle emitter thorium-227, which decays to radium-223. The biodistribution of iv administered BAY1862864 in Cynomolgus monkeys of both sexes was measured by gamma counting after a single dose of 100kBq/kg thorium-227, and antibody doses of 0.029, 0.143 and 0.75mg/kg, and the %injected dose calculated. The absorbed doses in organs in the 0.143mg/kg dose group were calculated using OLINDA-EXM. These calculations assume that the spatial distribution of radionuclide emissions in organs is uniform. However, this is not the case for alpha-particles since the distance they travel in tissue is in the μm range (2-10 cell diameters). Accordingly, alpha-particle emission dose estimates were obtained outside of OLINDA-EXM, and then added to the electron and photon dose contribution obtained from OLINDA-EXM. Curve fitting to obtain TIAC was performed outside of OLINDA-EXM. **Results:** The blood concentration time curves of thorium-227 and antibody were parallel over the study duration, indicating good in vivo stability of the thorium-227 labelled antibody-chelator conjugate. Blood clearance was not affected by antibody dose. The greatest thorium-227 absorbed doses were observed in the spleen>liver>bone osteogenic cells. The highest radium-223 + daughters absorbed doses were bone osteogenic cells>spleen & liver. The dosimetry assessment shows that after a single dose of BAY1862864, spleen, liver and osteogenic cells receive the highest absorbed doses. However the red marrow is expected to be dose limiting due to its low tolerance to radiation. With the exception of osteogenic cells, small intestine and red marrow, the absorbed doses are predominantly determined by the dose contribution from thorium-227. As the data for alpha-particle are scarce, caution must be used in comparing the absorbed dose estimated to tolerance doses that are mainly derived from external beam radiation and beta-emitter treatments. **Conclusion:** BAY1862864 was shown to be stable in blood with a slow clearance typical for iv administered antibodies that was independent of protein dose. The absorbed dose estimates for tissues after a dose of 100kBq/kg BAY1862864 (7MBq/patient) were well below the tolerance limits established for external beam radiation. This work contributes to the greater understanding and further development of dosimetry for alpha-emitting radiopharmaceuticals.

OP-386**Feasibility study of applying ICRP biokinetic models for pharmacokinetic modelling of alpha-emitter thorium-227 used in targeted radionuclide therapy**

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Aim: Targeted radionuclide therapy with Th-227 conjugated with novel antibodies, e.g. CD33 and CD70 has been pre-clinically used for treatment of myeloid leukaemia and renal cell carcinoma, respectively. Furthermore, PSMA-targeted Th-227 conjugate PSMA-TTC was recently developed for preclinical pharmacological study of treatment of prostate cancer. The imaging of alpha-emitter labelled radiopharmaceuticals in clinical practice is challenging. Therefore theoretical modelling of bio-distributions of Th-227 and its immediate decay product Ra-223 and other progeny is highly desired. Especially radiolabelled metabolites or unconjugated daughters may lead to toxicity but also might be beneficial in the case of unconjugated Ra-223 targeting metastatic bone lesions. **Materials and methods:** The current ICRP systemic biokinetic model structure and transfer parameters of thorium were taken as the prior model and parameters for pharmacokinetic modelling. Because the immediate decay product Ra-223 is another high LET alpha-emitter which can potentially be toxic to healthy tissues, the biokinetic model of radium was coupled to that for Th-227. By doing so, the bio-distributions of Th-227 and Ra-223 in human body can be simultaneously monitored. Furthermore, other decay products were as well taken into account and connected to Ra-223 as independent biokinetic models. **Results:** Model predictions show that 67% of Th-227 leaves blood with a clearance half-life of 6 h and deposits on the bone surface, 6% of Th-227 deposits in the liver and 4.5% of Th-227 deposits in the kidneys. The progeny Ra-223 deposits a similar activity in the alimentary tract and in the liver as the parent Th-227. The retentions of Ra-223 as progeny in kidneys and testes are about 8% of that of parent Th-227. **Conclusion:** The modelled pharmacokinetic bio-distributions of Th-227 and its decay products can be used as start distributions for local kinetic analysis, such as bone surface, volume, marrow and blood. The bio-distributions of decay products can be further used for patient dosimetry assessments.

1007 Monday, October 15, 2018, 16:30 - 18:00, Hall 1

Teaching Session 4 - Interactive Clinical Cases: Lung TNM 8 and Function of the Lung MDM

OP-387a**TNM of Lung Cancer 8th Edition**

A. Eccles; Guy's and St. Thomas' Hospitals NHS Foundation Trust, London, UNITED KINGDOM.

OP-387b**TNM of Lung Cancer 8th Edition**

T. Lynch; Belfast, UNITED KINGDOM.

OP-388**What do the Respiratory Physicians want from your Report?**

N. Magee; Belfast City Hospital, Consultant Respiratory Physician, Belfast, UNITED KINGDOM.

OP-389**What do the Surgeons want from your Report?**

K. McManus; Belfast Health and Social Care Trust, General Thoracic Surgeon, Belfast, UNITED KINGDOM.

OP-390a**Nodal Stations - Which Stations can be Reached and What Methods are Available**

N. Magee; Belfast City Hospital, Consultant Respiratory Physician, Belfast, UNITED KINGDOM.

OP-390b**Nodal Stations - Which Stations can be Reached and What Methods are Available**

K. McManus; Belfast Health and Social Care Trust, General Thoracic Surgeon, Belfast, UNITED KINGDOM.

1008 Monday, October 15, 2018, 16:30 - 18:00, Hall 4

Clinical Oncology: PSMA Ligand Therapy of Prostate Cancer

OP-391**Radioligand Therapy with 7.4 GBq ¹⁷⁷Lu-PSMA-617 in patients with mCRPC in a 6 weekly interval**

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Background: Radioligand Therapy (RLT) using ¹⁷⁷Lu-PSMA-617 is generally well tolerated and shows respectable PSA response rates and seems to prolong survival. Initially an injected dose of 6 GBq ¹⁷⁷Lu-PSMA-617 at an 8 weekly interval was recommended. The aim of this study was to evaluate response and safety of a shortened cycle interval combined with slightly elevated therapeutic activity. **Methods:** A total number of 30 patients with mCRPC were treated with approx. 7.4 GBq ¹⁷⁷Lu-PSMA-617 every 6 weeks (range 6.0 - 7.7 GBq). All patients had exhausted conventional therapeutic options (median age, 67.6 years; range, 50.9 - 82.1). Data were analyzed with respect to response and safety according PCWG3 and common toxicity criteria. **Results:** In median 7.2 GBq of ¹⁷⁷Lu-PSMA-617 was injected every 6 weeks. In 23 cases at least 3 cycles of RLT were performed. In 7 patients no 3rd cycle was performed due to progression or death. A PSA decline of 50% or more occurred

in 17 (65%) patients out of 26 patients included in the analysis. Any PSA decline occurred in 19 patients (73%). The estimated median survival was not reached. Compared to previously published data, patients treated with shorter intervals and higher doses had a greater chance to reach a relevant PSA decline of more than 50% (65% compared to 50%). The rate for any PSA decline was nearly equal (73% compared to 75%). There were no acute severe Adverse Events (CTCAE °3/°4) in account of blood system disorders (Hemoglobin, Platelet count, White blood cell) detected. **Conclusions:** Preliminary results from 30 patients show that shorter therapy intervals combined with slightly elevated doses may be more effective with respect to relevant PSA decline. Regarding acute severe Adverse Events toxicity is not elevated. The median overall survival was not reached.

OP-392

De novo Radioligand Therapy using Lu-177 labelled PSMA Small Molecules in Patients with Metastatic Prostate Cancer

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Purpose: The aim of this study was to evaluate the efficacy of very early Lu-177 prostate specific membrane antigen (PSMA) targeted radioligand therapy (PRLT) in patients with castration-naïve metastatic prostate cancer (mPC). **Methods:** A retrospective cohort of 11 castration-naïve patients (age 50–80 y, mean age 68 ± 9.7 y) treated with Lu-177 labelled PSMA small molecules, was analyzed prospectively. The patients with histologically confirmed mPC had undergone prostatectomy, only prostate biopsy (for diagnostic confirmation) or radiation therapy, but no androgen deprivation therapy or orchiectomy. Molecular response was evaluated by Ga-68 PSMA PET/CT according to European Organization for Research and Treatment of Cancer (EORTC) criteria, and morphological response on CT/MRI according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1). Imaging was performed prior to each PRLT cycle and for restaging. Disease Control Rate (DCR) was defined as complete remission (CR), partial remission (PR) and stable disease (SD). Best objective response rate (ORR) was defined as CR and PR. **Results:** The median follow-up time was 21.7 months (range 10.9–40.8 months). Based on EORTC criteria, DCR at 3 months (2.6 ± 0.7 m) post-PRLT was 90.9 %, including CR in 1/11 (9.0 %), PR in 6/11 (54.5 %) and SD in 3/11 patients (27.5 %). Best ORR was 63.5 %. By RECIST, DCR at 3 months (2.8 ± 0.9 m) post-PRLT was 100 %, encompassing CR in 1/11 (9.0 %), PR in 4/11 (36.5 %) and SD in 6/11 patients (54.5%). Best ORR was 45.5 %. The median PFS based on EORTC criteria and RECIST was 30.9 months. All of the 11 patients (100 %) demonstrated reduction in PSA. Decline in PSA by more than 50% was seen in 9/11 (82 %) patients. The median PSA-PFS was 20.0 months. Patients tolerated PRLT extremely well, no CTCAE grade 3–4 toxicity was observed. **Conclusion:** De novo PSMA radioligand therapy is feasible, safe and effective in metastatic prostate cancer. Early introduction of PRLT, probably in combi-

nation with androgen deprivation therapy, might provide an additional beneficial effect and further prospective randomized controlled studies are warranted to establish its place in the management of mPC.

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Discrete evaluation of multi-cycle Lu-177-PSMA-617-therapy effects on bone versus lymph node metastases in patients with metastasized castrationresistant prostate cancer (mCRPC)

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Purpose: The objective of this study was to separately evaluate the specific effects of Lu-177-PSMA-617-therapy on lymphatic (LM) and osseous metastases (OM) in patients with mCRPC. **Methods:** 20 patients with mCRPC (average values for age: 73.1 years, Gleason-Score: 8.1, disease duration: 6.6 years) underwent up to 3 cycles of PSMA therapy in our clinic and received Ga-68-PSMA-PET/CT scans (PET-Scan) before, during and after therapy. a) The response of LM was evaluated according to RECIST 1.1. PSMA-positive lesions with a diameter of > 1.0 centimeters were used as target-lesions, the SUVmax of all PSMA-positive LM was determined. b) To evaluate the OM load, we used the automated quantification tool 'EBONI'. It determines total PSMA-positive OM volume, SUVmean, SUVmax and number of OM. Patients were divided into 3 groups: PSA-Responder (PSAR)= decrease of $\geq 50\%$, PSANonresponder (PSAN)= increase of $\geq 20\%$ and stable (PSAS) with PSA levels in between. **Results:** 9 patients were PSAR, 4 PSAS and 7 PSAN. All patients showed OM, 11 showed LM suitable for RECIST evaluation (5 PSAR, 3 PSAS, 3 PSAN). 1.) SUVmax declined (avg. -22% , $p < 0.01$) in most OM, total PSMA-positive OM volume increased in most cases, even after 3 cycles (avg. $+150\%$, $p < 0.01$). 2.) SUVmax decreased in LM on avg. by 49.9% ($p < 0.01$). Diameters of LM decreased on avg. by 17.4% ($p < 0.05$). According to RECIST-criteria, this decrease qualified for therapy response in 15% of patients (3 PSAR) and for stable disease in 35% of patients. In 5 patients new LM emerged during therapy despite showing SUV-response. 3.) PSA-response did not allow to differentiate between therapy responders and non-responders in terms of PSMA-uptake, tumor diameter or volume. **Conclusion:** Lu-PSMA-therapy shows therapeutic effect on the viability of OM (in terms of max. PSMA-expression) in most cases, however without completely preventing expansion of metastatic disease. Regarding LM, PSMA-therapy appears to result in more distinct regression in size and SUVmax. However 25% of patients showed new LM despite response of existing lesions. RECIST-criteria for response and stable disease were met in 55% of cases with LM. Furthermore, therapy effects on SUV, affected bone volume and lymph node diameters were mostly independent of PSA response, also questioning the value of PSA-monitoring as a suitable response parameter. Generally these findings imply a complex therapeutic response to Lu-PSMA therapy which depends on the pattern of metastatic disease and requires a differentiated monitoring strategy, ideally involving PSMA-PET.

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Clinical Outcomes Of ^{177}Lu -PSMA Radioligand Therapy In Taxane Chemotherapy Pretreated And Taxane Chemotherapy Naïve Patients With Metastatic Castration Resistant Prostate Cancer

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Purpose: To evaluate clinical outcomes of ^{177}Lu -labelled prostate-specific membrane antigen radioligand therapy (^{177}Lu -PRLT) in taxane chemotherapy pretreated (T-pretreated) and taxane chemotherapy naïve (T-naïve) patients with metastatic castration resistant prostate cancer (mCRPC). **Subjects and Methods:** A retrospective analysis was performed on 167 patients with mCRPC who underwent ^{177}Lu -PRLT between March-2013 and December-2016. Patients were classified as either T-pretreated or T-naïve depending on whether they had received taxane based chemotherapy prior to ^{177}Lu -PRLT. Clinical outcome for T-pretreated and T-naïve patients was assessed by overall survival (OS), radiographic progression free survival (rPFS) and prostate-specific antigen (PSA) response rate. Univariate and multivariable analyses were performed for both T-pretreated and T-naïve patients to determine predictors of outcome. Toxicity was categorised by the common toxicity criteria for adverse events (version 4.03) and compared between the two groups. **Results:** Of the 167 patients treated with ^{177}Lu -PRLT, 83 were T-pretreated and 84 were T-naïve. At baseline, T-pretreated patients had overall poorer performance status, a higher prevalence of bone metastases, higher PSA levels, lower haemoglobin levels and higher ALP levels compared to T-naïve patients. Median OS was 10.7 months (95%CI: 7.9-13.5 months) for T-pretreated patients and 27.1 months (95%CI: 18.4-35.8 months) for T-naïve patients ($p<0.001$). Median rPFS was 6.0 months (95%CI: 3.2-8.8 months) for T-pretreated patients and 8.8 months (95%CI: 7.1-10.6 months) for T-naïve patients ($p=0.003$). PSA response assessment was evaluable in 132 patients and seen in 25/62 (40%) T-pretreated patients and 40/70 (57%) T-naïve patients ($p=0.054$). Significant determinates of OS in multivariable analysis for T-pretreated patients were poorer performance status (HR=2.71, 95%CI: 1.22-6.03), higher cumulative administered activity (HR=0.37, 95%CI: 0.20-0.69) and lower baseline haemoglobin (HR=2.76: 95%CI: 1.11-6.89). Higher baseline ALP was the only significant determinate of OS in multivariable analysis for T-naïve patients (HR=11.7: 95% CI: 2.92-47.15). Overall ^{177}Lu -PRLT was safe with minimal adverse effects evident during follow-up including grade 3 or 4 anaemia, leukopenia, thrombocytopenia and nephrotoxicity in an additional 5%, 2%, 2% and 0% of T-pretreated patients and 1%, 0%, 1% and 1% of T-naïve patients respectively. **Conclusion:** ^{177}Lu -PRLT is a promising treatment in

mCRPC with favourable outcomes and minimal associated toxicity observed in both T-naïve and T-pretreated patients.

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^{177}Lu -labeled PSMA-617 radioligand therapy for metastatic castration-resistant prostate cancer: which pre-treatment parameters would predict response?

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Purpose: ^{177}Lu -labeled PSMA-617 is a promising new therapeutic agent for radioligand therapy (RLT) as part of a theranostic approach for metastatic castration-resistant prostate cancer (mCRPC). Our aim was to find pre-treatment parameters that would predict a therapeutic response after the first treatment and define the most eligible patient for PSMA-RLT. **Materials & Methods:** In a retrospective single center study, we enrolled between January 2017 and February 2018, 20 mCRPC men (mean age 75 years, range 57-91) who were referred to first RLT cycle. All patients presented distant metastases and progressive disease with no other therapeutic options. All were ECOG $\leq$ 2 performance score and treated with mean and median of 6 GBq. ^{68}Ga -PSMA-11 PET/CT was performed up to 6 weeks before RLT and showed PSMA avid disease in all patients, including bone lesions (n=20), loco-regional/distant adenopathies (n=9), prostate/prostate bed uptake (n=8), liver disease (n=5), adrenal (n=3) and lung, brain, peritoneal and penis involvement (n=2). SUVmax and SUVmean were determined using region of interest for cancer lesions, physiologic uptake in liver, kidney, spleen, salivary and lacrimal glands as well as background and bladder radioactive urine. Complete blood counts, Gleason Score, PSA at cancer diagnosis and pre-RLT, renal and liver function assessments, disease location, C-reactive protein, Lactate dehydrogenase, Alkaline phosphatase (ALK), previous therapies, time from diagnosis to RLT and SUVs were included in the analysis (mean values for responders vs refractory were calculated, as well as p, AUC and cut-off values). Patients with PSA reduction two month after RLT associated with pain improvement were classified as responders. **Results:** Ten of 20 (50%) patients showed PSA reduction two month after therapy within 7 (35%) had more than 50% reduction. All responders reported pain improvement. Significant pre-RLT parameters to predict response were lower ALK values (mean 107.4 vs 251.2 IU/L, $p=0.01$, AUC 0.82, cutoff 210), lower platelets count (mean 219 vs 319 K/microL, $p=0.02$, AUC 0.8, cutoff 310) and high SUVmean of radioactive urine in the bladder (mean 22.9 vs 7.7, $p=0.027$, AUC 0.82, cutoff 17). Bone marrow involvement on ^{68}Ga -PSMA-PET was associated with worse prognosis ($p=0.06$) and was correlated to high ALK values. **Conclusions:** ^{177}Lu -labeled PSMA-617 RLT is a promising therapy option for mCRPC. Present study showed response in 50% of patients after one cycle of therapy. Lower ALK and platelets values as well as higher bladder urine SUVmean were associated with response. Future prospective studies are warranted to elucidate the survival benefit of therapy.

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¹⁷⁷Lu-DKFZ-PSMA-617 Therapy In Metastatic Castration Resistant Prostate Cancer: Safety, Efficacy And Quality Of Life Assessment

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Purpose: The objective of this study was to evaluate the efficacy and safety of a novel theranostic agent, ¹⁷⁷Lu-DKFZ-PSMA-617 therapy in metastatic castration resistant prostate cancer (mCRPC). **Subjects & Methods:** 72 mCRPC patients with progressive disease despite second line hormonal therapy and/or Docetaxel chemotherapy were recruited for the study. All patients underwent diagnostic ⁶⁸Ga-PSMA-HBED-CCPET/CT, prior to inclusion for therapy. Included patients underwent quarterly ¹⁷⁷Lu-DKFZ-PSMA-617 therapy. Hematological, kidney function, liver function tests and serum PSA levels were recorded before and after every therapy at 2 weeks, 4 weeks and 2 month intervals. Biochemical response was assessed using trend in serum PSA levels. Metabolic response was assessed by PERCIST 1 criteria. Clinical response was assessed by visual analogue score (VASmax) analgesic score (AS), Karanofsky's performance status (KPS) and Toxicity and response criteria of the Eastern Cooperative Oncology Group (ECOG) criteria. **Results:** The mean age of patients was 65.6±10.2 years (range: 30-83 years). The mean activity administered was 8330 ± 5106 MBq with a median of 3 cycles. There was a decline in the mean serum PSA levels from the baseline (baseline: 312.12 ng/ml, post 1st cycle therapy: 180 ng/ml). Based on biochemical response criteria 7/72 (9.7%), 20/72 (27.7%), 18/72 (25%), and 27/72 (37.5%) had near complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD), respectively. Metabolic response revealed 6/34 (17.6%) patients with near CR, 12/34 (35.2%) patients with PR, 6/34 (17.6%) patients with SD, mixed response in 2/34 (5.8%) and 8/34 (23.5%) with PD. The mean VASmax score decreased from 7.8 to 3.3. The mean analgesic score reduced from 3 to 1 after therapy. The mean KPS score improved from 40 to 70 after therapies. The mean ECOG performance status improved from 3 to 2 after therapy. Seven patients experienced grade I and grade II hemoglobin toxicity which was transient. **Conclusion:** ¹⁷⁷Lu-DKFZ-PSMA-617 radionuclide therapy is a safe and effective approach in the treatment of mCRPC patients.

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Initial clinical experience performing sialendoscopy for salivary glands protection for patients under ²²⁵Ac-PSMA-617-RLT

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Purpose: Main side effect of prostate-specific membrane antigen targeting alpha-therapy (PSMA-TAT) is the dry-mouth-syndrome. Inflammations of the parotid glands and consecutive reduced salivation function were already reported for patients after radioiodine therapy. Beneficial effects of steroids for radiation inflammation to tissue are well known. Thus, sialendoscopy and injection of steroids (prednisone) were performed before or after ²²⁵Ac-PSMA-617-TAT to reduce inflammation effects in the salivary glands and prevent xerostomia. **Methods:** Eleven male patients with metastatic castration-resistant prostate cancer (mCRPC) and a mean age of 68.5 years (range 58-80 y) underwent sialendoscopy and steroid injection before or after application of ²²⁵Ac-PSMA-617-TAT for every cycle. Sialendoscopy and steroid injection was performed by an ENT senior physician. Quality of life assessment was evaluated using a standardized report form. **Results:** In all 11 patients both parotid- and both submandibular glands were affected due to radiation sialadenitis and sialendoscopic treatment applied. Patients treated with sialendoscopy showed a significant improvement in health related quality of life (HRQOL) measurements regarding the XQ and XI. After sialendoscopy the XQ score decreased significantly from 77.7 ± 13.6 to 42.7 ± 14.8 (p=0.003) and the XI score decreased from 44.5 ± 6.9 to 25.8 ± 12.8 (p=0.003). Due to our limited number of patients we only describe tendencies. We did not experience any complications after sialendoscopy. **Conclusion:** Sialendoscopy and steroid injection had beneficial effects to the salivation function and quality of life for patients under ²²⁵Ac-PSMA-617-RLT. However, even with sialadenoscopic support after multiple cycles of TAT, salivary gland function was reduced and xerostomia was present. Therefore not only the inflammation but also the direct radiation is causative for the dry mouth. Further research is necessary to cope the main side effect of PSMA-TAT.

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A new clinical setting: ⁶⁸Ga-PSMA PET/CT after Radium-223-Dichloride as therapy assessment and selection for PSMA-RLT

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Aim: our purpose was to investigate the role ⁶⁸Ga-PSMA PET/CT in the management of patient treated with Radium-223-Dichlo-

ride (^{223}Ra), to assess response and to select patients potentially eligible for PSMA-RLT. **Material and Methods:** 60 patients are currently in follow up in our Hospital, after completing 6 ^{223}Ra therapy. Among these 60 patients, we have retrospectively enrolled 12 patients (age mean 74.3 yr, range 59–79) with these inclusion criteria: 1) 6 cycles treatment with Radium-223-Dichloride; 2) ^{68}Ga -PSMA PET/CT performed after 6th cycle of ^{223}Ra (range 1–6 months after therapy) with clinical evidence of disease progression. ^{68}Ga -PSMA PET/CT before treatment was also performed in 4/12 patients. Clinical and laboratory follow-up were performed for all the patients once a month. PSA and Alkaline Phosphatase (ALP) trend were evaluated during follow up. Our patients were divided in two subgroups: patients with other therapeutic options according to EAU Guidelines 2017 (Group A), or patients without any suggested therapy after ^{223}Ra (Group B). **Results:** Among the 60 patients, median overall survival after 223-Ra treatment was 21.2 months (longer than Alsympca Study). ^{68}Ga -PSMA PET/CT performed after ^{223}Ra demonstrated 2/12 liver metastases, 6/12 Ln progression. Bone Progression was observed in all patients, without significative bone marrow rebound or flare. Pre-Therapy PSMA PET/CT did not increased or facilitate therapy assessment. Patients in group A were 7: 3 treated with Enzalutamide and 4 with CHT after ^{223}Ra . Patients in group B were 4, eligible only for compassionate experimental PSMA-RLT: 2 Patients were treated with 225-Actinium-PSMA with complete or partial response; 3 Patients are scheduled for ^{177}Lu -PSMA (2) and ^{225}Ac -PSMA (1). **Conclusion:** patients after ^{223}Ra treatment represent a new clinical setting for their longer overall survival, with a different sequence of therapy before ^{223}Ra , but fewer therapeutic options after ^{223}Ra treatment. ^{68}Ga -PSMA PET/CT was an useful tool for therapy assessment and detection of bone/visceral metastases. Therefore ^{68}Ga -PSMA PET/CT is an option for patients with advanced state of disease, eligible only for possible experimental PSMA-RLT. In our small group of patients alpha emitter-PSMA-RLT was the best option chosen, because of the diffuse bone marrow infiltration that is a common finding in this particular clinical setting. Limitations of our study are the limited number of patients evaluated with PSMA and eventually treated with PSMA-RLT.

1009 Monday, October 15, 2018, 16:30 - 18:00, Hall 6

Thyroid: Thyroid Cancer - From Pathology to Personalized Treatment

OP-399

Comparison between the 7th and 8th edition of the AJCC TNM staging system for differentiated thyroid cancer and clinical and prognostic impact: a single center experience.

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Aim: Aim of our study was to compare patients with differentiated thyroid cancer (DTC) previously treated with total thyroid-

ectomy and radioiodine (RAI) therapy before and after restaging according to 8th AJCC TNM staging system by disease outcomes. **Methods:** We have retrospectively evaluated 981 DTC patients who underwent total thyroidectomy and RAI therapy from January 1997 to December 2003 in our department. We declassified them according to the 8th TNM/AJCC edition and compared with the 7th edition focus on the main clinical features and disease outcome. **Results:** Using the 8th edition, patients classified as T1 or T2 passed from 634 to 843 and patients classified as T3 from 319 to 122. Considering patients classified as T1-T2 according to 8th edition, T1-T2 according to 7th edition and T3 according to 8th edition, we didn't find any statistically significant difference in terms of first dose of RAI administered, median age, gender and antithyroglobulin levels before RAI ($p>0.05$). Instead, the total number of RAI treatments ($p<0.01$), Tg level at ablation ($p<0.01$) and disease free survival ($p<0.05$) were significantly different in T1-T2 group according to 8th edition than T1-T2 according to 7th edition. These evidences was not confirmed comparing T1-T2 acc. 8th edition and T3 according to 8th edition ($p>0.05$). When switched to the 8th edition, 947 patients were classified as stage I or stage II compared to 710 according to 7th edition. Among these two groups no statistically significant difference were found in first dose of RAI, median age, distribution of sex, antithyroglobulin levels before RAI, total numbers of RAIs, Tg levels before RAI and disease free survival. **Conclusions:** With the 8th AJCC TNM staging system, a significant number of patients have been downstaged despite patients classified as T1-T2 with this new classification seem to have a similar behavior and outcome compared to T3. Moreover T1-T2 according to 8th edition look like more aggressive and with worse prognosis than T1-T2 according to 7th edition. In our opinion RAI therapy should be still consider in this group of patients.

OP-400

Is low-dose radioiodine treatment sufficient for a successful remnant tissue ablation in low-moderate risk thyroid cancer patients?

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Introduction: The American Thyroid Association (ATA) 2015 guideline recommends low-dose radioactive iodine (RAI) therapy in low and moderate risk groups. The aim of our study is to evaluate the ablation success of LD RAI treatment. **Subjects & Methods:** Low and moderate risk well differentiated thyroid cancer (WDTC) patients who received ablation therapy between December 2014 and August 2016 were included in the study. The patients were divided into two groups according to RAI activity given (high-dose (HD) group: 100 mCi RAI and low-dose (LD) group: ≤ 50 mCi RAI). TSH, thyroglobulin (Tg) and Anti-Tg values before and 6 months after RAI ablation and 5 mCi whole body scintigraphy (WBS) after 6 months were recorded. Patients with negative 5 mCi WBS and $\text{Tg}<2$ ng/dl at 6 months were accepted as successfully ablated. For the patients who were not ablated at the first RAI, ablation success was assessed

in the second and higher RAI treatments. Chi-square test and student's t test were applied using SPSS program. **Results:** 206 patients (100 LD and 106 HD group) were involved in the study. The failure rates were 21% in LD group and 10.4% in HD group ($p < 0.05$). Although there were more patients with unsuccessful ablation after 30 mCi RAI compared to those with 50 mCi RAI, the difference was not statistically significant. 81% of LD group patients with ablation failure had remnant tissue uptake on 5 mCi WBS. Whereas only 55% of HD group patients had remnant uptake on 5mCi RAI WBS. In patients with elevated Tg values (> 2 ng/dl) at 6 months post-RAI, only 37.5% achieved successful ablation in the second RAI, while in patients with remnant uptake on 5mCi WBS at 6 months this rate was 80% ($p < 0.05$). There was no evidence of recurrence in the follow-up of ablated patients. When considering the second ablation dose of patients, only a mean 6.5% cost increase was detected in the HD group, while the total hospitalization days were reduced in HD group. **Conclusions:** The ATA 2015 guideline states that LD RAI ablation therapy may be applied in low and moderate risk WDTC patients. In our study, increased rate of ablation failure was observed in LD group compared to HD group. This causes repetitive RAI treatments in non-ablated patients, which causes increased duration of hospitalization. For this reason, we recommend LD RAI treatment only in selected cases after performing cost-benefit analysis.

OP-401

Dosimetry in Radiometabolic Therapy for Differentiated Thyroid Cancer; could relationship between dosimetric value and clinical parameters address the patient management?

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Purpose: The aim of this work is to address the use of dosimetry pre and during therapy for the Red Marrow (RM) and for the Whole Body (WB) in Differentiated Thyroid Cancer (DTC) and to focalize the relationship between clinical parameters and dosimetric results. **Methods and materials:** We enrolled in dosimetry 120 patients (139 dosimetries) with DTC from March 2012 to December 2017. We make double dosimetric studies (PreTherapy PreT and Post Therapy PosT) Some patients underwent multiple treatment and dosimetries. We consider a total of 98 double dosimetries with complete clinical data and follow up. In PreT we administer 19 MBq trace activity of ¹³¹I, collecting serial Blood samples and WB counts according to the AIFM Italian dosimetric protocol and EANM SOP. In PosT we administer a range of 1019–9342 MBq, mean 6253 MBq, median 6208 MBq. With a regression analysis we studies the prediction capability of residence times (tau) and mGy/MBq of RM and WB before treatment respect to the post therapy ones (Graph 1). We moreover consider a multivariate multiple regression model to consider in the variability the clinical values such as sex, age, histology and

variant, multifocality, bilaterality, biochemical and hormonal assessment of thyroid (Tsh lpo, Tg lpo, FT4), staging and presence of another tumour. **Results:** All the variables pre-treatment have a significant role in explaining the levels of the corresponding variables post-treatment (Figure 1). For all the variables, a PRE unitary increase determines a much smaller increase in post values (from 0.3 to 0.5). When considering all the variables as possible predictors (Table 1), none of them seems to have an effect on WBposttau, apart from WBprettau. For RMposttau, instead, we found correlation with RMprettau, WBprettau, age and the presence of another tumour. Concerning WBpostmGyMBq and RMpostmGyMBq, both appear to be reduced for N1b staging; WBpostmGyMBq reduced for advanced tumours and increased for large values of WBprettau. RMpostmGyMBq increases with age and RMprettau. A large parte of the total variability of WBpostmGyMBq and RMpostmGyMBq remains unexplained **Conclusion:** Dosimetry connected with clinical values could be a useful tool to help in patient management. Moreover the next step is to follow up considering all these variables to have a more complete, safe and effective therapeutic approach.

OP-402

Shifting paradigms in the management of pediatric differentiated thyroid cancer from static to dynamic risk stratification: a step forward toward precision medicine

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Introduction: This study aimed to assess the usefulness of a risk-adopted management system known as dynamic risk stratification (DRS) in comparison with the American (ATA) and European Thyroid Associations' (ETA) risk classifications in the management of pediatric patients with differentiated thyroid cancer (DTC). **Materials and Methods:** The current study included 50 pediatric patients with DTC who were treated with total or near total thyroidectomy and radioiodine ablation whose risk assessment was initially defined according to the ATA and ETA guidelines. During the two years after initial treatment, patients were reclassified according to their DRS. Three other risk stratification systems: MASIC, AGES, and AMES were also compared with the final outcome. **Results:** The study showed that the ability of the DRS system to predict the final outcome was superior to that of the ATA and ETA guidelines. The observed variance in predicting final outcome was 2.3% for ETA, 14.8% for ATA, and 83.4% for DRS. The other three risk stratification systems, MASIC, AGES, and AMES, were found not to be applicable in the pediatric subgroup. In intermediate/high-risk patients, according to the ATA/ETA guidelines, an excellent response to initial therapy resulted in a noteworthy reduction (about 40%) for detection of structural disease at the time of final follow-up. The risk of structural dis-

ease at the time of final follow-up was significantly higher in the structural incomplete response group (HR = 23.34, $P = 0.00$) and biochemical incomplete response group (HR = 13.83, $P = 0.03$) than in the excellent response group. **Conclusion:** The data documented the signifying of re-stratifying pediatric patients with DTC on the basis of the findings obtained at the time of or after their initial therapy (total thyroidectomy and radioiodine ablation), predominantly in the intermediate/high-risk patients. In addition, DRS helped to better modulate the later follow-up, excluding a large number of intermediate/high risk patients from needless intensive workups, allowing personalization of follow-up management.

OP-403

Recombinant human thyrotropin vs thyroid withdrawal in radioactive iodine therapy of pN1 thyroid cancer patients: a large multicenter retrospective, non inferiority matched cohort study

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Context: Recombinant human thyrotropin (rhTSH) has been shown to be as effective as thyroid hormone withdrawal (THW) in the preparation for radioactive iodine (RAI) therapy in differentiated thyroid cancer (DTC) patients without distant metastasis, including patients with locoregional nodal metastatic disease (N1 DTC). However, there is lack of consensus regarding the degree of nodal involvement which optimally responds to rhTSH stimulated ablation. **Objectives:** The primary objective of the study was to demonstrate non-inferiority of rhTSH vs. THW in terms of disease-free status (basal ultrasensitive Tg < 0.2 ng/mL and/or stimulated-Tg ≤ 1 ng/mL, absence of TgAb and normal neck US) at the first follow-up control performed at 6-18 months post RAI therapy in the real-life setting in pT1-3, N1, M0 DTC. Other objectives included identification of prognostic factors for disease status and description of clinical and biological medium-term outcomes. **Design, patients:** This was a French multicenter retrospective, matched cohort study. Groups were matched in each participating center according to the age (<45 vs. ≥45 years), number of metastatic locoregional nodes (≤5 vs. >5 LN) and stage of tumour (pT1-T2 vs. pT3 according to pTNM 2010). **Results:** The cohort consisted of 404 pT1-T3 thyroid cancer patients with locoregional lymph node metastases and no evidence of distant metastasis at the time of RAI

therapy, prepared with either rhTSH stimulation (n=205) or THW (n=199). Cumulative RAI administrated activities were 3.7 ± 0.5 GBq and 3.3 ± 1.0 in the THW or rhTSH arms, respectively. Most patients had 5 LN or less (90.7% in rhTSH, and 91.9% in THW). At the first follow-up control, disease-free patients rate was not inferior in the rhTSH group (75.1% [95% CI: 68.6; 80.9]) compared to the THW group (71.9% [95% CI: 65.1; 78.0]). Biochemical incomplete response was observed in 10.2% and 14.6%, and structural incomplete response in 10.2% and 6.5%, in rhTSH and THW groups, respectively. The remaining cases were classified as undetermined response. At the last follow-up control (29.7 ± 20.7 in rhTSH group and 36.7 ± 23.8 months in the THW group), 83.5% (rhTSH group) and 81.5% (THW group) of patients achieved a complete remission status. This result was found not to be influenced by any of the known prognostic factors. **Conclusions:** rhTSH was non-inferior to THW for RAI therapy in our series of DTC patients staged pT1-T3/N1/M0 on disease free status outcome both at the first control at 6-18 months and on a medium-term basis.

OP-404

Effects of the updated TNM staging in differentiated thyroid cancer: does microscopic extrathyroidal extension affect the ablation success in patients with newly diagnosed DTC

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Background: According to the updated UICC/AJCC TNM classification for differentiated thyroid cancer (DTC), the T-stage depends on the tumor size, whereas microscopic extrathyroidal extension (ETE) no longer affects T-stage. However, the impact of ETE on ablation success after radioiodine therapy remains unclear. We therefore compared response rates of patients initially classified as T1/T2 DTC without ETE (T1/2-ETE) with patients reclassified as T1/T2 DTC with ETE (T1/2+ETE). **Methods:** Patients formerly classified as pT3 DTC solely due to ETE were reclassified according to the updated 2017 UICC/AJCC TNM criteria into patients with T1/T2+ETE. These patients were compared to a control group consisting of DTC patients classified as T1/T2-ETE according to the former and updated TNM classification. Patients were considered non-responders to radioiodine ablation after six months in case of persisting thyroglobulin (TG) ≥ 0.5 ng/ml, relevant iodine-uptake in diagnostic I-131 imaging and clinical need of re-therapy. **Results:** 185 patients were re-classified as T1/2+ETE and compared to 408 control patients classified as T1/2-ETE. Both groups were statistically indifferent in terms of age (48 ± 16 vs. 47 ± 14 years, $p = n.s.$), sex (female 71% vs. 73%, $p = n.s.$), tumor size (15.8 ± 8.6 mm vs. 15.5 ± 9.1 , $p = n.s.$) and TSH-stimulation by rhTSH at time of radioiodine ablation (40% vs. 47%, $p = n.s.$). T1/2+ETE showed a significantly higher rate of patients with N1-stage (49.2% vs. 24.8%, $p < 0.05$), R1-stage (15.7% vs. 7.6%, $p < 0.05$) and higher I-131 activities (4929 ± 2196 vs. 3537 ± 1382 MBq, $p < 0.05$). Irre-

spective of ETE, non-responders were equally distributed in both groups (70/185 (37.8%) +ETE vs. 124/408 (30.4%) -ETE, $p=n.s.$). In the N0/NX subgroup non-responders were also equally distributed in both groups (22/94 (23.4%) +ETE vs. 71/307 (23.1%) -ETE, $p<0.05$). The same was the case in the N1 subgroup (48/91 (52.7%) +ETE vs. 53/101 (52.5%) -ETE, $p<0.05$), though with higher non-responder rates as compared to the N0/NX subgroup. **Conclusion:** Patients with ETE show a significantly higher rate of lymph node metastases and R1-resections. The latter one probably due to the more challenging operation conditions. Ablation success is achieved irrespective of ETE, however, patients with lymph node metastases show higher non-responder rates. Presumably not the presence of ETE itself is a risk factor for being a non-responder, but the higher risk for systemic disease in this subgroup. An important confounder are the higher radioiodine activities used in the T1/2+ETE, which warrants further prospective investigation.

OP-405

Long Term Outcome Of Radioiodine Therapy In Hurthle Cell Carcinoma : Single Center Large Cohort Study

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Purpose: It is generally believed that hurthle cell carcinoma(HCC) is an aggressive variant of differentiated thyroid cancer(DTC), and also tend not to take up radioiodine compared to other variants of DTC. This prospectively collected data that is retrospectively analyzed to evaluate the effectiveness of radioiodine in HCC. **Subjects and Methods:** This retrospective cohort study was conducted between 1996-2017 with a mean follow-up duration of 74.84 months(range: 12-226 months). All patients of HCC who had total thyroidectomy with/without nodal dissection, post-surgical I-131 remnant ablation/therapy with a minimum follow-up of 12 months were included. Follow-up was done by (Diagnostic Whole Body Scan)Dx-WBS initially, and neck sonography, serum thyroglobulin(Tg) and anti-thyroglobulin(ATA) levels, subsequently. **Results:** From our institutional DTC patients' data-base, 101/7411 (1.36 %) patients were presented with tissue diagnosis of HCC. However, 26 patients were excluded from the study for various reasons. In remaining 75 patients, 28 were males and 47 were females with mean age of $45.9\pm 13.2y$ (range: 21-72y). At initial Dx-WBS, 64 showed remnant thyroid tissue, 5 had regional lymph nodes, 1 had distant metastasis, and 2 showed both lymph nodes and distant metastases. Interestingly, 3 patients in this series were not treated with I-131 as Dx-WBS showed no neck uptake or distant sites, and Tg and ATA were negative (surgically ablated) but just put on TSH-suppressive doses of thyroxine. The mean administered activity of I-131 at the initial presentation and its cumulative dose at the end of follow up were 42.8 (SD $\pm$ 29.97) mCi and 72.1 (Median = 40) mCi, respectively. At first follow-up (6-8 months following RRA), 62/75 (82.6 %) were successfully ablated. Among 13/75 (17.4%) patients who did not achieve remission at first follow-up, six achieved remission on second administration, while 7 patients could not achieve remission at all (6-persistent disease and 1-progression in spite of repeat-

ed I-131 administrations). Among 68 (62+6 =68) patients who were successfully ablated, on follow-ups, 4 had recurrence (2 in thyroid bed; 1 in thyroid bed with regional lymph nodes; and 1 presented with lung metastases). Among these 4, one patient with recurrence in thyroid bed, got ablated by further management, but 3 showed persistent disease. Therefore, 65/75(86.6 %) HCC patients achieved complete remission with the help of radio-iodine with mean follow-up of 75-month. **Conclusion:** We conclude, radioiodine therapy is an effective treatment modality even in 87% of HCC, an aggressive variant of DTC, that is characterized by an excellent long term remission rates.

OP-406

Impact of ATA 2015 in the management of Differentiated Thyroid Cancer patients, in a practical setting

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Introduction: The American thyroid association (ATA) 2015 guideline has introduced new histopathological parameters in the risk stratification (RS) of differentiated thyroid cancer (DTC) patients, introduced the concept of dynamic risk stratification (DRS) and redefined the use of radio-active iodine (RAI) in treatment algorithm. The aim of this retrospective audit was to assess the practical implications of these modifications in management of DTC, in a tertiary care centre. **Methods:** In this retrospective study, 138 DTC patients (underwent total thyroidectomy and RAI therapy) were risk stratified according to ATA 2009 and 2015 guidelines. Percentage of patients changing RS, was calculated and the resultant change in RAI use, was evaluated. Compliance in administration of the RAI dose according to ATA guidelines was assessed. Follow up data of patients at 1 year of post RAI treatment was audited to assess how the DRS modified the initial risk estimate. **Results:** According to the 2009 RS criteria, 24 out of 138 patients were low risk (LR), 85 intermediate risk (IR) and 29 high risk (HR). However according to the 2015 modification 26 were LR, 69 were IR and 43 were HR. Overall 11.6 % patients changed their RS categories. These patients were all IR patients according to 2009 guidelines and had lymph node metastasis (LNM). 14 (10.1 %) got upstaged to HR, and 2 got downstaged to LR. As for the intention of RAI use goes, 3 (2.17 %) patients got downstaged to remnant ablation from adjuvant therapy. Significant deviation in the use of RAI dosage occurred in the treatment of 9.4% of patients, according to ATA 2009 guidelines. However, according to 2015 guidelines, 31 % of patients had received significantly more than the recommended upper limit. At 1 year follow up according to DRS 84% of LR, 75% of IR and 44% of HR patients showed excellent response (ER); whereas 6.1 % of IR and 3.8% of LR continue to show persistent structural disease. **Conclusion:** IR patients with LNM were primarily affected by the modified RS. Changed RS changed the intention of RAI use in only 2.17% of patients. In current practice, significantly higher dosage of RAI is being administered to patients. The effect of DRS in modifying the initial RS is most prominent in IR, almost 3/4th of them show ER to initial therapy. Long-term follow-up is needed for proper understanding of the modified RS.

1010 Monday, October 15, 2018, 16:30 - 18:00, Hall 28

Neuroimaging - Rapid Fire Session: Cognitive Impairment & Neuro-Degeneration

OP-407

Amyloid Imaging using 18F-FIBT PET: a pilot study

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Purpose: 2-(p-Methylaminophenyl)-7-(2-[18F]fluoroethoxy)imidazo[2,1-b]benzothiazole (18F-FIBT) has been reported as a promising marker for imaging cerebral amyloid deposition using PET. For further clinical integration, the imaging protocol and corresponding evaluation method are compared with ¹¹C-PiB and optimized in this pilot study. **Methods:** Six patients with different clinical-pathophysiological phenotypes underwent dynamic PET imaging for 90 min in Siemens Biograph mMR. For the comparison of different calculation methods, the patients imaged with dynamic ¹⁸F-FIBT were compared to four patients scanned with dynamic ¹¹C-PiB. For the comparison of SUVRs, each case imaged with ¹⁸F-FIBT was compared to a group of matched patients (five patients/group) imaged with ¹¹C-PiB. The image data were spatially normalized based on MRI using PMOD. Images were analyzed by comparing standardized uptake value ratios (SUVR), binding potentials (BP) obtained using reference tissue model, and distribution volume ratio (DVR). Cerebellum was selected as reference tissue region. The effect of MRI-based partial volume correction (PVC) on interpretation was also compared. **Results:** Specific binding was detected in the cases with underlying AD pathology. The intensities of BP and SUVR were associated with clinical severity for ¹⁸F-FIBT, which was not observed for ¹¹C-PiB. SNRs were substantially higher in FIBT than in PiB imaging. The optimal imaging time for ¹⁸F-FIBT was found between 40–60 min. Cases with non-AD pathology did not show specific binding. BP has higher contrast than SUVR. However, SUVR is more consistent with the clinical interpretations. **Conclusion:** SUVRs PVC correction seemed to be an easy and robust analyzing technique, making FIBT a favorable amyloid marker for clinical routine.

OP-408

Clinical validation of ¹⁸F-PI-2620 for *in vivo* quantification of tau in subjects with Alzheimer's disease

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Aim: Intracellular tau deposition is a key pathologic feature of Alzheimer's disease (AD) and other neurodegenerative disorders. ¹⁸F-PI-2620 is a novel tau PET-tracer with a high binding-affinity for aggregated tau. Pre-clinically, ¹⁸F-PI-2620 binds to 3R and 4R tau isoforms and is therefore able to depict

tau-deposits in AD brain sections from different Braak stages, as well as deposits in PSP. To extend the utility of PI-2620 for use in therapeutic clinical trials, a Test/Retest study with arterial sampling was performed and simplified quantification methods were explored. **Materials and Methods:** In an ongoing clinical imaging study, participants diagnosed with mild AD, as well as non-demented controls (NDCs) undergo dynamic PET imaging for 180 minutes. 3 NDC and 3 AD underwent a Test/Retest study including repeat-scanning and arterial sampling with metabolite correction. Distribution volume ratios (DVRs) were determined using full tracer kinetic models and reference tissue models. Standardized uptake value ratios (SUVR) were determined at different time points p.i. using cerebellar cortex as reference region. Test-retest variability was calculated as percent difference between test and retest scans. **Results:** Imaging data show robust brain uptake and fast wash-out in non-target regions with peak SUVs > 4 similar to what has been observed before. There was no increased off-target binding, and no age-related increase seen in cortical and subcortical brain regions like basal ganglia as noted for first generation tau agents. Focal asymmetric uptake was evident in temporal and parietal lobes, precuneus, and posterior cingulate in AD subjects. The time-activity curves were well described by the 2-tissue-compartment model (2TC). SUVR measured at 60–90 min p.i. correlated well with 2TC (slope 1.37, $r^2 = 0.97$) and non-invasive Logan plot (slope 1.3, $r^2 = 0.93$). The average test-retest variability in AD was 2.1 % $\pm$ 8.0 (2TC), 3.3 % $\pm$ 6.1 (non-invasive Logan) and 7.8 % $\pm$ 8.6 (SUVR). SUVRs at 60–90 min were significantly lower in non-demented controls (SUVR 1.0–1.2) than in AD subjects (SUVRs up to 4) in the same brain regions. **Conclusion:** ¹⁸F-PI-2620 PET data in AD and NDC demonstrate favorable kinetics and high target specificity with low off-target activity and high signal in regions of expected tau pathology. Non-invasive quantification using SUVR at 60–90 min p.i. provides significant discrimination between NDC and AD subjects. The excellent test-retest variability confirms the utility of PI-2620 to evaluate change of tau deposition in longitudinal studies.

OP-409

Association between White Matter Lesions and Cerebral Glucose Metabolism in Patients with Cognitive Impairment

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Background: White matter lesions (WMLs), detected as hyperintensities on T2-weighted MRI, are considered potential risk factors for memory and cognitive impairment in the elderly. It has not been sufficiently evident that cognitive impairment in patients with Alzheimer's disease is caused by WMLs as well as amyloid pathology. The aim of this study was to evaluate relationship between WMLs and cerebral glucose metabolism in patients with cognitive impairment after adjustment of cerebral β -amyloid ($A\beta$) burden. **Methods:** Eighty-three patients with cognitive impairment, who underwent brain MRI, F-18 florbetaben positron emission tomography (PET), and F-18 fluorodeoxyglucose PET, were included prospectively: 19 patients

exhibited cognitively normal (CN), 30 exhibited mild cognitive impairment (MCI), and 34 exhibited Alzheimer's disease dementia (ADD). The Fazekas scale was used to quantify WMLs on brain T2-weighted MRI. The cerebral A β burden and cerebral glucose metabolism were quantitatively estimated using volume-of-interest analysis. Multiple linear regression analysis adjusted for the cerebral A β burden was performed to evaluate the relationship between the Fazekas scale score and cerebral glucose metabolism. **Results:** The glucose metabolism in the bilateral frontal, temporal, and parietal cortices and limbic lobes was significantly lower in patients with ADD than in patients with SCI and those with MCI. The Fazekas scale score exhibited a significant negative correlation with the glucose metabolism in the bilateral frontal, temporal, and left parietal cortices and bilateral limbic lobes and was an independent determinant of the glucose metabolism in the bilateral frontal and temporal cortices and limbic lobes. **Conclusion:** WMLs are associated with the cerebral glucose metabolism in patients with cognitive impairment. Chronic microvascular ischemia may contribute to cognitive impairment with cerebral A β accumulation.

OP-410

Central nervous system damage in HIV patients: combined FDG PET and MRS study

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The combined examination using different neuroimaging methods could help better understanding the mechanism of HIV-mediated cognitive dysfunction. In our previous PET studies, metabolism reduction in anterior cingulate cortex (ACC) early after disease onset was revealed. The purpose of this research was to study MRS metabolites ratios in HIV and compare metabolic changes revealed by FDG PET and MRS. **Methods:** 56 HIV-positive patients (25–45 years) in different disease stages and 23 healthy volunteers were examined. PET-FDG was performed on Gemini TF Base scanner and standard protocol, relative estimation of glucose cerebral metabolic rate (CMRglu) in regions of interest (ROI) corresponding to Brodmann areas (BA) were calculated by WFU PickAtlas. Multivoxel proton MRS was performed on Achieva 3T scanner (2D PRESS H-MPC, TE/TR=144/1500 ms) in supraventricular white matter (WM) and medial cortex (8x9 voxels 10x10x15 mm). NAA/Cr, NAA/Cho ratios (NAA - N-acetylaspate, Cr - creatine, Cho - choline) in 6 of WM (anterior, medium and posterior for each hemisphere) and 3 ROIs in medial cortex were analyzed. **Results:** MRS revealed decrease in NAA/Cr and NAA/Cho ratios in ACC in HIV-infected patients compared to the control group. In the white matter adjacent to this zone bilaterally, increase in the value of the ratio Cho/Cr was revealed. The most significant NAA/Cr decrease was revealed in HIV patients with co-morbid hepatitis C. According to the FDG PET data, CMRglu decrease was revealed in cingulate cortex (BA24,32), and in group with co-morbid hepatitis C - also in frontal (BA8,10,46), parietal cortex (BA7), caudate nuclei and thalamus. NAA/Cr in ACC correlated positively with the CMRglu in the same areas (BA 24&32, left and right, $r=0.6$, $p<0.0001$) and in frontal cortex

(BA 8-10) bilaterally, $r=0.5$, $p<0.01$. NAA/Cr in WM also correlated positively with CMRglu in frontal (BA8) and cingulate (BA24,32) cortex; Cho/Cr correlated negatively with CMRglu in left angular gyrus ($r=-0.4$, $p<0.05$). **Conclusion:** The results show that local metabolic changes appear in a number of ROIs even at the early stage of HIV infection and rise with the increase of disease severity. Correlations of MRS and PET data show the connection between supraventricular white matter integrity and cortex metabolism. Since both MRS and PET revealed metabolic changes in ACC, and NAA/Cr (neuronal integrity marker) correlated positively also with glucose metabolism in other cortical areas, it may be concluded that changes in cingulate cortex play important role in the HIV associated cognitive decline.

OP-411

Impact of Delirium in Remission on the Performance of Brain FDG PET for etiological Diagnosis of clinically uncertain cognitive Impairment

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Purpose/Introduction: The majority of studies on the use of brain FDG PET for the etiological diagnosis of clinically uncertain cognitive impairment (CUCI) have focused on memory clinic outpatient settings. The role of FDG PET in patients hospitalized in a geriatric unit for an acute or subacute illness is less clear. Typical presentations include patients with prolonged cognitive impairment during recovery from surgical treatment on a geriatric unit, although they had no cognitive problems prior to hospitalization. A considerable fraction of these patients suffer from atypical and prolonged courses of delirium. In the acute phase of fulminant delirium, alterations of FDG uptake have been observed that mimic neurodegenerative disease. The present study evaluated if prolonged delirium in remission impairs diagnostic performance of brain FDG PET for differentiation between neurodegenerative and non-neurodegenerative causes of CUCI. This is clinically relevant, as the suspicion of first manifestation of a neurodegenerative disease should be assessed before the patient is finally discharged from the acute care geriatrics unit. **Methods:** 88 inpatients (81.4 $\pm$ 5.4y) with newly manifested CUCI during hospitalization in a geriatric unit for an acute indication were included in the study (DRKS00005041). Presence of delirium as assessed via Nursing Delirium Screening Scale and Delirium Rating Scale Revised was not an exclusion criterion. However, at the time of enrollment, delirium was not considered the only cause of cognitive impairment. Brain FDG PET was performed on average 3 days after enrollment (IQR 1–4d). Cases were categorized as neurodegenerative or non-neurodegenerative etiology based on visual interpretation of the PET images. Clinical diagnosis at follow-up after ≥ 12 months was used as standard of truth to compare the accuracy of brain FDG PET between patients with and without delirium in remission. **Results:** Twenty-six patients (30%) had manifested a delirium during their current hospital stay.

Fifty (57%) of the cases were categorized as neurodegenerative based on baseline FDG PET with a tendency towards a higher fraction of neurodegenerative cases amongst patients with delirium (69% vs. 52%, $p=0.128$). Sixty-eight patients were available for follow-up after 16.0 ± 3.1 months, which confirmed the baseline classification in 61 patients (90%, 3 false negative and 4 false positive cases with respect to detection of neurodegeneration). The fraction of correct baseline classification was not different between patients with delirium in remission and patients without delirium (86% vs. 91%, $p=0.469$). **Conclusion:** Brain FDG PET is useful for etiological diagnosis of clinically uncertain cognitive impairment also during delirium in remission.

OP-413

Amyloid Load and Cognitive Performances in a Non-Demented Elderly Population: a 18F-Flutemetamol PET Study

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Previous studies have shown that between 20 and 50% of asymptomatic elderly subjects had high amyloid load. The aim of this study was to explore the relationship between amyloid load and cognitive performance, and its modulation by educational level in a non-demented elderly population. **Methods:** This is the final results of the EDUMA study (NCT02196116), including 119 subjects. The amyloid load was assessed by 18F-flutemetamol PET-CT. Patients had 6-year clinical follow-up (every 2 years) before and simultaneously with PET/CT scan. We collected for each subject: age, sex, ApoE status, educational level, dependence on Instrumental Activities of Daily Living, Global Memory Score (MMSE test), Episodic Memory Score (Grober and Buschke test), Semantic Memory Score (Isaacs set-test), and slopes of cognitive decline during the 6-year follow-up for each test. We compared subjects with normal and pathological PET/CT in visual analysis. **Results:** 25% of the subjects had a pathological 18F-Flutemetamol PET-CT in visual analysis. They were significantly older ($p=0.003$), ApoE-mutated ($p=0.006$), with dependence on at least one instrumental activities of daily living ($p=0.025$), and alterations of episodic and semantic memories ($p<0.001$ and $p=0.045$, respectively). They also presented a more important decline in the episodic and semantic memory ($p=0.025$ and $p=0.040$, respectively). There was no difference concerning MMSE test. Subjects with high level of education presented better performances in MMSE test and semantic memory ($p<0.001$ for both), even though they were older ($p<0.001$) and with comparable amyloid load ($p=0.822$). There was no difference concerning episodic memory ($p=0.749$), and instrumental activities of daily living ($p=0.531$). Moreover, there was no difference concerning cognitive decline. **Conclusion:** In a non-demented elderly population, a high amyloid load is associated with alterations of episodic and semantic memories

and more important decline in memory performances in the 6 years before PET/CT scan. These results confirm the interest of evaluation of amyloid load for the early diagnosis of Alzheimer disease, notably in the subjects with a high level of education which had delayed onset of symptoms.

OP-414

18F-FDG PET (rather than DAT SPECT) predicts clinical trajectories in cognitive onset Lewy-body disease patients

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Introduction. A small number of patients with mild cognitive impairment (MCI) may later develop a Lewy body diseases (LBDs). Actually, patients with under-threshold PD motor symptoms may ask for neurological consultation because of cognitive rather than for motor impairment. A "Park cognitive subtype" has been proposed in which both cortical LB deposition and neurodegeneration are prominent presenting as early MCI and progressing to frank dementia over few years. This construct is increasingly recognized but has large overlap with the construct of dementia with Lewy bodies (DLB) in its prodromal (or MCI) stage. There is no agreement on whether is possible to identify a patient with MCI who later develops Parkinsonism and eventually dementia. Furthermore, it is still unclear how to predict at baseline which phenotypic pathway patients will subsequently follow. The aim of our work was to investigate baseline clinical, neuropsychological and neuroimaging features of a group of MCI patients and to follow-up their different trajectories toward the development of LBD. **Subjects and Methods:** We retrospectively selected thirteen LBD patients with MCI preceding (2.9 ± 1.9 y) Parkinsonian signs and symptoms and dementia (in 6 of them after 4.6 ± 1.6 y). Neuropsychological tests, DAT SPECT and 18F-FDG-PET were compared with healthy controls and with a pure motor *de novo* PD group without cognitive impairment (PD-MOT). MRI, DAT SPECT and FDG-PET were analyzed both at group and individual level. **Results:** patients with prodromal LBD showed impairment in several neuropsychological tests in multiple cognitive domains which further worsened at the time of Parkinsonism onset. At group level, they showed significant posterior temporo-parieto-occipital hypometabolism compared to healthy controls while PD-MOT group did not. By contrast, DAT basal ganglia uptake did not differ between prodromal LBD and PD-MOT. After the onset of Parkinsonism, the 6 patients developing dementia compared to those remaining with MCI were older, tended to have a higher UPDRS-III score, and more often presented medial temporal lobe atrophy and

extended association cortex hypometabolism in both anterior and posterior regions. Moreover, they all developed at least another clinical core feature to fulfill the diagnostic criteria for DLB. **Conclusion:** neuroimaging features and clinical trajectories seem to differ among patients with MCI subsequently developing a LBD. As highlighted by FDG PET, patients developing DLB exhibit since the first evaluation more severe signs of neurodegeneration than those receiving later a diagnosis of PD (thus affected by a peculiar cognitive onset phenotype).

OP-415

Diagnostic Utility of Cardiac MIBG for DLB Diagnosis in a UK Population Using an HMR Cut-off Derived from Images of Local Healthy Control Subjects

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Objective: To determine the utility of cardiac ¹²³I-metaiodobenzylguanidine (MIBG) scintigraphy in differentiating dementia with Lewy bodies (DLB) from Alzheimer's disease (AD) in a clinically representative UK population, comparing findings with ¹²³I-ioflupane (FP-CIT) SPECT (DaTSCAN™). **Methods:** We recruited subjects over 60 years old with probable DLB (n=17; 77.4±8.0 years) and probable AD (n=15; 76.6± 6.8 years) from clinical services. Each participant underwent detailed clinical and neuropsychological examinations, cardiac MIBG and FP-CIT. Participant diagnoses were confirmed using validated consensus criteria, but without using MIBG or FP-CIT results. We subsequently recruited 29 age-matched healthy controls (75.2±8.3 years), who underwent the same detailed cognitive tests and physical examination as the participants with dementia. Subjects were scanned using Siemens Intevo or Symbia S gamma cameras with MEGP collimators for MIBG and LEHR for FP-CIT. Cardiac MIBG uptake was measured on the early and delayed planar images via the heart-to-mediastinum ratio (HMR), with results <2.25 defined as abnormal. This cut-off was determined by adapting the result of 2.10 obtained in a multicentre study by Yoshita *et al.* for our cameras via phantom calibration. An independent cut-off was set as two standard deviations (SD) below the mean of the control subject HMRs. FP-CIT scans were assessed according to a visual rating scale with 0 classed as within normal limits and values of 1-3 assigned to abnormal uptake, including "balanced loss". **Results:** MIBG had a sensitivity of 71%, a specificity of 80% and an overall accuracy of 75% for distinguishing DLB from AD when applying the *a priori* cut-off of 2.25 for both the early and delayed images. 3/29 controls had HMRs below 2.25 on early images and 5/29 on delayed suggesting this cut-off is too high. The mean control HMR was 2.78 and two SD below mean 1.86. Applying the lower cut-off improved the performance of cardiac MIBG on delayed images, raising specificity (87%) and overall accuracy (78%) without compromising sensitivity (71%). The overall accuracy on early images remained 75%

(sensitivity 65%; specificity 87%). FP-CIT had a sensitivity of 88%, specificity 75% and overall accuracy 82%. **Conclusion:** These results do not support a change from FP-CIT to cardiac MIBG in the UK for first-line DLB investigation. The cardiac MIBG HMR cut-off adapted from the multicentre study appears too high for a UK population. Applying our cut-off derived from control studies improved MIBG specificity, exceeding FP-CIT in this sample. Early MIBG imaging gave similar results to delayed imaging.

1101 Tuesday, October 16, 2018, 08:00 - 09:30, Plenary Hall

CME 9 - Translational Molecular Imaging & Therapy / Oncology: Imaging Targets for Cancer Immunotherapy

OP-416

Role of Imaging in Cancer Immunotherapy

N. Aide; Service de Médecine Nucléaire, Centre Régional de lutte contre le cancer François Baclesse, Caen, FRANCE.

OP-417

SPECT-CT Imaging of PD-L1 Expression in Cancer

S. Heskamp; Radboud University Medical Center, Nijmegen, NETHERLANDS.

OP-418

PET Imaging of Targets for Immunotherapy: Implications for Radiotherapy

G. Niedermann; University of Freiburg, Department of Radiation Oncology, Freiburg, GERMANY.

1102 Tuesday, October 16, 2018, 08:00 - 09:30, Hall 2

Joint Symposium 17 - Dosimetry / ICRU: Target Practice - Conditions for Personalized Treatment Planning in Radionuclide Therapy

OP-419

Essential Radiobiology for Radionuclide Therapy

M. Konijnenberg; Erasmus MC, Rotterdam, NETHERLANDS.

OP-420

Uncertainties in Absorbed-Dose Estimates - Which are the Key Contributors?

J. Gear; The Royal Marsden NHS Foundation Trust, Department of Nuclear Medicine, Sutton, UNITED KINGDOM.

OP-421

Treatment Volume Definitions for Tumours and Organs at Risk

K. Sjögreen-Gleisner; Lund University, Medical Radiation Physics, Lund, SWEDEN.

OP-422

Setting the Standards for Treatment Planning ICRU Task Group 31

G. Sgouros; Johns Hopkins Medicine, Department of Radiology and Radiological Science, Department of Radiation Oncology and Department of Oncology, Baltimore, UNITED STATES OF AMERICA.

1103 Tuesday, October 16, 2018, 08:00 - 09:30, Hall 3

Joint Symposium 18 - Oncology / JSNM: Targeted Alpha Therapy - Prospect of Networking, Partnership, and Logistics

OP-423

Targeted Alpha Therapy in Japan - Where we are in 2018

N. Oriuchi; Fukushima Medical University, Advanced Clinical Research Center, Fukushima, JAPAN.

OP-424

Development and Future Perspective of the Targeted Alpha Therapy in Japan

T. Watabe; Osaka University Graduate School of Medicine, Department of Nuclear Medicine and Tracer Kinetics, Suita, Osaka, JAPAN.

OP-425

Access to Alpha Radionuclides in Europe

A. Morgenstern; DG Joint Research Centre (JRC), Nuclear Safety and Security, Karlsruhe, GERMANY.

OP-426

Commercial Perspective of Alpha Emitters Including Distribution and Regulatory Hurdles

S. Marx; ITG, Garching, GERMANY.

1104 Tuesday, October 16, 2018, 08:00 - 09:00, Hall 5

Technologists: Oral Presentations 2

OP-428

Semi-quantitative criteria for the diagnosis of the myocarditis using ^{99m}Tc -Pyrophosphate SPECT/CT

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Aim: To determine the semi-quantitative criteria for diagnostic of the myocarditis by use a SPECT/CT with ^{99m}Tc -pyrophosphate (PYP). **Methods:** We examined 34 patients with isolated atrial fibrillation (AF). Cardiac SPECT was performed 18-20 hours after intravenous injection of 370 MBq ^{99m}Tc -PYP with hybrid SPECT/CT GE Discovery NM/CT 570c (USA) equipped with cadmium-zinc-tellurium detectors. Moreover, all patients underwent MDCT of the left atrium and pulmonary veins. For evaluation and interpretation of both the examinations results, as well as to determine the localization of the radiopharmaceutical accumulation the scintigraphic and x-ray images were fused by using Advantage Workstation 4.6 (GE software Fusion QC). The

localization of the ^{99m}Tc -PYP uptake within the myocardium was assessed. Additionally the following semi-quantitative indexes were calculated: "focus/lung", "focus/spine", "focus /sternum", "focus /costa", "focus/ left ventricle blood pool" and "focus/intact myocardium". To the histological verification of the myocarditis, the endomyocardial biopsy (EMB) was performed during catheter radiofrequency ablation in all patients. **Results:** According to the EMB results, the myocarditis was verified in 25 (74%) patients. The visual approach to compare the results of ^{99m}Tc -PYP SPECT/CT with the histological data, revealed 21 true-positive, 8 true-negative, 1 false positive and 4 false-negative results. Thus, the sensitivity of the method was 84%, specificity 88%, accuracy 88%. The positive predictive value was 95%, negative predictive value - 66%. According to the the ROC analysis the sensitivity and the specificity of the semi-quantitative SPECT indexes for the myocarditis identification were the following: «focus/lung» ≥ 1.47 (Se=88%, Sp=66.7%, and AUC= 0.814, p-level =0.01); «focus/ left ventricle blood pool» ≥ 1.26 (Se=78.9, Sp=91.7 AUC= 0.846, p-level =0.0001); «focus/intact myocardium» ≥ 1 (Se=89.1, Sp=66.7, AUC= 0.754, p-level =0.009), and «focus /spine» ≥ 0.11 (Se=85.7, Sp=88.9, AUC= 0.857, p-level =0.0002). Using a combination of visual and semi-quantitative evaluation criteria, we were able to exclude false positive and 2 false-negative results, which allowed to improve the sensitivity, specificity and accuracy to 91%, 100% and 94%, respectively. The positive predictive significance of the method was 100%, negative predictive relevance to 83%. **Conclusion:** The use of semi-quantitative analysis of hybrid ^{99m}Tc -PYP SPECT/CT allows improving the diagnostic efficiency of the myocarditis diagnosis in patients with isolated AF.

OP-429

Comparison of Gastric Emptying Results Using 60min, 90min and 120min Protocol - A Retrospective Study

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Aim: The aim of this study is to compare the differences of Gastric Emptying (GE) results using protocols of 60min, 90min compared with the current 120min protocol. **Materials:** A retrospective study was performed on 84 patients scanned in our department in 2017. Six patients were excluded due to complications during the scan or not enough information was accessible for the study. The patients fasted from midnight the previous day, they were instructed not to smoke or use chewing gum. Medications were not stopped, but were noted. The radioactive meal contained cornflakes and milk, labelled with 12MBq of ^{99m}Tc -Dowex. Pictures were acquired with the patient in an erect position, every 15min until 120min and processed by a trained Technologist using Hermes Software. **Methods:** All the patient's pictures were processed individually for 60min, 90min and 120min. A retrospective analysis was performed comparing the diagnostic results ($T_{1/2}$) and classified them as Normal (30-90min), Borderline (90-95min) and Delayed GE (>95min). **Results:** This study included 78 patients, 31% males and 69% females, with ages between 16 and 84 years old. There were several reasons for the referral of these patients, including vomiting (51%), diabetes (37%), abdominal pain (27%), nausea and

early satiety (15%), reported weight loss (10%), bloating (9%), gastroparesis (6%), tenderness and diarrhoea (3%), botox surgery (1.3%), reflux (<1%), opiate (<1%), oesophageal dysmotility (<1%) and Ehlers-Danlos Syndrome (<1%). We found using a 60min protocol instead of 120min, we have changes of the report in 22% of the patients. The minimum and maximum changes in values of $T_{1/2}$ were -159% and 128% with average of overestimation of 23%. For the 90min protocol, changes to the report classification occurred in 10% of patients. Most of these involved the borderline classification. The $T_{1/2}$ values differed by an average of 13% (minimum and maximum changes were -122% and 42%). **Conclusions:** We can conclude that a 60min protocol is not appropriate to report the GE results with accuracy, since there is a change within the report classification in 22% of patients. Regarding the 90min protocol, even though the alterations of the report were lower (10%) we cannot guarantee the 90min protocol to be totally accurate for the patients. Therefore the additional 30 minutes demonstrated to be of value and as three patients can be booked simultaneously, this still allows for effective use of scanner time.

OP-430

Brain F-18-Choline PET/CT: a first interim analysis of the impact on clinical management in patients with brain lymphoma

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Aim: Assessment of the clinical utility of the brain F18-Choline (FCH) PET/CT for detection of brain lymphoma and prediction of response to chemoimmunotherapy. **Materials:** This is a retrospective study which evaluates the clinical utility of performing brain FCH PET/CT in a cohort of 13 patients with histologically confirmed brain non-Hodgkin's lymphoma lymphoma (NHL) (11 primary and 2 secondary) submitted to four cycles of chemoimmunotherapy (MATRIX regimen). All patients had pre-treatment brain FCH PET/CT and MRI. 7 out of 13 patients underwent end of treatment FCH PET/CT imaging and MRI and 6 patients had MRI only. Dynamic brain FCH PET/CT was acquired for 30 minutes. Static PET/CT images were reconstructed from the last 20minutes of the dynamic data. SUVmax was calculated from the static PET data for all lesions and SUV_{Delta} (the percentage change of SUVmax between the pre- and post-treatment FCH PET/CTs) for lesions shown on the end of treatment FCH PET/CT. All FCH PET/CT scans were compared with the pre- and post-treatment MRI. **Results:** There were a total of 22 brain lesions detected equally on FCH PET/CT and MRI. Of the 13 patients, 4 had complete response (CR) to treatment (11 lesions), 6 had partial response (PR) (7 lesions) and 3 showed progressive disease (PD) (4 lesions). 7/11 of the lesions with CR had SUV_{max} on baseline scan lower than 4.0 and 4/11 had SUV_{max} more than 4.0. Of the 7 lesions with PR, only one had SUV_{max} lower than 4.0. All lesions with PD (4/4) had SUV_{max} higher than 4.0. Of the 7 patients (7/15) with pre- and post-treatment brain FCH PET/CTs, a total of 15 lesions were detected and 11/15 had SUV_{Delta} 100% (CR) and 4/15 had SUV_{Delta} higher than 30% (partial

metabolic response). 64% of the lesions with SUV_{Delta} 100%(CR) had SUV_{max} lower than 4.0 on the baseline scan. The 4 lesions showing metabolic disease progression (SUV_{Delta} higher than 30%) all had SUV_{max} higher than 4.0. **Conclusion:** Brain FCH-PET/CT appears a useful tool for staging and restaging (at end of treatment) of brain NHL. SUV_{max} of 4.0 on the pretreatment PET/CT appear to be a cut off point for predicting treatment response to chemoimmunotherapy.

OP-431

T2 mapping sequence for the study of prostate cancer with simultaneous PET/MR 11C-Choline and MR multiparametric protocol

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Aim: To assess T2 quantification as a predictor of malignancy on PET/MR C11-Choline protocol and MR multiparametric (mp-MR) in the analysis of diagnosis in prostate cancer (PC).

Material and Method: Sixteen patients diagnosed with suspected PC were underwent to PET/MR C11-Choline WB scan, simultaneously MRAC, T1LAVA, T2 SSFSE and DWI sequences were acquired. Next, mp-MR study to obtain T2W, T1W, DWI, DCE images and T2-MAP sequence was performed localized in prostate region. All studies were analyzed by two qualified physicians in both Nuclear Medicine and MRI. The suspected tumor tissue (STT) in Periferical Zone (PZ) and Central Zone (CZ) in prostate was detected with correlation of C11-Choline pathology uptake, hypointensity T2W images, hiperintensity DWI images at b1400, ADC maps, enhancement curve and K-trans maps. Then mean T2 values from Volumes of interest (VOIs) in all STT ($T2_{meanSTT}$) and normal tissue ($T2_{meanNT}$) from T2 mapping images was obtained. **Results:** A total of 34 suspected tumor lesions was detected in prostate PZ (n=17) and CZ (n=17). T2 mean quantification $\pm$ standard deviation for STT was $T2_{meanSTT} = 63.83 \pm 12.02$ ms and in normal tissue $T2_{meanNT} = 101.80 \pm 11.78$ ms respectively. Normalization and Student's T test was performed. It concluded that $T2_{meanSTT}$ was significant less than $T2_{meanNT}$ ($P < 0,05$). Prostate cancer for all suspected lesions was then confirmed by anatomical pathology. **Conclusion:** This preliminary study, low T2 quantifications in prostate tissue in PZ and CZ could be a good predicted of malignancy. T2-MAP sequence contributes to more accurate in the detections of tumor lesion in the diagnosis prostate cancer patients. Therefore, the described protocol is proposed as a new powerful clinical tool. These promising results should be consolidated with a larger number of studies.

OP-432

Use of 18F-FDG PET/CT as a Predictive Biomarker of Outcome in Patients with Head-and-Neck Cancer

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Purpose/Introduction: 18F-fluoro-2-deoxyglucose (18F-FDG) positron emission tomography/ computed tomography (PET/

CT) is valuable in baseline staging, treatment planning, and therapy response assessment and follow-up after therapy; according with Xu et al. (2012) the sensitivity and the specificity for PET/CT to detect head-and-neck cancer are 83% and 90%, respectively. The aim of this retrospective observational study is to discuss the value of 18F-fluoro-2-deoxyglucose (18F-FDG) positron emission tomography/ computed tomography (PET/CT) imaging biomarkers in patients with squamous cell carcinoma (SCC) and papillary thyroid carcinoma (PTC) when the primary tumour and/or metastasized lymphatic nodes are located in the head and neck area. **Subjects and Methods:** This study was performed in a total of 93 patients (86 patients with SCC (19 females, 67 males) and 7 patients with PTC (5 females, 2 males)) that underwent to 18F-FDG PET-CT. Each patient followed the protocol according with the gold standard protocol for 18F-FDG PET/CT scan, therefore patients were scanned at 60 minutes post 18F-FDG administration with head and neck and half body scan. In addition to maximum and mean standardized uptake values (SUV_{max} and SUV_{mean} , respectively), the descriptive variables were also studied. These parameters will be evaluated with respect to their potential role as non-invasive markers for patient risk stratification and correlated with the histological results (according with the TNM system for SCC and PTC). **Results:** A total of 7 patients (5 females, 2 males) were studied in PTC and obtain the following results: T2 ($SUV_{max}=2.52$; $SUV_{mean}=1.39$, average age=54 years), T3 ($SUV_{max}=8.94$; $SUV_{mean}=5.42$; average age=41.50), T4 ($SUV_{max}=13.74$; $SUV_{mean}=8.02$; average age=70.67 years). A total of 86 patients (19 females, 67 males) with SCC were studied and obtained the following results: T1 ($SUV_{max}=8.26$; $SUV_{mean}=5.12$; average age=58.72 years), T2 ($SUV_{max}=9.12$; $SUV_{mean}=4.94$; average age=58.70), T3 ($SUV_{max}=9.80$; $SUV_{mean}=5.96$; average age=59.17), T4 ($SUV_{max}=7.28$; $SUV_{mean}=4.20$; average age=58.23). All the SUV units are presented in g/mL. **Discussion/Conclusion:** In PTC patients, SUV_{max} and SUV_{mean} increases proportionally to the TNM classification. In SCC patients, the SUV_{max} and SUV_{mean} behaviour is the same from T1 to T3, but it decreases in T4. This way, in both type of tumours, SUV_{max} and SUV_{mean} had a predictive significance related to SCC and PTC differentiation. SUV_{max} will be the best option for choosing the best treatment for the patient considering that it allows access to the highest uptake in the area, which matches with the result already obtained by Zhu, Lee & Shim, (2011).

OP-433

Added Value Of Combined Visual And Quantitative Analysis For Localizing Epileptic Regions With FDG PET Imaging

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Aim: FDG Brain PET is a precious paraclinical tool for the evaluation of patients with epilepsy who are underassessment for surgical treatment. With the widespread availability of PET, identifying the functional deficit and preoperative evaluation of partial epilepsy has become a practical routine method. The aim of our study was to assess the efficacy of quantitative software-aided approach in localizing epileptic brain disorders using 18F-FDG Brain PET scan in addition to the physician qualitative interpretation. **Material and Methods:** The subject selection in our study was concentrated on patients who suffered from epilepsy disorders and referred for brain PET imaging. Thirteen patients (6 men -5 women; 25 ± 11 YO) underwent PET scan. Quantitative analysis was investigated using Scenium software, a statistical analysis tool providing z-score(1). The hypometabolic foci are defined as more than 2SD from the average of count/voxel for each region of the brain cortex using a standard database. The patients were categorized into normal cerebral gray matter (N=5) and local cerebral lesion (N=6) on the basis of MRI findings. Two physicians reported the qualitative findings of PET scans. Kappa concordance measure was used for statistical analysis. Ethics approval code: (IR.SSU.MEDICINE.REC.1395.293). **Results:** The Kappa index value for the localization agreement between MRI and PET/CT was 0.8 for both assessment methods. In the absence of MRI abnormality, the relative frequencies of localized spots were 60 and 89 for qualitative and quantitative diagnosis, respectively. Furthermore, these values were 83 and 91 while the MRI demonstrated abnormal foci. **Conclusion:** Destructive effects of epilepsy, declines the quality level of life, thus accurate diagnosis becomes very important(2). The foregoing study shows the added value of quantitative analysis on a diagnosis of epileptogenic sites alongside visual analysis. In fact, it can be a potent supplementary to other modalities like MRI and EEG in surgical treatments of epilepsy disorders(3).

OP-434

Need for Randomization in Side-by-side FDG-PET Comparison Studies

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Aim: With the introduction of digital PET/CT systems, side-by-side FDG-PET comparison studies are performed to evaluate the clinical impact of such novel systems. Some studies use a fixed scan-order, which may introduce a bias in results when considering FDG-uptake measurements, since it is known that FDG-uptake can further increase up to 100 minutes after FDG-administration. We evaluated the impact of a fixed scan-order on standardized uptake values (SUVs) in a side-by-side FDG-PET comparison study. **Methods:** We performed a prospective side-by-side PET comparison study in 20 patients referred for a FDG-PET/CT scan. For each patient, scans were acquired with a conventional scanner (cPET, Ingenuity TF PET/CT, Philips) and

a digital scanner (dPET, Vereos PET/CT, Philips Healthcare). For both scanners, an optimized high-resolution PET reconstruction was used. The PET scanning order was randomized per patient. Group 1 consisted of 10 patients who were first scanned on cPET, 65±9 minutes after FDG-administration. The second scan, on dPET, was acquired 99±12 minutes after FDG-administration. Group 2 consisted of 10 patients who were first scanned on dPET, 66±12 minutes after FDG-administration. The second scan, on cPET, was acquired 95±12 minutes after FDG-administration. Per patient, FDG-positive lesions were included up to a maximum of 5. For each lesion, we measured mean and maximum standardized uptake values (SUVmean and SUVmax), and Δ SUVmean and Δ SUVmax from cPET to dPET were calculated. Lesion axial diameters were measured on CT. **Results:** In group 1 where we included 40 lesions, the average size was 14 mm (range 5–45 mm). From cPET to dPET, SUVmean and SUVmax increased on average with 1.9 (+43%) and 2.7 (+43%), respectively. In group 2, 28 lesions were included with an average size of 15 mm (range 4–30 mm). From cPET to dPET, SUVmean and SUVmax increased on average with 0.2 (+8%) and 0.4 (+10%), respectively. Between group 1 and group 2, the average increases in SUVmean and SUVmax were significantly different ($p<0.001$). **Conclusion:** A fixed scanning order strongly influence SUV measurements in side-by-side FDG-PET comparison studies. Without randomization of the scan order, results of the second scan may greatly overestimate the true benefit in lesion detectability. In side-by-side comparison studies, a randomized scan order is therefore crucial for a valid comparison.

OP-435

Influence of motion artifacts on myocardial blood flow with [13N]Ammonia PET/CT imaging

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Purpose: Dynamic positron-emission-tomography/computed-tomography(PET/CT) is considered the gold standard non-invasive technique for *in vivo* measuring myocardial blood flow(MBF); despite this, artifacts due to patient motion during dynamic acquisition of PET/CT can alterate the measures of MBF. The purpose of this study was to quantify the prevalence of body motion in a clinical setting and to evaluate the effects of motion on MBF and coronary flow reserve(CFR). **Material and Methods:** A cohort of 60 sequential stress/rest PET/CT, injected with 370 MBq of [13N]Ammonia, was analyzed for patient motion(120 datasets in total) and MBF evaluation. Each study was performed at rest and during Regadenoson induced hyperemia. The exams were acquired by a GE Discovery690 scanner in list mode. Stress and rest images were reconstructed into 32 dynamic frames(24x10s, 4x30s, 4x60s), corrected for attenuation and reconstructed using ordered subsets expectation maximization. The patients were analyzed by Corridor 4DMv2015 and a 1:1 kinetic model. The presence of motion artifacts and direction of motion was recorded for each affected frame. **Results:**

Among the 1920 stress frames, 491 were corrected for motion artifacts (25,6%).The directions of the motion were cranial for 213 frames, caudal for 230,anterior for 37 and posterior for 11.Between the 1920 rest frames,73 were corrected(3,8%). The directions of the motion were cranial for 42 caudal for 18, anterior for 8 posterior for 5. The whole sample, considering the four directions, has a quadratic mean motion±standard deviation of 5.49±2.06mm. The difference in MBF for stress PET/CT was statistically significant for the left anterior descending artery(LAD), for the right coronary artery(RCA) and for the global MBF(TOT) ($p<0.05$) but not for the left circumflex artery(LCX) ($p=n.s.$). There were no statistically significant difference for the three coronary territories ($p=n.s.$). The CFR was statistically significant for LAD and TOT ($p<0.05$), but not for the LCX and RCA ($p=n.s.$). Difference between motion corrected and non corrected showed a wide range from -72% to +228% for MBF and CFR, respectively. The confidence intervals at 95%(95%CI) for stress LAD, LCX and RCA were: 0.0566|0.1170, -0.0289|0.0292, -0.1078|0.0219, respectively. The rest 95%CI of LAD, LCX and RCA were: -0.0549|0.0225, -0.0227|0.0086, -0.1362|0.0178. The CFR 95%CI were 0.0745|0.2049, -0.0244|0.0720, -0.0772|0.0906 for LAD, LCX and RCA, respectively. **Conclusions:** The motion artifacts have a high incidence in stress/rest [13N]Ammonia-PET/CT with a caudo-cranial direction prevalence and wide variability. Motion correction is mandatory to avoid statistically significant differences in the quantification of MBF and CFR, with errors up to 228%.

OP-436

Benefits of head tilting for brain PET-CT examinations

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The main goal of the current study is to think over the aspects of head positioning for brain examinations, focusing on mainly one field of view (FOV) PET/CT acquisitions. The image quality, radiation exposure of the eye lenses, streaking artefact due to the beam hardening of the skull, patient comfort, orientation of the reconstructed images were all considered in this study. **Method:** while the brain centered in the PET field of view, the degree of tilting the patient's chin toward to the chest were examined. Reconstructed CT images of anonymized patients were retrospectively evaluated. From the perspective of PET image quality the PET FOV on the CT image were simulated, then the number of significant voxels of the brain tissue close to the FOV borders were plotted as a function of the tilt angle. On the same way the path of the radiation exposure in the brain were analysed. We introduced a simple wedge-shape insert placed under the head holder into our routine brain examinations according to our initial results. Patients were reported in connection with the comfort during the examination. **Results:** we found that the range of 20 -25 degree is the optimal range to tilt the head toward to the chest. As a result of tilting the head, the reconstructed axial slices for both the CT and the PET are fit for supra orbito-meatalis line. It decreases the asymmetries caused by wrong orientation, and can take unnecessary the re-orientation of the images as a post-processing step, prior the

medical reporting. In most cases it results that the eyes are out of the CT scan range, which is particularly important, since the eyes have high risk for radiation exposure. The location of CT streaking artefacts moves down to the direction of cerebellum. In general because the tilting of the head, the perpendicular projection of the brain to the scan axis is significantly shorter, which means 10–15% dose reduction. Furthermore the noise – as a result of the low sensitivity of PET on the FOV borders – has smaller effect on the diagnostic value of reconstructed PET image. There is no noticeable advantage or disadvantage related to the patient comfort. **Conclusion:** tilting the head with 20–25 degree results an overall improvement in image quality and dose reduction. Our results are relevant not for PET/CT only, but for SPECT/CT examination too.

1105 Tuesday, October 16, 2018, 08:00 – 09:00, Hall X

M2M: AD-PD - It's in the brain!

OP-437

Radiolabelling and Evaluation of Butyrylcholinesterase Inhibitors as Early Biomarkers for Alzheimer Disease

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Introduction: Butyrylcholinesterase (BChE) is an enzyme responsible for the hydrolysis of choline-based esters, such as acetylcholine (ACh). Up to 30% increase of BChE has been observed in the brains of patients with Alzheimer disease (AD) compared to healthy individuals, suggesting that BChE is a promising target for an early diagnosis of AD. In this work we report ¹¹C-labelling, evaluation of the metabolism and *in vivo* positron emission tomography (PET) studies in control and diseased animals with a recently reported potent selective BChE inhibitor. **Subjects and methods:** The BChE inhibitor was radiolabelled with ¹¹C-methylation on the alcohol position of the corresponding precursor using [¹¹C]CH₃I as the labelling agent. Metabolite studies were performed on blood and brain samples of wild type (WT) rats at t = 5, 10, 30, and 60 min after intravenous injection using high performance liquid chromatography (HPLC) and radioactive detection. To assess the ability of the radiotracer to bind to BChE *in vivo* a longitudinal PET imaging study has been conducted in an animal model of AD (Tg6799) at 4, 6 and 7 months of age. Control animals with the same genetic background but with an absence of the disease (C57BL/6J) were investigated at the same time points. Beta amyloid plaque deposition has been evaluated *in vivo* using [¹⁸F]florbetaben. **Results:** Radiolabelling of the BChE inhibitor could be achieved with non-corrected radiochemical yield of 20%. Metabolism studies showed the presence of unidentified metabolites. The parent compound accounted for >80% and >20% of the radioactivity in blood at t=10 and 60 min post injection, respectively. No metabolites could be detected in brain samples. *In vivo* studies showed excretion through the intestine and the bladder. The tracer successfully crossed the blood brain barrier (BBB) and was rapidly

washed from the brain. PET studies using the BChE inhibitor showed increased uptake in different brain regions in AD but not WT animals at late time points. Studies performed with [¹⁸F]florbetaben showed significant differences between AD and WT animals both in the cortex and the hippocampus, confirming the presence of amyloid beta plaques in diseased animals. **Conclusion:** The selected BChE inhibitor sufficiently undergoes radiolabelling with ¹¹C, crosses the BBB, and is quickly washed out of the brain of WT mice. Comparison between AD and WT mice show an accumulation of the radiotracer in affected areas of the brain, confirming that the selected radiotracer can be used to study AD progression.

OP-438

Preclinical characterization of two promising PET tracers for imaging tau neurofibrillary tangles (NFTs)

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Introduction and Aim: The aim of this study was to evaluate preclinically, the properties of two promising PET tracers for imaging tau in Alzheimer's Disease. Tau is a microtubule-associated, natively unfolded protein with little tendency for aggregation. In AD, however, it becomes hyperphosphorylated, misfolded and begins to form insoluble aggregates which exhibit a disease-specific spatio-temporal distribution in the brain, which has been shown to be associated with cognitive impairment. It is hoped that the application of tau PET tracers will allow researchers to confirm the mechanism of action of drugs directly targeting pathological tau; monitor the effects of disease modifying AD therapies more broadly, gain a better understanding of the pathophysiology of AD, and select patients for future clinical trials. **Material and Methods:** Tau binding and selectivity vs. Aβ was assessed using human AD brain tissue homogenates, with [³H]MK-c6 and [³H]PIB, respectively. Selectivity against MAO-A and MAO-B was assessed using adult rat brain (cortex) tissue homogenates, using [³H]harmine and [³H]selegiline, respectively. Autoradiography studies were performed using tritiated or F-18 labeled compounds **1** and **2** on human AD and non-AD brain sections. The degree of non-displaceable binding was assessed by self-block or blocking with T808, RO-6958948, and MK-6240. PET studies were performed in anesthetized cynomolgus monkeys with arterial blood sampling. The total volume of distribution (V_t) was estimated using a 2-tissue compartment model and Logan graphical method with metabolite corrected plasma input function in ROIs defined on a subject specific MRI using a NHP brain atlas. Both radiotracers were prepared to high radiochemical yield and specific activity by nucleophilic displacement of the chloroheteroarene precursor with [¹⁸F]KF/K222. **Results:** Compounds **1** and **2** were identified as high affinity (K_d<1nM) and highly selective (9–10μM vs. Aβ, >800x vs. MAO-A, >600x vs. MAO-B) ligands for NFTs. Autoradiography experiments demonstrated that both radiotracers showed similar levels of high displaceable binding in AD brains, regardless of

the blocking compound. Conversely, *in vitro* studies in non-AD brains showed no displaceable binding. PET studies of these two ligands in non-human primates showed high brain penetration and homogeneous distribution across regions ($V_T=2.29\pm0.25$ for **1**, $V_T=5.06\pm0.46$ for **2**) with rapid washout kinetics. **Conclusion:** Compounds **1** and **2** possess *in vitro* and *in vivo* properties consistent with their being suitable PET tracers to quantify tau aggregates in the human AD brain. Further evaluation in clinical studies is warranted.

OP-439

Comparative Longitudinal Evaluations of [^{18}F]AV-1451 and [^{18}F]NM-AV-1451 as PHF-Tau Protein Imaging Agents with a Alzheimer's Disease Transgenic Mouse: a Preliminary Results and Unexpected Uptake of the Olfactory Bulbs

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Purpose: [^{18}F]AV-1451 ([^{18}F]T807) has been proven to be a promising PHF-Tau protein tracer for studying Alzheimer's disease (AD) [1, 2]. In order to improve its brain uptake and binding specificity, we have synthesized three *N*-alkyl analogs of [^{18}F]AV-1451 and found that both the lipophilicities and whole brain uptake of these analogs in normal mice were higher than that of [^{18}F]AV-1451 itself. *In vitro* autoradiographic studies on post-mortem human brain slices of a healthy control and an AD patient showed that *N*-methyl analog of [^{18}F]AV-1451, [^{18}F]NM-AV-1451, had highest specific binding in frontal lobe of AD patient [3]. We reported herein the distribution of [^{18}F]AV-1451 and [^{18}F]NM-AV-1451 in a normal aging mouse and an age matching 3xTg AD mouse at different time intervals using microPET. **Methods:** The [^{18}F]AV-1451 and [^{18}F]NM-AV-1451 were synthesized with TraceLab F_{SN} module as reported previously [3]. A female normal aging mouse and an age matching 3xTg-AD mouse were used for microPET imaging at different time intervals (16, 19 and 22 months old for normal aging mouse; 19 and 22 months old for 3xTg-AD mouse). Mice were injected with a bolus of about 200 μCi of each ligand and imaged with an Argus PET/CT scanner. Dynamic sinograms were produced with 12 x 10 sec, 3 x 60 sec, 3 x 300 sec, 4 x 6000 sec and 2 x 900 sec frames. The regional brain uptake and kinetics of these two ligands in mice were analyzed with PMOD, and standardized uptake value ratios (SUVr) were calculated using cerebellum as a reference region. **Results:** The RCYs of [^{18}F]AV-1451 and [^{18}F]NM-AV-1451 were 13 ± 4 ($n=15$) and 7 ± 6 ($n=4$) with a radiochemical purity of >95 % and specific activity of 151 ± 52 and 100 ± 108 GBq/ μmol , respectively. For both tracers, the SUVr of AD mouse were higher than those of age matching normal mouse (Fig. 1 and 2). The regional SUR differences of [^{18}F]AV-1451 decreased with time (Fig. 1). In contrast, the regional SURs of [^{18}F]NM-AV-1451 in 3xTg-AD mouse were significantly increased with time compared to those in normal aging mouse (Fig. 2). Moreover, PET studies showed that

both [^{18}F]AV-1451 and [^{18}F]NM-AV-1451 tracer had significant uptake in olfactory bulb and the regional SUVr of [^{18}F]NM-AV-1451 were higher than those of [^{18}F]AV-1451 (Fig. 3). **Conclusions:** This preliminary results suggested [^{18}F]NM-AV-1451 may be a better AD imaging agent than [^{18}F]AV-1451. The validations of [^{18}F]NM-AV-1451 as a PHF-tau imaging agent continue.

OP-440

Development of a novel reversible F-18 labelled SL25.1188 analog for the detection of MAO-B activity

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Introduction: Monoamine oxidase-B (MAO-B) is an important enzyme for regulating the levels of monoaminergic neurotransmitters by catalyzing their deamination. Inhibition of MAO-B has been widely used in the treatment of Parkinson's disease (PD). Carbon-11 (^{11}C) labelled MAO-B inhibitors, such as [^{11}C]L-deprenyl and [^{11}C]SL25.1188, have been used in PET studies to image the distribution of available MAO-B in the human brain. The short half-life of ^{11}C (20.4 min) makes these radioligands less suited for distribution to PET centers without an on-site cyclotron. The aim of this study was to develop a novel reversible ^{18}F -labeled analog of SL25.1188 ([^{18}F](S)-3-(6-(3-fluoropentyloxy)benzo[d]isoxazol-3-yl)-5-(methoxy methyl)oxazolidin-2-one; [^{18}F]FSL25.1188), and to perform its biological evaluation in *vitro* and *in vivo* for detection of binding to MAO-B. **Methods:** Precursor and reference compound were synthesized *via* a multi-step synthesis. Radiolabeling was achieved by one-step nucleophilic substitution reaction. The reaction was carried-out in CH_3CN at 100°C for 10 min. [^{18}F]FSL25.1188 was first evaluated in *vitro* by human whole hemisphere autoradiography (ARG) experiments. Furthermore, dynamic PET imaging with [^{18}F]FSL25.1188 was performed *in vivo* in a non-human primate (NHP) to investigate regional brain uptake and enzyme binding kinetics. Total distribution volumes (V_T) were calculated with 2-TCM, and radiometabolites were measured in monkey plasma using radio-HPLC. **Results:** Reference and precursor compounds were synthesized in 6-steps starting from 2-fluoro-4-hydroxybenzonitrile. [^{18}F]FSL25.1188 were produced and isolated in high radioactivity, radiochemical purity (>99%), and high molar activity (>100 GBq/ μmol). In the ARG assay, [^{18}F]FSL25.1188 binding was observed in MAO-B rich regions. Co-incubation with L-deprenyl and SL25.1188 inhibited radioligand binding in regions having high MAO-B density, such as thalamus (32% and 40%, resp.) and caudate nucleus (38% and 42%, resp.). The PET imaging study of [^{18}F]FSL25.1188 in NHP showed high brain uptake ($\text{SUV} = 2.8$ at peak) followed by a progressive washout. The regional uptake also reflects the known distribution of MAO-B, with the highest accumulation in thalamus ($V_T = 5.6$) and striatum ($V_T = 4.6 - 4.7$), moderate accumulation in the cortical regions ($V_T = 4.3 - 4.6$), and lowest in cerebellum ($V_T = 3.7$). Radiometabolite studies demonstrated that only polar radiometabolites were formed

with 20% unchanged radioligand at 60 min. **Conclusion:** A high yielding radiosynthesis method to produce [^{18}F]FSL25.1188 was developed. [^{18}F]FSL25.1188 displays favorable properties for *in vivo* imaging of MAO-B, including blocking effect *in vitro*. There was a high blood-brain-barrier permeability, regional uptake in accordance with known MAO-B distribution, and fast washout from the NHP brain *in vivo*.

OP-441

Longitudinal Assessment Of Dopamine Progenitor Cell Engraftment In A Preclinical Model Of Parkinson's Disease

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Introduction: Great strides have been made in the development of cell therapies for Parkinson's disease (PD) with the aim of restoring functional dopaminergic neurotransmission. Clinically, cell therapy derived from human fetal tissues have shown significant, long term benefit, however, clinical use is stymied by ethical and logistical issues. Dopaminergic progenitor cells derived from human embryonic stem cells (hESC-DAs) are a renewable and viable alternative, able to mature into functional midbrain dopaminergic neurons *in vivo*. Here we longitudinally follow the integration of hESC-DAs in a preclinical model of PD using clinically relevant methodologies including MRI, MRS and PET as well as behavioural measures and histology to assess engraftment and functional recovery. **Materials and Methods:** The floor plate-based protocol was used to produce functionally active hESC-DAs. Athymic nude rats were lesioned with 6-hydroxydopamine (6-OHDA) in the nigrostriatal projection, subsequently animals with >90% lesion efficacy and >5 rotations per minute (RPM) received either vehicle or hESC-DA neurosphere transplant. Multimodal imaging, including MRI, MRS, PET (^{18}F -FBCTT as a radiopharmaceutical for the presynaptic dopamine transporter and ^{18}F -Fallypride as a tracer for the occupancy of post synaptic D2/D3 receptors) were used to assess initial lesion and transplant efficacy over a 6 month period post transplantation as well as behavioural measures (amphetamine induced rotation) and histology. **Results:** MRI and MRS show surviving transplants that increase in volume over time indicating proliferation and maturation of neuron rich cells. The 6-OHDA lesioned striatum initially showed a greater than 90% reduction in ^{18}F -FBCTT binding, while ^{18}F -Fallypride binding was significantly increased indicative of a pronounced decrease in DA release. At 6 months post-transplant ^{18}F -FBCTT clearly shows re-innervation with a ~40% increase in binding and ^{18}F -Fallypride binding was normalized to intact levels indicating an improvement in functional dopamine release. After lesion, amphetamine induced rotations were >5 RPM, by 3 months a significant recovery was observed and maintained at the 6 months in line with previous data. Histological analysis complemented the imaging data confirming neuron-rich transplants expressing tyrosine hydroxylase and markers of midbrain do-

paminergic neurons. **Conclusion:** These data prove the ability of hESC-DA neurons to re-innervate the lesioned striatum and restore dopaminergic neurotransmission within 6 months of transplant.

OP-442

Synthesis and biological evaluation of a novel mGluR5 radioligand: [^{18}F]AZD9272

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Introduction: The metabotropic glutamate receptor subtype mGluR5 has been proposed as a potential drug target for CNS disorders such as anxiety disorder, depression, Parkinson's disease and epilepsy. The AstraZeneca compound AZD9272 has previously been labelled with carbon-11 and used as a PET radioligand for determination of mGluR5 receptor binding and occupancy (1,2). The aim of this study was to develop ^{18}F -labeled AZD9272 (3-fluoro-5-(3-(5- ^{18}F)fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl)benzonitrile), and to examine its binding characteristics *in vitro* and *in vivo*. **Methods:** The nitro-precursor and the cold reference standard were provided by AstraZeneca. Radiolabeling was achieved by a classical one-step fluorine-18 nucleophilic substitution reaction. The detailed regional distribution [^{18}F]AZD9272 binding was evaluated using autoradiography on human brain whole hemisphere sections and PET measurements in four non-human primates (NHPs). After intravenous injection of [^{18}F]AZD9272, brain radioactivity was measured for 123 minutes using a high resolution PET system. Radiometabolites were measured in monkey plasma using gradient radio HPLC. **Results:** [^{18}F]AZD9272 was successfully synthesized from nitro precursor and the incorporation yield of the fluorination reactions was >55%. The radiochemical purity was higher than 99% at EOS. Molar activity was 94 ± 103 GBq/ μmol at time of administration. The radioligand was stable, with a radiochemical purity of >99% at 2h after formulation in a sterile phosphate buffered solution (pH = 7.4). The percentage of parent radioligand in monkey plasma was 59&64% (n=2) at 120 min after injection, consistent with the high metabolic stability previously reported for ^{11}C -labeled AZD9272 (1). After injection of [^{18}F]AZD9272 the maximum whole brain radioactivity concentration was 4.9-6.7 % of injected dose (n=4) and reached within 5.5-13.5 minutes of data acquisition. PET images for [^{18}F]AZD9272 showed a pattern of regional radioactivity consistent with that previously obtained for [^{11}C]AZD9272 (2). Regional binding was highest in striatum and thalamus, whereas lower binding was observed for the cerebellum and occipital cortex. Autoradiography images of the human brain *in vitro* showed an anatomical distribution pattern consistent with that for the NHP brain *in vivo*. **Conclusions:** The radioligand [^{18}F]AZD9272 shows suitable properties for *in vivo* and *in vitro* imaging of mGluR5 binding in the primate brain. ^{18}F -labeled AZD9272 offers advantages over [^{11}C]AZD9272 in terms of higher image resolution, combined with

a longer half-life, thereby serving as an improved tool for quantitative assessment of AZD9272 binding sites using PET and autoradiography. **References:** (1) Andersson et al., 2013, Nucl. Med. Biol. 40:547–553. (2) Varnäs et al., 2018, Neuropharmacology, 135:455–463.

OP-443

Recent advances in translational study of ^{18}F -DABTA-11, a PET tracer for alpha-synuclein aggregates

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The ability to image alpha-synuclein aggregates (α -syn) in the living brain would enable to diagnose and track the degree and location of alpha-synucleinopathies over time. We have been developing several small molecule diagnostic probes based on 4,4'-diaryl-2,2'-bithiazole, DABTA, tracers suitable for quantification of α -syn by nuclear medicine imaging. Recently, we studied ^{18}F -DABTA-11 as a lead compound for noninvasive, specific imaging of α -syn as opposed to other proteopathies (e.g. $\text{A}\beta$ and tau). Here, we report the results of studies aimed at the clinical translation of the ^{18}F -DABTA-11 lead by μPET using α -syn E46K mutant rat model at age of 12 months as well as in nonhuman primates (NHP). **Methods:** The ^{18}F -DABTA-11 lead with low nanomolar affinity for α -syn ($K_i = 3 \text{ nM}$) and high selectivity (120 fold) for $\text{A}\beta$ and tau was labeled with the Neptis module using two-step ^{18}F -fluoro ethylation. The brain-specific binding kinetics were investigated in 12 month-old rats with E46K α -syn mutation and controls using dynamic PET coregistered to a 7T-MRI. Furthermore, we studied the ^{18}F -DABTA-11 and an ^{11}C -DABTA-3 leads' brain uptake kinetics and plasma stability in normal NHP. **Results:** The automation and CMC works for the two-step radiosynthesis of the ^{18}F -DABTA were established (RCY >15% and a purity >98%). Group comparisons of distribution volume (DV) in rats showed statistically significant differences between α -syn E46K rats and controls for the substantia nigra, cerebellum, thalamus, brainstem, corpus callosum, basal forebrain, neocortex, and striatum. In normal NHP both tracers showed initial brain uptake of up to 1.4% ID (1.3 SUV) and a quite rapid washout with marginally increases in later time points (up to 0.45SUV at 120min). Initial results of in vivo stability of ^{18}F - and ^{11}C -DABTA in monkey plasma were higher than 55% 120 min p.i. **Conclusion:** The favorable features of DABTAs encourage us to carry out translation into human studies. The fast washout from brain in NHP and the suitable uptake brain entry/clearance kinetics, target affinity, excellent accumulation in the α -syn rich regions in E46K rats suggests that DABTA-11 is promising selective α -syn tracer that may allow for the first non-invasive imaging of α -synuclein aggregates in patients with Parkinson's disease or de-

mentia with Lewy bodies. **Acknowledgment:** We are grateful for the excellent assistance of Zhisheng Jia, Prodip Datta and Mohammad Moein in NHP study.

OP-444

18F-Fluorodopa and 18F-Fallypride Assessment of Cell Grafts in 6-OHDA Lesioned Rats

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Introduction: 18F-Fluorodopa is a widely used radiotracer in clinical studies of cell replacement therapy in patients with Parkinson's disease, however it has not, to date, been shown that small cell grafts could be detected in rodent models of PD using this radiotracer. The aim of this study was to assess the ability of 18F-Fluorodopa and 18F-Fallypride to monitor therapeutic graft development in unilaterally 6-OHDA lesioned rats as measured against behavioural measures. **Materials and methods:** 26 lister-hooded rats received 6-OHDA lesions of the right medial forebrain bundle to induce unilateral dopamine loss and corresponding motor impairments. Rats were then split into 3 groups: lesion only (n= 10), lesion rats grafted with primary human fetal cells (hVM, n=10) and lesion rats grafted with clinical grade human embryonic stem cells differentiated to a dopaminergic phenotype (hESC-DA; n=6). Rats were scanned with 18F-Fluorodopa at 17–20 weeks post grafting. A subset were also scanned 12–15 weeks post graft with 18F-Fluorodopa or with 18F-Fallypride. 18F-Fluorodopa scans we carried out and analysed with patlak plots as described by Kyono *et-al.*¹ and 18F-Fallypride scans with logan reference plots as described by Ota *et-al.*² using a mediso nanoscan PET/CT scanner and vivoquant image analysis software. Ki values of the lesioned side were expressed as a % of the values in the intact side. Motor impairment and recovery were assessed using four tests of simple motor function (amphetamine-induced rotation, vibrissae-evoked touch test, adjusting steps test and cylinder test). Graft volumes and neuronal cell counts were analysed by histology at study endpoint. 18F-Fluorodopa and 18F-Fallypride were produced in house on a Trasis all-in-one system via adaptations of literature methods.^{3,4} **Results:** Group wise comparison of striatal regions of grafted groups vs control lesion only rats showed a statistically significant increase in uptake for 18F-Fluorodopa in the grafted groups. On an individual basis there was a statistically significant correlation between 18F-Fluorodopa uptake and behavioural tests. Groupwise comparison between grafted and lesion only groups showed a statistically significant normalisation effect of 18F-Fallypride uptake in the striatal regions in the grafted animals compared to the lesion only animals. Both grafted groups showed statistically significant improvements in all behavioural measurements compared to lesion only animals. **Conclusions:** 18F-Fluorodopa and 18F-Fallypride are useful in the analysis of graft function in this Parkinson's disease model. **References:** 1. Kyono, EJNMMI

Res 2011,1,25. 2. Ota, PsychiatryResNeuroimaging 2015,232,92-97. 3. Libert, JNuclMed 2013,54,1154-1161. 4. Mukherjee, NuclMedBiol 1995,22,283-296.

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Tuesday, October 16, 2018, 08:00 - 09:00, Hall Y

Do.MoRe: Data Analysis - Neurology

OP-445

Validation of non-invasive parametric methods for ^{11}C -UCB-J PET imaging using subcortical white matter as reference tissue

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Introduction: ^{11}C -UCB-J was developed as a specific PET ligand for quantifying presynaptic SV2A expression in vivo and is considered as an excellent proxy of synaptic density. A region-based analysis of ^{11}C -UCB-J PET dose occupancy data confirmed 1 tissue compartment model (1TCM) as the preferred kinetic model and identified subcortical (centrum semi-ovale) white matter as a valid reference region [1,2]. However, accurate parametric images are a prerequisite for clinical applications and a voxelwise analysis of ^{11}C -UCB-J PET. The purpose of this study was to evaluate different non-invasive methods for generating ^{11}C -UCB-J parametric maps representing binding potential (BP_{ND}) and relative tracer delivery (R_1) at a voxel level while using centrum semi-ovale as reference tissue. **Subjects & methods:** 10 healthy volunteers (8M/2F; age 27.6 ± 10.0 yrs) underwent a 90-min dynamic ^{11}C -UCB-J PET scan with full arterial blood sampling under baseline and SV2A-antagonist dosing conditions. A basis function approach (receptor parametric mapping: RPM2) of the simplified reference tissue model (SRTM) and a multilinear reference tissue model (MRTM2) were used for generating parametric BP_{ND} and R_1 maps. Both approaches used a fixed wash-out constant k_2 for the reference tissue determined by regional based SRTM analysis with k_2 coupled between all brain regions. In addition, reference Logan (rLogan) and standard uptake value ratios for several post injection time intervals ($\text{SUVR}_{60-90\text{min}}$, $\text{SUVR}_{50-80\text{min}}$ and $\text{SUVR}_{40-70\text{min}}$) were investigated. $\text{BP}_{\text{ND}}/\text{SUVR}-1$ and R_1 images were evaluated using correlation and Bland-Altman analyses, comparing regional parametric values to region-based 1TCM DVR-1 and R_1 values relative to centrum semi-ovale. **Results:** For all non-invasive parametric methods, highly significant correlations were found with regional 1TCM values for both $\text{BP}_{\text{ND}}/\text{SUVR}-1$ ($r \geq 0.97$) and R_1 ($r \geq 0.86$) parameters. RPM2 and MRTM2 presented a very similar small bias and 95% limits of agreement interval (1.6% bias and [-7.3%,10.5%] for MRTM2) and outperformed rLogan (10.5% bias and [-3.6%,24.6%]). For a SUVR based quantification, $\text{SUVR}_{60-90\text{min}}$ demonstrated the smallest bias and 95% limits of agreement interval (6.6% bias and [-9.0%,22.3%]). **Conclusion:** Both RMP2 and MRTM2 provided more robust ^{11}C -UCB-J parametric maps compared to rLogan and are therefore the preferred methods for voxel level analysis of dynamic ^{11}C -UCB-J PET studies using the centrum semi-ovale

as reference region. $\text{SUVR}_{60-90\text{min}}-1$ images relative to the centrum semi-ovale proved to be an excellent proxy for the ^{11}C -UCB-J BP_{ND} maps using only static ^{11}C -UCB-J PET imaging. [1] Finnema et al., Kinetic evaluation and test-retest reproducibility of [^{11}C] UCB-J, JCBFM, Jan 2017 [2] Koole et al., Neuroreceptor Mapping Conference, London, 2018

OP-446

Reliable quantification of ^{18}F -GE-180 PET neuroinflammation studies using an individually scaled population-based input function

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Aim: Measurement of the individual input-function by continuous arterial blood-sampling and metabolite analysis of ≥ 6 arterial blood-samples is the gold-standard for quantitative assessment of neuroinflammation by dynamic PET with translocator protein (TSPO) ligands. Aim of this study was to test a population-based input-function individually scaled by a single late blood-sample for simplified quantification of ^{18}F -GE-180 PET. **Methods:** Two healthy volunteers and eight liver-transplanted patients were enrolled (age 60 ± 8 years, 4 females, 4 smokers). All were scanned for 90min (Biograph mCT, Siemens) starting with the injection of $185\text{MBq } ^{18}\text{F}$ -GE-180. Automatic arterial blood-sampling was performed during the first 15min. Additional blood-samples were obtained manually at 4.5, 10, 17.5, 32.5, 65 and 85min p.i.. The latter were also used to determine the time-course of the plasma-to-whole blood ratio and the fraction of unmetabolized tracer in order to derive the input-function from the whole-blood time-activity-curve (TAC). Whole-blood curve and input-function were corrected for delay and dispersion using an image-derived TAC of the internal carotid. "Population-based" templates of whole-blood TAC and input-function were generated by averaging the individual curves after scaling to the respective value at 85min p.i.. Individual population-based blood-curves were obtained by multiplying the templates by the individual 85min values. The thalamus TAC was extracted from the dynamic PET-data using a predefined standard VOI in MNI-space after stereotactical normalization based on individual MPRAGE-MRI (SPM12). The 2-tissue-compartment-model with free fractional blood-volume was used to estimate the total distribution-volume (VT) of ^{18}F -GE-180 in the thalamus (PMOD). Measured or population-based blood curves were used for the modelling. In addition, the thalamus-to-cerebellum uptake ratio (60-90min p.i.) was computed. **Results:** Bland-Altman analysis revealed a tendency towards lower thalamic VT with the population-based input (0.146 vs. 0.170, $p=0.063$), particularly for higher VT values. However, tha-

lamic VT calculated with population-based or measured blood-curves were strongly correlated ($R^2=0.904$, $p<0.0001$). VT was significantly lower in smokers (with population-based blood-curves: 0.105 vs. 0.173, $p=0.021$). The thalamic uptake-to-cerebellum ratio did not correlate with VT based on measured input ($R^2=7*10^{-6}$, $p=0.994$), nor was it different between smokers and non-smokers (0.825 vs. 0.838, $p=0.438$). **Conclusions:** These results support the use of a population-based input-function scaled with a single late blood-sample for quantitative analysis of dynamic ^{18}F -GE-180 PET studies. High correlation to results obtained with complete measured blood-data and detection of an expected difference in TSPO binding related to smoking (Brody, *Neuropsychopharmacology* 2017;42:1630-9) could be achieved. In contrast, GE-180 uptake scaled to the cerebellum failed in both regards.

OP-447

Deep Learning approach for interpretation of ^{123}I -ioflupane SPECT images in patients with suspected Parkinson's Disease

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Purpose: Parkinson's disease (PD) is primarily characterized by dysfunction of the presynaptic dopaminergic system which can be analyzed at the striatal level using dopamine transporter imaging with ^{123}I -ioflupane SPECT (DaTscan). Typically, these images are interpreted either only visually or in combination with semi-quantitative analysis approach which requires age-matched reference values. We propose a deep learning-based approach for interpretation of DaTscan images in patients with PD. **Methods:** DaTscan images of 176 healthy controls (HC) and 390 PD subjects from the PPMI database (www.ppmi-info.org) were used to build a convolutional neural network (CNN) (Fig. 1) designed to refine image interpretation. Specifically, the network was designed to distinguish between DaTscan images of HC and PD subjects. Summed 2D semi-quantitative images around the basal ganglia were used through a 10-fold cross-validation to evaluate the network. No data augmentation was performed. For each subject, the reconstructed DaTscan image was affine-registered with a DaTscan template in the standard anatomical Montreal Neurological Institute (MNI) space, and scaled voxel by voxel to the mean uptake in the entire brain without striata, resulting in a distribution volume ratio (DVR) image. Subsequently, a 12-mm-thick transversal slab centered (in axial direction) at the striatum in the template space was extracted and averaged to create a 2D DVR-image. Finally, a rectangular mask encompassing the striata in the MNI space was applied to crop a 47x34 DVR patch (Fig. 1) which was used as input to the network. We tested our network using as ground truth the gold standard diagnosis of PPMI cohort. In addition, we used Striatal Analysis software (*syngo.via*, Siemens-Medical-Solutions, USA, Inc., Knoxville, TN) to build a database of reference regional binding ratios from 101 HC subjects and used it to classify new PPMI data (59 HC and 87 PD). The performances of the two approaches (normal DB and proposed CNN) were

compared. **Results:** Using the database of quantitative reference values, optimal classification accuracy (CA) using Youden index and area under receiver-operating-characteristic curve (AUC) were: putamen (CA=92%, AUC=0.96), caudate (CA=77%, AUC=0.92), and striatum (CA=87%, AUC=0.93). However, better results were achieved using the proposed network (AC=96.5%, AUC=0.986). **Conclusion:** We built a deep learning network and trained it to classify subjects into HC or PD based on their DaTscan data. Such a network can potentially assist in resolving inter-observer variability of visual reads of DaTscan images and substituting a normal database of binding ratios required for meaningful clinical quantification of dopamine transporter availability.

OP-448

Assessment of the Accuracy of Volumetric Statistical Amyloid Burden (VSAB) for Identifying Amyloid Positive and Negative Subjects with ^{18}F -Flutemetamol PET

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Purpose: Previous studies have shown that VSAB, the volume of gray matter exceeding a z-score threshold compared to a database of amyloid negative healthy controls, is a useful metric for quantitative assessment of amyloid PET brain scans. Applying a probabilistic gray matter mask (GMM) for VSAB calculation further improves the utility of this metric in quantifying amyloid images and has demonstrated high accuracy and excellent agreement with expert visual reads using Florbetapir and Florbetaben. Here, our goal is to evaluate the use of VSAB for distinguishing between amyloid positive and negative patients with Flutemetamol PET scans. **Methods:** Flutemetamol PET scans for 109 clinically diagnosed healthy controls (M:F-47:62; mean age 72.1 years) and 18 AD subjects (M:F-10:8; mean age 74.2 years) were acquired from the Australian Imaging, Biomarkers & Lifestyle Study of Aging (AIBL) (www.aibl.csiro.au). All normals were further classified as amyloid negative by an expert reader. After registration to common template space, z-scores were computed for each voxel of every PET scan as previously described. Z-score thresholds at 1.65, 3, and 5 were considered for the computation of VSAB, defined as the percentage of voxels within the GMM exceeding the z-score threshold. The probabilistic GMM, defined as the region where voxels are at least 50% more likely to contain gray matter than white matter, was created using FreeSurfer for the segmentation of MRIs. ROC curves created at each z-score threshold determined the optimal VSAB cutoff, resulting in the highest sensitivity and specificity. AUC, sensitivity, specificity, and accuracy were calculated for VSAB at each z-score threshold. **Results:** Using a z-score threshold of 5, VSAB correctly classified scans with 99.2% accuracy at 100% specificity and 94% sensitivity, and AUC value of 0.970 (17/18 correctly classified amyloid positive and 109/109 correctly classified amyloid negative). Z-score thresholds of 1.65 and 3 resulted in 98.4% accuracy at 100% specificity and 89% sensitivity, with AUC values of 0.937 and 0.961 respectively (16/18 correctly classified amyloid positive, and 109/109 correctly classified amyloid negative). **Conclusion:** VSAB using a probabilistic GMM cor-

rectly classified amyloid negative from amyloid positive patients with excellent accuracy and high sensitivity and specificity, with only one incorrectly identified amyloid positive subject. Future studies are warranted to further explore this metric using the derived VSAB cutoffs found here on a larger test set.

OP-449

ViQuant: A fully-automated non-invasive absolute quantification pipeline for [18F]FDG PET/MRI of the human brain

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Purpose: To introduce ViQuant, a clinically viable fully automated PET/MR based software pipeline that allows non-invasive determination of the cerebral metabolic rate of glucose (CMRGlc) using an image-derived input function (IDIF), followed by the calculation of patient-specific abnormality maps (Z-maps). **Material and Methods:** The ViQuant pipeline is a MATLAB based tool consisting of individual software blocks that perform the following tasks: (1) dynamic PET image reconstruction based on motion matched attenuation maps (Siemens e7 tools), (2) extraction of an image derived input function (IDIF) by performing an MR-based motion correction and partial-volume correction, (3) generation of CMRGlc images using Patlak analysis, and (4) generation of a normative database (NormDB) and patient-specific z-maps. To evaluate the performance of the software pipeline, 10 non-lesional epilepsy patients ((27±7) y, (70±10) kg, 5M/5F) underwent dynamic [18F]FDG PET/MRI examinations in a fully-integrated PET/MRI (Siemens, Biograph mMR). The 60min imaging protocol consisted of simultaneous acquisition of PET list mode data, MRA, T1 MR as well as sparsely-sampled MR navigators for motion correction. A low-dose CT was performed for the purpose of attenuation correction. No arterial input function (AIF) was obtained from the patient cohort as the IDIF methodology was already validated using healthy volunteers. The obtained patient data together with CMRGlc images from 20 healthy volunteers (demographics similar to NLE patients) were passed to the ViQuant pipeline for the non-invasive calculation of patient-specific CMRGlc images. Spatial normalization of all images was performed using DARTEL (SPM 12), allowing the pixel-wise comparison of patient images against the NormDB. The obtained z-maps were subsequently transformed back into patient space where they were evaluated side-by-side with SUV images (40-60min p.i) by an experienced nuclear medicine physician. **Results:** Patient-specific z-maps provided important imaging clues with respect to both hypo- and hypermetabolic areas in the corresponding SUV images, significantly adding to the visual evaluation of image asymmetries. In particular, the identification of hypermetabolic areas in epilepsy patients, only poorly appreciated in the past, might offer important mechanistic clues about the origin and spread of the seizure discharge, likely to provide added clinical value in challenging cases of

extratemporal lobe epilepsy. Moreover, z-maps also provided additional clues about white matter abnormalities that might be related to low-level inflammation. **Conclusion:** Our work demonstrates that the developed automatic pipeline allows for a fully-quantitative [18F]FDG-PET/MRI assessment of brain function in a clinical setting which might provide added value in the clinical management of neurology patients.

OP-450

Diagnostic Performance of Regional Cerebral Blood Flow Images Derived from Dynamic PIB Scans in Alzheimer's Disease

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Introduction: Several tools have been created to support clinician's diagnosis decision for Alzheimer's disease (AD). These tools make use of the hypometabolism pattern as seen in 2-[¹⁸F]-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) scans. Studies have shown, however, that regional cerebral blood flow (rCBF) images derived from ¹¹C-labelled Pittsburgh Compound B (PIB) PET scans may be good surrogates for FDG scans. The aim of this study was to explore whether rCBF images, derived from dynamic PIB scans, could be used for diagnosis of AD using the PALZ tool from PMOD. **Subjects and Methods:** Nine patients diagnosed with AD, ten with mild cognitive impairment, and eleven healthy controls underwent static FDG and dynamic PIB PET scans. Three sets of images were generated, all normalized to cerebellar grey matter values: from the FDG images, (1) standardized uptake value ratios (SUVR); and from the dynamic PIB images, (2) the ratio of tracer influx relative to reference region (R_1) (through the simplified reference tissue model 2), and the time-weighted average of initial frames (ePIB; with time interval of (3) 20-130s, and (4) 1-8min). The images were analysed with the PALZ tool from PMOD (v3.9, PMOD Technologies LLC), providing an AD score. SUVR scores were used as a reference to compare with rCBF scores. Correlations of the methods were drawn, and receiver operating curves (ROC) were made to explore sensitivity and specificity outcomes. **Results:** Both R_1 and ePIB(20-130s) presented a good correlation when compared to SUVR ($R^2=0.78$ and 0.75 , respectively), with linear regression slopes of 0.74 and 0.71 , while ePIB(1-8min) showed a worse correlation ($R^2=0.46$), and a slope of 0.44 . All ROC curves exhibited a similar shape, with an area under the curve (AUC) of 0.95 for ePIB(20-130s), 0.94 for R_1 , 0.93 for SUVR, and 0.87 for ePIB(1-8min), and no statistically significant differences were found between curves. However, R_1 and ePIB(1-8min) showed to have the highest sensitivity, of 100% , while SUVR and ePIB(20-130s) presented 89% . Meanwhile, SUVR had the highest specificity, of 76% , while R_1 had a specificity of 67% , and both ePIB, 57% . **Conclusion:** Due to its high sensitivity and the fact that its ROC curve was not statistically significantly different from those seen with FDG SUVR, rCBF images suggested to be a good surrogate for FDG scans for diagnostic purposes. Therefore, rCBF (using R_1) seems to be a valid method for the diagnosis of AD patients.

OP-451**FDG PET/MR brain imaging: Impact of different MR attenuation correction methods on the image-derived input function**

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Aim: To evaluate the impact of different MR attenuation correction (AC) methods on the accuracy of an image-derived input function (IDIF) obtained from [18F] FDG PET/MR imaging of the human brain. **Material and Methods:** Ten healthy volunteers (PROVIDE AGE) underwent test-retest [18F]FDG PET/MRI examinations in a fully-integrated PET/MRI scanner (Siemens, Biograph mMR). The imaging protocol consisted of a 60 min list-mode PET acquisition simultaneously acquired with the following MR sequences: Dixon and UTE acquisitions for AC, 3D time-of-flight MR angiography (TOF-MRA) for segmentation of the internal carotid arteries (ICAs) and sparsely sampled MR navigators for motion correction. Apart from the vendor-provided AC maps, RESOLUTE based AC maps were calculated. A low-dose brain CT was also acquired as the AC reference standard. The PET data was reconstructed based on four different AC maps using the OSEM algorithm (PET-DIXON, PET-UTE, PET-RESOLUTE and PET-CT). The arterial input function (AIF) was collected as a reference standard for comparison with the generated IDIFs. The IDIF generation pipeline included the following tasks: (1) automatic segmentation of the petrous segment of the ICAs from TOF-MRA images, (2) MR-navigator based motion compensation and (3) MR based partial volume correction. IDIFs (IDIF-Dixon, IDIF-UTE, IDIF-RESOLUTE and IDIF-CT) were obtained from the corresponding images. The ratio of the area-under-the-curve (R-AUC) between each calculated IDIF and the AIF was used as a similarity measure between the input functions. **Results:** The R-AUC for IDIF-Dixon, IDIF-UTE, IDIF-RESOLUTE and IDIF-CT was found to be 0.71 ± 0.14 , 1.09 ± 0.14 , 0.97 ± 0.07 and 1.00 ± 0.04 respectively. As expected, the IDIF-CT was in excellent agreement with the AIF. The IDIF-DIXON severely underestimated the AIF due to suboptimal correction for bone attenuation, whereas the IDIF-UTE overestimated the AIF due to moderate overcorrection for bone. In addition, both these methods displayed a large variability of +14% (SD). In contrast, the IDIF-RESOLUTE showed good agreement with the AIF, with a slight average underestimation of 3% and a moderate variability of +7% (SD). **Conclusion:** Our work demonstrates that the RESOLUTE MR-AC can be considered as a reasonable alternative to CT-AC with respect to an accurate determination of an IDIF. The RESOLUTE MR-AC obviates the need for an additional CT-AC scan, thus allowing the non-invasive determination of cerebral metabolic rate of glucose solely using a fully-integrated PET/MRI scanner. **Acknowledgement.** This study was supported by the Austrian Science Foundation KL482-B31. **Keywords.** Image-derived Input Function, PET/MRI, Attenuation correction, Neuroimaging

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Tuesday, October 16, 2018, 08:00 - 09:30, Hall 1

Pitfalls & Artefacts 5 - Interactive Clinical Cases: Thyroid: Pitfalls in Parathyroid Detection with Nuclear Medicine Imaging**OP-452****Dual-Phase, Subtraction and SPECT/CT with MIBI**

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OP-453**PET/CT with 11C-Methionine**

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OP-454**PET/CT with 18F-Fluorocholine in Primary Hyperparathyroidism**

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OP-455**PET/CT with 18F-Fluorocholine in Secondary Hyperparathyroidism**

J.-N. Talbot; Hôpital Tenon, Nuclear Medicine, Paris, FRANCE.

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Tuesday, October 16, 2018, 08:00 - 09:00, Hall 4

Clinical Oncology - Rapid Fire Session: Prostate - Not Just 68Ga-PSMA**OP-456****Detection efficacy of [¹⁸F]PSMA-1007 PET/CT in 251 Patients with biochemical recurrence after radical prostatectomy**

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Introduction: Recently, prostate-specific membrane antigen (PSMA) targeted PET-imaging has gained significant interest for staging and restaging of prostate cancer. Most published studies have investigated the diagnostic potential of ⁶⁸Ga-labeled PSMA-agents. [¹⁸F]PSMA-1007 is a novel PSMA-ligand with excellent preclinical characteristics which is not excreted by the urinary tract, a potential advantage for pelvic imaging. The aim of this study was to investigate the diagnostic efficacy of [¹⁸F]PSMA-1007 in biochemical recurrence (BCR) after radical prostatectomy (RP). **Methods:** 251 patients from three academic centers with BCR after radical prostatectomy were evaluated in a retrospective analysis. Patients who had received second line androgen deprivation therapy and/or chemotherapy were

excluded, however prior first line ADT exposure was allowed. The median PSA-level was 1.2 ng/ml (range: 0.2–228 ng/mL). All patients underwent a PSMA-PET/CT after injection of 301 ± 46 MBq [^{18}F]PSMA-1007 at 92 ± 26 min post injection. The detection rate of presumed recurrence sites was correlated with PSA-level and original primary Gleason score. A comparison to a subset of patients treated previously with androgen deprivation therapy (ADT) was undertaken. **Results:** 204 of 251 patients (81.3%) patients had evidence of recurrence on [^{18}F]PSMA-1007 PET/CT. The detection rates were 94.1% (79/84), 90.1% (50/55), 74.5% (35/47) and 61.5% (40/65) for PSA-levels of ≥ 2 , $1 < 2$, $0.5 < 1$ and $0.2 < 0.5$ ng/mL, respectively. [^{18}F]PSMA-1007 PET/CT revealed local recurrence in 43.7% (62) of patients. Lymph node metastases were present in the pelvis in 40.6% (102), in the retroperitoneum in 19.5% (49) and in supradiaphragmatic locations in 12.0% (30) of patients. Bone and visceral metastases were detected in 40.2% (101) and 3.6% (9) patients. In higher Gleason score tumors (≤ 7 vs. ≥ 8) detection efficacy trended higher (76.3% vs. 86.7%) but was not statistically significant ($p=0.32$). However, detection efficacy was higher in patients who had previously been on ADT (91.7% vs. 78.0%) within 6 months prior to imaging ($p=0.0179$). **Conclusion:** [^{18}F]PSMA-1007 PET/CT offers high detection rates in BCR after radical prostatectomy which is comparable or higher than results data published for ^{68}Ga -labelled PSMA-ligands.

OP-457

Evaluation And Preliminary Radiation Dosimetry Of [^{18}F]PSMA-11 For PET Imaging Of Prostate Cancer

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Introduction: Prostate specific membrane antigen (PSMA) is highly overexpressed in prostate cancer (PCa). Many PSMA radiotracers for PET/CT imaging of secondary PCa staging have been developed but encounter difficulties in achieving high radiochemical yields or precursor availability. [^{18}F]PSMA-11 has been successfully radiosynthesized by Kersemans *et al.*¹, but no first-in-human results are available yet. The aim of this study is to evaluate the safety of administration and the radiation dosimetry of [^{18}F]PSMA-11. Here we present the preliminary results of a phase-1, open label study in prostate cancer patients. **Subjects and methods:** [^{18}F]PSMA-11 was synthesized as described by Kersemans *et al.*¹ Six patients (median 66.5y, range 62–68y) with suspected PCa recurrence after previous treatment were injected with 2 MBq/kg [^{18}F]PSMA-11 followed by PET/CT_{low-dose} imaging at 0, 20, 50, 90 and 300 min post injection (p.i.). To evaluate the safety of administration, vital parameters (body temperature, blood pressure and heart rate) were monitored. To assess toxicity, blood count and biochemical parameters such as sodium, creatinine, ALT/AST and alkaline phosphatase were determined. Radiation dosimetry analysis was performed using the

RADAR method as implemented in the OLINDA/EXM software. For blood activity measurement, small samples of venous blood were collected at 5, 10, 20, 30, 50, 70, 90 and 300 min p.i. The free ^{18}F fraction was determined in plasma 20, 50 and 90 min after administration to evaluate the metabolism of [^{18}F]PSMA-11. **Results:** No study drug related adverse events were observed. After injection, [^{18}F]PSMA-11 is rapidly cleared from the blood with 29.0 ± 5.9 % of the activity excreted in urine 5h p.i. The free ^{18}F fraction increased from 9.7 ± 1.0 % 20 min p.i. to 22.2 ± 1.5 % 90 min p.i. Dosimetry is reported for 2 patients. The calculated mean effective dose of 0.012 ± 0.001 mSv/MBq makes the total radiation exposure of [^{18}F]PSMA-11 lower compared to other ^{18}F -labeled PSMA PET agents and similar to ^{68}Ga -PSMA-11. The highest tracer uptake was observed in kidneys, lacrimal and salivary glands, spleen and liver. **Conclusion:** [^{18}F]PSMA-11 can be safely administered and results in a mean effective dose of 0.012 ± 0.001 mSv/MBq. Therefore, the total radiation dose is lower compared to other ^{18}F -PET agents and in the same range of [^{68}Ga]PSMA-11. 1. Kersemans, K. *et al.* Automated radiosynthesis of Al[^{18}F]PSMA-11 for large scale routine use. *Appl. Radiat. Isot.* 135, 19–27 (2018).

OP-458

Biodistribution and radiation dosimetry of the novel ^{18}F -labeled prostate-specific membrane antigen-ligand PSMA-7 for PET/CT in prostate cancer patients

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Objectives: We investigated the whole-body distribution and the radiation dosimetry of ^{18}F -PSMA-7, a novel ^{18}F -labeled PSMA-ligand for the PET/CT imaging of prostate cancer. **Methods:** Ten patients with prostate cancer and biochemical recurrence were examined with 329 – 384 MBq (mean 359 ± 17 MBq) ^{18}F -PSMA-7. Eight sequential positron emission tomography scans were acquired from 30 minutes to 3 hours after injection with IRB approval. Kidneys, liver, spleen and salivary glands were segmented into volumes of interest using the QDOSE dosimetry software suite (ABX-CRO, Germany). Absorbed and effective dose were calculated using the ICRP endorsed IDAC 1.0 package. PSMA-positive lesions were evaluated separately by analysis of maximum (max) and peak SUV values. The gluteus maximus muscle served as a reference region for the calculation of the tumor-to-background ratios (TBR's). **Results:** Physiologic radiotracer accumulation was observed in the salivary and lacrimal glands, liver, spleen and intestines, in a pattern resembling the distribution known from other PSMA-tracers with excretion via biliary and urinary pathways. The effective dose from ^{18}F -PSMA-7 for the whole body was calculated with 9.75×10^{-3} mGy/MBq. The highest radiation dose was observed in the kidneys (1.74×10^{-1} mGy/MBq), followed by the liver (7.11×10^{-2} mGy/MBq),

salivary glands ($4.82\text{E-}02$ mGy/MBq) and spleen ($1.44\text{E-}02$ mGy/MBq). Six out of ten patients were scored as PSMA-positive. A total of nine suspicious lesions were analyzed. The values for the SUV_{max} (mean 7.59 ± 3.92) and SUV_{peak} (mean 3.85 ± 2.35) in the PSMA-positive lesions increased until 60 min p.i. (SUV_{max} 12.81 ± 7.69 , SUV_{peak} 5.75 ± 3.22) and remained at this intensity in the subsequent PET/CT scans. Due to the decreasing activity within the background, the highest TBR's were seen in the latest PET/CT scans (3 h p.i.). Compared to early PET/CT scans TBR's (1 h p.i. mean 10.32 ± 6.86 , 3 h p.i. mean 33.63 ± 15.81) were increased in mean by a factor of 3. **Conclusion:** Data from this initial study demonstrated that PET imaging with ^{18}F -PSMA-7 is safe and feasible in the clinical setting. Physiologic accumulation of the radiotracer corresponded to the known distribution of the PSMA-expressing organs. The radiation dose from ^{18}F -PSMA-7 was similar to that from other ^{18}F -labeled PSMA-ligands. The highest TBR was found three hours after injection. The high uptake in suspicious lesions in terms of absolute SUV_{max} and relative TBR values indicates potentially high sensitivity of the tracer for detection of prostate cancer manifestations.

OP-459

Comparison of 68Ga-PSMA-11 PET/CT and 18F-Fluciclovine PET/CT in recurrent Prostate Cancer.

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Aim: To compare the diagnostic performance of 68Ga-PSMA-11 PET/CT and 18F-Fluciclovine PET/CT in prostate cancer (PCa) patients with biochemical recurrence (BCR) after definitive therapy. **Methods:** An ongoing 68Ga-PSMA-11 PET/CT imaging phase-II trial in PCa patients with BCR (UCLA-IRB#16-001095; NCT02940262) was used to identify patients who also underwent 18F-Fluciclovine scans. The records of 435 patients enrolled from October 2016 to March 2018 have been analyzed. Inclusion criteria for this retrospective analysis were: no changes in therapy management and no more than 4 months between the two scans. 26 patients met the inclusion criteria and were analyzed. 13/26 (50%) patients underwent PET/CT for localization of recurrence after definitive therapy (9 after definitive prostatectomy and 4 after definitive RT), 9/26 (35%) for localization of recurrence after post-prostatectomy salvage RT and 4/26 (15%) for re-staging before systemic therapy. 5/26 (19.2%) were under ADT at the time of the scans. 46.1% (12/26) had a Gleason Score >7. Detection rates (DR) were determined per patient and per region (local: prostate bed + pelvic lymph nodes; distant: extra-pelvic lymph nodes + other soft-tissues + bone). **Results:** The median interval between 68Ga-PSMA-11 PET/CT and 18F-Fluciclovine PET/CT was 1.2 months (range 0.2 - 4.1 months). Mean/median PSA levels were 5.2/3.1 ng/mL (range 0.17-25.1; SD±6.1) at the time of 18F-Fluciclovine PET/CT and

6.5/3.5 ng/mL (range 0.21-34.6; SD±8.8) at the time of 68Ga-PSMA-11 PET/CT. The mean/median PSA difference between the 2 scans was 1.33/0.13 ng/mL (range 0.0-16.3). The detection rate of 18F-Fluciclovine PET/CT was 30.7% (8/26). Local recurrence was identified in 11.5% (3/26), while distant disease was observed in the 19.2% (5/26) of patients. 68Ga-PSMA-11 detected sites of recurrence in 84.6% (22/26) of patients. Local recurrence was identified in 23.1% (6/26), while distant disease was observed in the 61.5% (16/26) of patients. Concordantly negative scans occurred in 15.6% (4/26) of patients while concordantly positive scans were seen in 30.7% (8/26). In 7 of these 8 patients, 68Ga-PSMA-11 PET/CT detected additional lesions not observed on 18F-Fluciclovine scans. No case of positive 18F-Fluciclovine and negative 68Ga-PSMA-11 scans was identified. **Conclusion:** This retrospective analysis suggests that 68Ga-PSMA PET/CT detects recurrence sites with a higher sensitivity than 18F-fluciclovine PET/CT. While far from definitive evidence of superiority, these unexpected findings encouraged us to initiate a prospective single-center, phase-II trial to compare the diagnostic performance of 68Ga-PSMA-11 with that of 18F-Fluciclovine PET/CT in patients with BCR and low serum PSA levels after radical prostatectomy (UCLA-IRB#17-001885; NCI-2018-00546).

OP-460

Evaluation Of High-risk Prostate Cancer Patients At Initial Staging With Al¹⁸F-PSMA-HBED-CC: Intraindividual Comparison With ⁶⁸Ga-PSMA-HBED-CC

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In the setting of primary disease, ^{68}Ga -PSMA appears to preferentially identify treatment-relevant intermediate and high-risk prostate cancer (PC). Besides, ^{68}Ga -labeled compounds are produced with generators providing limited activity per synthesis whereas ^{18}F -labelled tracers, like Al ^{18}F -PSMA-HBED-CC, can be produced in large scales with a lower positron energy that potentially offers higher image quality. Thus, we compared on a head-to-head basis the image quality and detection performance of both radiopharmaceuticals in a sample of high-risk PC patients at initial staging. We enrolled 28 patients (median age: 63, range: 51-78 years) who underwent both ^{68}Ga -PSMA and Al ^{18}F -PSMA PET/CT scanning within a time window of 1-2 weeks, 60 minutes after the i.v. administration of 2.0 and 4.0 MBq/kg, respectively. Studies were performed with a 64-slice PET/CT scan with TOF correction. All patients had high-risk biopsy proven PC prior therapy (Gleason > 7) with a median PSA level of 20.7 ng/mL (range: 1.7-137.0 ng/mL). The study was approved by the institutional Ethics Committee. We measured the SUV_{max} in all abnormal foci as well as the SUV_{max} ratio (SR) in all coincident lesions, defined as SUV_{max} lesion/ SUV_{max} background. Gluteal musculature was selected as background. Al ^{18}F -PSMA and ^{68}Ga -PSMA PET/CT demonstrated abnormal findings in 26 and 25 patients (93% and 89%), respectively. Images of Al ^{18}F -PSMA were of high visual quality. Moreover, 11/28 patients (39%) submitted for initial staging had evidence of metastatic disease. Abnormal foci (n=106) were seen in the fol-

lowing sites: prostate gland (n=31), lymph nodes (n=23), bone (n=50) and lung (n=2). At the prostate gland 31 abnormal foci were observed with ^{18}F -PSMA and 29 with ^{68}Ga -PSMA (94%). Seventeen bone lesions were positive only with ^{18}F -PSMA (34%) whereas 3 bone lesions were positive only with ^{68}Ga -PSMA (6%). Five abnormal lymph nodes (22%) were identified only with ^{68}Ga -PSMA PET/CT, while the remaining 18 were also abnormal for ^{18}F -PSMA. For concordant lesions (n=79), we did not find a significantly different SR for both tracers: 7.5 (2.4–23.4) and 7.2 (2.5–33.6), median (range), for ^{68}Ga -PSMA and ^{18}F -PSMA, respectively. ^{18}F -PSMA PET/CT is a promising imaging technique for the evaluation of PC patients at initial staging with the potential to detect patients with metastatic disease that contraindicates surgery. Further studies are needed to confirm these preliminary results.

OP-461

Imaging of Metastatic Castration-Resistant Prostate Cancer - Comparison of ^{68}Ga -RM2 and ^{68}Ga -PSMA PET/CT

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Introduction: In recent years ^{68}Ga -PSMA-PET/CT has become the standard procedure for imaging prostate cancer (PCa). Additionally, PSMA can serve as target for radionuclide therapy using ^{177}Lu -PSMA. Besides PSMA, the use of new PET radiopharmaceuticals addressing other targets such as the GRPr, e.g. RM2, are promising for restaging of prostate cancer. RM2 has shown a high detection rate in early recurrent PCa and high overlap with PSMA in this population (Minamimoto et al. JNM 2016). It can equally be labeled with ^{68}Ga for PET/CT imaging as well as ^{177}Lu for therapy in the sense of a theranostic approach. Aim of our retrospective study was an intra-individual comparison of lesion detection as well as uptake of ^{68}Ga -RM2 and ^{68}Ga -PSMA in patients with metastatic castration-resistant prostate cancer (mCRPC). **Subjects and Methods:** In total 20 mCRPC patients referred for radionuclide treatment were scanned with ^{68}Ga -PSMA as well as ^{68}Ga -RM2 in order to identify PSMA and/or RM2 positivity - as prerequisite for ^{177}Lu -PSMA or ^{177}Lu -RM2 therapy, respectively. We visually and semiquantitatively (SUVmax and SUVpeak) compared uptake in 116 metastatic reference lesions (4 local, 35 lymph nodes, 63 bone, 13 liver, 1 lung). **Results:** In the visual assessment 1/20 patient showed higher RM2 uptake compared to PSMA in all lesions. 1/20 patient showed mixed RM2-positive / PSMA-negative and RM2-negative / PSMA-positive lesions. 8 patients showed a much higher PSMA than RM2 uptake, 8 patients showed a high PSMA uptake but no RM2 uptake. 2 patients showed neither RM2 nor PSMA positive lesions. In the semiquantitative assessment SUVmax and SUVpeak were significantly higher for PSMA than for RM2 subsuming all reference lesions ($p < 0.001$) as well as in separate analysis of lymph node ($p = 0.001$), osseous ($p < 0.001$) and liver metastases ($p = 0.039$). **Conclusion:** In the majority of included advanced mCRPC patients ^{68}Ga -PSMA showed a much higher uptake compared to ^{68}Ga -RM2 in visual and semiquantitative assessment. Nevertheless, a small number of patients showed no or only faint PSMA uptake but high RM2 uptake in metastatic le-

sions. Therefore, ^{68}Ga -RM2-PET/CT could be helpful in restaging ^{68}Ga -PSMA-negative prostate cancer patients and identifying those patients who would benefit from a ^{177}Lu -RM2-therapy.

OP-462

^{68}Ga -RM2 PET vs. ^{68}Ga -PSMA-11 PET: Prospective Comparison in Patients with Biochemical Recurrence of Prostate Cancer

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Purpose: Detection of prostate cancer (PC) after biochemical recurrence (BCR) remains a great challenge. RM2 is a synthetic bombesin receptor antagonist, which targets gastrin-releasing peptide receptors (GRPr). PSMA is a well-established membrane antigen expressed on prostate cancer cells. Here we present comparative data from two novel PET compounds, ^{68}Ga -RM2 and ^{68}Ga -PSMA, in patients with BCR with prior equivocal or non-contributory conventional imaging. **Methods:** Twenty-nine men (range: 60–83 year-old; mean $\pm$ SD: 71.3 $\pm$ 5.7) with BCR PC were imaged with ^{68}Ga -RM2 and ^{68}Ga -PSMA-11 PET. Areas of abnormal uptake were recorded for each scan by two experienced PET readers. **Results:** All patients had rising PSA (range: 0.2–36.4 ng/mL; mean $\pm$ SD: 6.9 $\pm$ 8.2) and non-contributory conventional imaging (CT; MRI; ^{18}F NaF PET/CT or $^{99\text{m}}\text{Tc}$ MDP bone scan). ^{68}Ga -PSMA found sites of disease in 22/29 patients and ^{68}Ga -RM2 identified recurrent prostate cancer in 20/29 patients. ^{68}Ga -PSMA-11 was positive and ^{68}Ga -RM2 was negative in 3 patients; ^{68}Ga -PSMA-11 was negative and ^{68}Ga -RM2 was positive in 2 patients. More lesions were seen on ^{68}Ga -PSMA-11 than on ^{68}Ga -RM2 in 4 patients, while ^{68}Ga -RM2 identified more lesions than ^{68}Ga -PSMA-11 in 3 patients. PSA was 0.4–36.4 ng/mL; mean $\pm$ SD: 8.3 $\pm$ 8.8) in patients with positive ^{68}Ga -PSMA-11 and 0.3–36.4 ng/mL; mean $\pm$ SD: 8.8 $\pm$ 9.1) in patients with positive ^{68}Ga -RM2 (P : 0.86). PSA was 0.2–8.2 ng/mL; mean $\pm$ SD: 2.5 $\pm$ 3.2) in patients with negative ^{68}Ga -PSMA-11 and 0.2–8.2 ng/mL; mean $\pm$ SD: 2.7 $\pm$ 2.9) in patients with negative ^{68}Ga -RM2 (P : 0.90). **Conclusions:** ^{68}Ga -PSMA-11 and ^{68}Ga -RM2 are promising PET radiopharmaceuticals for localization of disease in patients with BCR PC and non-contributory conventional imaging. The differences in target density, biodistribution and clearance pathways may result in the superiority of one of the two tracers in different patients. ^{68}Ga -RM2 shows similar sensitivity to ^{68}Ga -PSMA-11 (69% vs. 76%) but without 100% overlap of positive cases, therefore suggesting that larger studies are needed.

OP-463

^{68}Ga -RM2 PET/MRI Detection of Recurrent Prostate Cancer in Patients with Negative Conventional Imaging

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Purpose: ^{68}Ga -RM2 is a synthetic bombesin receptor antagonist that targets gastrin-releasing peptide receptors (GRPr). GRPr are highly overexpressed in several human tumors, including pros-

tate cancer (PCa). We present data from the use of ^{68}Ga -RM2 in patients with biochemical recurrence (BCR) of PCa and negative conventional imaging (CI). **Methods:** We enrolled 67 men with BCR PCa, 59–83 year-old (mean $\pm$ standard deviation (SD): 69.3 $\pm$ 5.7). Imaging started at 40–89 minutes (mean $\pm$ SD: 52.1 $\pm$ 9.5 after injection of 127.5–152.6 MBq (mean $\pm$ SD: 141.5 $\pm$ 5.3) of ^{68}Ga -RM2 using a time-of-flight (TOF)-enabled simultaneous positron emission tomography (PET) / magnetic resonance imaging (MRI) scanner. T1-weighted (T1w), T2-weighted (T2w) and diffusion-weighted images (DWI) were acquired. **Results:** All patients had rising prostate specific antigen (PSA) (range: 0.2–124 ng/mL; mean $\pm$ SD: 8.7 $\pm$ 21) and negative CI (CT or MRI, and $^{99\text{m}}\text{Tc}$ MDP bone scan) prior to enrollment. The observed ^{68}Ga -RM2 PET detection rate was 77.1% (42.1% for PSA < 1 ng/mL, 50% for PSA 1–2 ng/mL, 73.3% for PSA 2–5 ng/mL and 92.3% for PSA > 5 ng/mL). ^{68}Ga -RM2 PET identified recurrent PCa in 47 of the 67 participants, while the simultaneous MRI scan identified findings compatible with recurrent PCa in 21 of the 67 patients. PSA velocity (PSAv) values were 0.32 $\pm$ 0.47 ng/ml/year (range: 0.03–1.9) in patients with negative PET scans and 2.32 $\pm$ 2.04 ng/ml/year (range: 0.13–8.68) in patients with positive PET scans (P : 0.0006). **Conclusions:** ^{68}Ga -RM2 PET identifies GRPr expression in patients with BCR PCa. High uptake in multiple areas compatible with cancer lesions suggests that ^{68}Ga -RM2 is a promising PET radiopharmaceutical for localization of disease in participants with BCR PCa and negative CI. ^{68}Ga -RM2 may identify higher risk patients given the highly statistically significant difference PSA velocity values between patients with negative and positive scans.

OP-464

^{18}F -FDHT PET/CT as a predictor of treatment response in mCRPC treated with enzalutamide

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Introduction: Metastasized prostate cancer has only palliative treatment options of which androgen deprivation is the mainstay of treatment. However, the majority of patients will develop progressive disease despite castrate levels of testosterone; castration-resistant prostate cancer (CRPC). In vivo determination of androgen receptor status by $^{16}\beta$ -[^{18}F]-fluoro-5 α -dihydrotestosterone (^{18}F -FDHT) PET/CT could be of use to predict treatment response timely and objectively. The objective of this study is to predict treatment response of enzalutamide (semi) quantitatively by early ^{18}F -FDHT PET/CT. **Subject and Methods:** This pilot study was performed in 18 chemotherapy naïve men ($\geq$ 50 years) with mCRPC. ^{18}F -FDHT PET/CT was performed at baseline and after 4 weeks of treatment. Standard Uptake Value (SUV)_{max} and SUV_{peak} of the 5 most intense and/or all bone, pleura and lymph node metastases were determined per patient. Response was determined at 12 weeks of treatment according to Prostate Cancer Clinical Trials Working Group. Area under the curve (AUC), sensitivity (Se), specificity (Sp), true positive rate and false positive rate of different characteristics of ^{18}F -FDHT PET/CT were performed by ROC analysis. An AUC of 1

represents a perfect test and an AUC of 0.5 represents same as guessing at random. **Results:** A total of 477 lesions (411 bone, 3 pleura and 63 lymph node) were found. At 12 weeks, response was seen in 16 patients, whereas 2 patients showed no response. Characteristics of potential ^{18}F -FDHT PET/CT predictors of treatment response are shown in table 1. Optimal accuracy was obtained using median SUV_{peak} at baseline of all metastatic lesions in comparison to the 5 most intense lesions and in comparison to PSA (AUC of 0.79, AUC of 0.65 and AUC of 0.09 respectively). **Conclusions:** ^{18}F -FDHT PET/CT can identify treatment response in mCRPC treated with enzalutamide. Optimal accuracy was obtained using median SUV_{peak} at baseline of all metastatic lesions in comparison to the 5 most intense lesions and in comparison to PSA. Baseline ^{18}F -FDHT PET/CT is accurate for determining treatment response, no additional ^{18}F -FDHT PET/CT is needed.

OP-465

Minimal-invasive robot-assisted resection of $^{99\text{m}}\text{Tc}$ -PSMA I&S positive nodes - radioguidance, a logical next step in the technical evolution of targeted prostate cancer surgery

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Aim: With the rising use of PSMA-targeted molecular imaging approaches as complementary tool to PSA measurements, the desire to explore the use of PSMA as target for interventions has grown. While in general interventional efforts focus on radioisotope therapies, some have already pioneered the use of PSMA tracers for surgical guidance; especially the tracer $^{99\text{m}}\text{Tc}$ -PSMA I&S has proven a valuable tool for salvage lymph node dissections during open surgery. Minimal-invasive robot-assisted laparoscopic surgery has become an established technique for the management of prostate cancer and is increasingly gaining popularity. However, until recently, this technology lacked compatibility with radioguided surgery concepts. To allow for targeted robot-assisted resection of $^{99\text{m}}\text{Tc}$ -PSMA I&S labeled lesions, we used a novel innovative DROP-IN gamma probe that can be maneuvered using standard robotic surgical instruments. **Materials and methods:** Patients with biochemical recurrent prostate cancer and PSMA-PET positive lymph nodes were scheduled for targeted salvage surgery. These patients received an injection of $^{99\text{m}}\text{Tc}$ -PSMA I&S (Scintomics) the day prior to surgery followed by SPECT/CT at the day of surgery. Concurrency between the PET/CT and SPECT/CT findings was established, based on which the surgical targets and their anatomical locations were identified. Surgery was performed using a da Vinci X robot and gamma tracing was realized using a prototype DROP-IN gamma probe (Eurorad). **Ex vivo** a conventional gamma probe for open surgery was used for validation. **Results:**

^{99m}Tc -PSMA I&S SPECT/CT allowed for accurate identification of the tumor-infested lymph nodes initially identified on PET/CT. During surgery, port placement was optimized for use with the DROP-IN probe. After insertion, the DROP-IN could intuitively be handled and positioned to discriminate “hot” nodes from background (e.g. urine in the ureters). The combination of the wristed Prograsp® surgical tool and DROP-IN gamma probe design supported nodal tracing with a superior rotational freedom within the lower pelvis and the iliac region. Despite relatively low signal to background values and confined spaces, the DROP-IN probe could be accurately maneuvered so that ^{99m}Tc -PSMA I&S avid lymph nodes could be accurately identified and dissected.

Conclusion: Here, we describe the successful first in-human application of a DROP-IN gamma probe for minimal-invasive PSMA radioguided surgery. By introducing the DROP-IN gamma probe technology, radioguided resections have translated into the realm of robotic surgery, further expanding the impact of this technology. Robotic targeted salvage surgery procedures might thus cause less morbidity - however, equivalent oncological outcomes have to be demonstrated.

OP-466

The influence of intraprostatic vs. intratumoral tracer deposition in sentinel node procedures in prostate cancer patients; A phase II randomized comparison study

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Introduction: One of the treatment options of intermediate- and high-grade prostate cancer is a robot assisted radical prostatectomy (RARP), supplemented by a sentinel node (SN) biopsy procedure and an extended pelvic lymph node dissection (ePLND). Previous studies indicated that the location and the amount of detected SNs are influenced by the injection technique.¹ To validate this concept, a prospective randomized phase II trial was performed wherein the relation between detection of lymph node (LN) metastases and intratumoral (IT) or intraprostatic (IP) SN tracer deposition was studied. **Methods:** Prostate cancer patients with a >5% risk of lymphatic involvement according to Briganti nomogram and treated with RARP (n=113) were included and randomized between an ultrasound guided transrectal injection of indocyanine green- ^{99m}Tc -nanocolloid in 2 intratumoral depots of 1 mL (n=55, IT-group) or in 4 depots of 0.5 mL in the peripheral zone of the prostate (n=58, IP-group). Preoperative lymphoscintigraphy and SPECT/CT were performed to define the locations of the SNs. SNs were dissected using a combination of radio- and fluorescence-guidance, followed by an ePLND. The number of surgically removed SNs and pathologically proven tumor positive SNs were registered and compared between the two groups. **Results:** Patients in both groups had comparable average tumor characteristics, Briganti score (13.5 (IT) vs. 10.8 (IP), p=0.117), SNs on SPECT/CT (3.0 (IT) vs. 4.0 (IP), p=0.489) and number of removed SNs (3.4 (IT) vs. 4.2 (IP),

p=0.184). Unilateral (12 vs 6, p=0.0001) and bilateral non-visualization (3 vs 1, p=0.032) were significantly more observed in the IT-group. Two patients wherein the intratumoral tracer deposition failed showed false negative results. The number of pathologic node-positive (pN1) patients was significantly higher in the IT-group (23 vs. 14, p=0.045) and significantly more positive lymph nodes were found in the ePLND specimens of the IP-group (10 vs. 36, p=0.010). **Conclusions:** Results from this study indicate that the classification of pN1 prostate cancer patients is improved by intratumoral tracer deposition, when compared to intraprostatic tracer administration. At the same time, intratumoral tracer deposition potentially improves the oncological benefit of the SN procedure by increasing the harvesting accuracy of lymphatic metastases.

1109

Tuesday, October 16, 2018, 08:00 - 09:00, Hall 6

Other Clinical Studies: Non Oncology

OP-467

Prediction of post-operative pulmonary function: Performance of quantitative SPECT/CT and planar Tc^{99m}-MAA scintigraphy and segment counting in 42 lobectomy patients

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Purpose: The aim of this study was to compare the performance of quantitative analysis of SPECT/CT (QLUNG) and planar (PL) Tc^{99m}-MAA perfusion scintigraphy, and segment counting (SC), in predicting post-operative (PO) pulmonary function in patients undergoing lobectomy. **Subjects and methods:** Patients planned for lobectomy were prospectively enrolled from December 2016 to December 2017. Patients who completed pre-operative forced expiratory volume capacity (FEV1), diffusing capacity of the lung for carbon monoxide (DLCO) and Tc^{99m}-MAA perfusion scintigraphy, underwent video-assisted thoracoscopic surgery (VATS) lobectomy, and completed PO-FEV1 and PO-DLCO, were included. The final population consisted of 42 patients (69% male, average age 66±8 years). Predicted post-operative (pPO)-FEV1 and pPO-DLCO were derived from the pre-operative measurements multiplied by the percentage of lung tissue remaining after lobectomy. The percentage was calculated for each patient by three methods: QLUNG, PL and SC. Pearson correlation, paired T-test and Bland-Altman analysis were used to assess the performance of the three methods compared to the true post-operative (tPO) measurements: tPO-FEV1 and tPO-DLCO. **Results:** Nineteen patients had right lobectomy and 23 left lobectomy. The mean and standard deviation of resected lung tissue calculated by PL and QLUNG respectively was 11±5% and 17±6% on the right (p=0.002), and 23±5% and 21±3% on the left (p=0.066). All three methods showed significant correlation (p<0.001) between predicted and true FEV1 and DLCO: QLUNG r=0.729, r=0.599; PL r=0.697, r=0.552; SC r=0.729, r=0.585. There was no significant difference

between the three methods but QLUNG had the highest r values overall. The accuracy for predicting a postoperative FEV1 or DLCO of <40% was identical for all 3 methods - 81%. The deviation of predicted values from the true PO-FEV1 and PO-DLCO was smallest for QLUNG by Bland-Altman analysis, 95% confidence intervals are (-24.4,+22.7) and (-24.4,+24.4) respectively for QLUNG, (-24.9,+25.4) and (-25.6,+28.0) for PL, (-26.5,+21.2) and (-26.4,+23.3) for SC. **Discussion:** In this homogenous population of 42 patients undergoing VATS lobectomy, although there was a significant difference between quantitation by PL and QLUNG in right lobectomy patients, there was no significant difference among the three methods used to predict PO-FEV1 or PO-DLCO. QLUNG presented the best correlation to, and smallest deviation from the true values. A larger population is required to establish if there is a significant difference in methods used to predict PO lung function.

OP-468

First-in-man Study in Lung Perfusion Imaging with the New CZT SPECT Camera (VERITON®)

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Introduction: Based upon the breakthrough of cardiac CZT cameras, there is now an interest to apply this same technology to other SPECT imaging targets. Recently, an organ specific CZT-SPECT scanner (VERITON® Spectrum Dynamics, Caesarea, Israel) that utilizes a focused body/organ and contouring detector technology has been introduced, interesting for lung-imaging. In this study, we compare perfusion lung SPECT imaging between a conventional gamma camera and the VERITON® camera. **Subjects and methods:** With the approval of the ethical committee, on patients undergoing the routine clinical procedures as part of their clinically referred care, lung perfusion SPECT imaging have been acquired with a conventional gamma camera and the VERITON® camera, with no additional injection of radiopharmaceutical to patients. The lung perfusion SPECT data was acquired for 10min in body contouring mode using 12 CZT detectors and 240 to 300 projections per detector. The images were reconstructed using OSEM iterative algorithm with resolution recovery, 2.46mm voxel size, 8 iterations, 8 subsets. **Results:** To date, perfusion lung SPECT imaging have been acquired in 6 patients (age 63+/-3) followed for pulmonary embolism and injected with 160 (+/-7.8) MBq of ^{99m}Tc-LYOMAA. Initial experience with the CZT-SPECT system has shown that it is possible to acquire a lung perfusion SPECT image in approximately 10 minutes, same time required by a conventional SPECT system, but with a better resolution. Diagnosis of sequelae of pulmonary embolism was done in all patients in both modalities. **Conclusion:** CZT technology has the potential to provide high resolution SPECT images with potentially lower time acquisition and/or radiation dose to the patient than when using conventional gamma camera technology. Further investigation is necessary to demonstrate the benefits of applying this new CZT-CT64 technology to SPECT lung-nuclear Imaging.

OP-469

Comparison of Galligas and ⁶⁸Ga-EDTA Aerosol Deposition in Respiratory Tract of Smokers and Nonsmokers

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Purpose: This study aims to compare the aerosol deposition in respiratory tract between smokers and non-smokers using both Galligas and ⁶⁸Ga-EDTA ventilation PET/CT. **Methods:** Thirteen volunteers, including 6 smokers (6 men, 0 woman; aged 35±8 years) and 7 non-smokers (4 men, 3 women; 38±7 years) with normal lung function tests (forced expiratory volume in 1 sec, forced vital capacity, flow volume curves, carbon monoxide transfer factor, bronchial provocation test and bronchial dilation test) were enrolled with Institute Review Board approval and written informed consent. Each volunteer underwent both galligas (particle size 30-60 nm) and ⁶⁸Ga-EDTA (particle size 0.5-2 μm) PET/CT scans within 1 week. After inhalation, the volunteers underwent 5 consecutive 3-minute 2-bed emission acquisitions within half hour. Volume of interests (VOIs) were drawn over the hilar bronchi and peripheral lungs and the mean bronchus-to-lung ratios (R) were calculated for comparison. **Results:** The aerosol deposition at hilar bronchi was significantly higher in smokers than in non-smokers for ⁶⁸Ga-EDTA (7.67±5.41 vs 2.65±1.63, P=0.038) but significantly lower for galligas (0.53±0.08 vs 0.66±0.06, P=0.008). In the same patients, deposition of ⁶⁸Ga-EDTA at hilar bronchi, as compared with peripheral lungs in each patient, was significantly higher than that of galligas in both smokers (d=7.14±5.38 P=0.023) and non-smokers (d=1.99±1.64, P=0.018). Within 30 minutes after inhalation, the change of ⁶⁸Ga-EDTA deposition at hilar bronchi over time, as compared with peripheral lungs in each patient, was significantly different between the smokers and non-smokers (P=0.02). The R value seemed increasing in smokers while relatively stable in non-smokers. **Conclusion:** Aerosol ⁶⁸Ga-EDTA, but not galligas, are more likely to deposit at hilar bronchi in smokers than non-smokers though both groups have normal lung function. The clearance of ⁶⁸Ga-EDTA from hilar bronchi also seems to be different between smokers and non-smokers. ⁶⁸Ga-EDTA PET/CT may be a valuable method to reflect the function of tracheo-bronchial cilia.

OP-470

Assessment of liver fibrosis with quantitative analysis of ^{99m}Tc-GSA SPECT/CT

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Purpose: Assessment of liver fibrosis is essential to manage treatment and to determine prognosis in patients with chronic liver disease. ^{99m}Tc-diethylenetriamine-pentaacetic acid-galactosyl human serum albumin (GSA) scintigraphy has been used to investigate liver functional reserve. Planar dynamic scintigraphy is commonly used for ^{99m}Tc-GSA imaging. However, absolute quantification of radioactivity in the liver cannot be achieved from planar scintigraphy. Recent works reported that absolute radioactivity in tissue can be quantified with SPECT/CT. The

aim of this study was to evaluate the usefulness of quantitative assessment of ^{99m}Tc -GSA SPECT/CT to estimate liver fibrosis, compared with conventional assessment of planar scintigraphy.

Subjects & methods: Forty-nine patients (mean age, 64 ± 14 years), who underwent hepatectomy and ^{99m}Tc -GSA imaging for the preoperative workup, were retrospectively studied. Following planar scintigraphy, ^{99m}Tc -GSA SPECT data (60 steps of 6 s/step, 360 degree, 128×128 matrix) was acquired 20 min after the tracer injection (185MBq) on a SPECT/CT scanner (Discovery 670). SPECT images were reconstructed with CT attenuation correction and scatter correction using OSEM (2 iterations; 10 subsets). Liver uptake ratio (LUR) defined as radioactivity in whole liver divided by injected radioactivity was measured with a dedicated software. LHL15 which is a conventional index on ^{99m}Tc -GSA planar scintigram was also measured. The LUR and LHL15 measurements were compared with the histopathological results of liver fibrosis staging (F0-F4: F0, absence of fibrosis; F4, severe fibrosis). **Results:** There was a significant correlation between liver fibrosis stage and the LUR ($p < 0.0001$, $r = 0.61$). The LUR measurements in F4 liver ($30.7 \pm 12.8\%$) were significantly lower than those in both F0-1 ($49.6 \pm 7.0\%$, $p < 0.0001$) and F2-3 ($46.0 \pm 9.6\%$, $p = 0.0004$), while no significant difference in LUR between F0-1 and F2-3 ($p = 0.48$) was observed. The areas under the ROC curve of LUR and LHL15 for differentiating F0-3 vs. F4 was 0.89 and 0.84, respectively. With an LUR threshold of 40.4%, the sensitivity and specificity of LUR for differentiating F0-3 vs. F4 was 90.9% and 89.5%, respectively. With an LHL15 threshold of 0.93, the sensitivity and specificity of LHL15 for F0-3 vs. F4 was 72.7% and 79.0%, respectively. **Conclusion:** LUR measured with ^{99m}Tc -GSA SPECT is correlated with the extent of liver fibrosis. Quantitative assessment of ^{99m}Tc -GSA SPECT permits accurate prediction of severe liver fibrosis, with both sensitivity and specificity of approximately 90%, and is superior to conventional measure on planar scintigram.

OP-471

A Method to Calculate MAG3 Renal Curves at Later Times to Compare with Measured Delayed Data Points

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Introduction: If obstruction is observed in a MAG3 renal study, a delayed image may be taken, possibly at 30-40mins after the standard renogram study. However quantitative interpretation of the delayed values is difficult. Our method predicts the kidney counts at any time after the renogram assuming the same physiology applies. This predicted renogram can help identify any renal changes that may have occurred during the delay time.

Method: Rutland-Patlak renal analysis gives the zero-excretion curve (kidney with no excretion). The difference between this curve and the renal curve gives the %excretion at any time, with the value at 20minutes often used [the Renal Output Efficiency (ROE)]. Plotting $\log(1 - \%excretion/100)$ against time gives a straight line fit in the last stage of the renogram. Extrapolated, this line gives the predicted %excretion for later times. Also, the 'blood' curve can be interpolated between the last renogram point and the delayed point. This gives the time-extended zero

excretion curve. From these two curves, the kidney counts at all times up to the delayed time can be calculated, assuming no change in physiology. A comparison can then be made with the measured delay point. **Results:** 98 kidney studies were examined. For those with $ROE < 85\%$ ($n = 48$) the mean (range) of the ROE was 72% (42%-85%) and at the delay time the measured excretion was 89% (60%-97.5%) and the calculated excretion was 93% (66%-100%). So at the delay time there is a significant increase in %excretion values, making this parameter less sensitive to any observed changes. A visual assessment was also made for a significant difference in delayed and calculated points. For these ($N = 18$), the absolute difference in %excretion values was $7.5\% \pm 2.7\%$ (std.dev.). For $N = 13$ studies, visual assessment judged a marginal difference (not considered clinically significant) and the absolute difference in %excretion values was $3.0\% \pm 2.6\%$. For the remainder ($N = 57$) the absolute difference in %excretion values was $1.4\% \pm 2.4\%$. **Conclusion:** Any delayed images obtained after a standard MAG3 study can be difficult to interpret. Our technique calculates the kidney curve up to the delayed time assuming no change in physiology from the standard renogram. This allows a comparison with the measured value for any changes. However the %excretion values continually increase with time, so this parameter becomes less sensitive to differentiate change at longer delay times. Visual assessment is still practical with this technique, but alternative measurement parameters are required, and this is being considered further.

OP-472

Ultrasound and CT angiogram measurement of kidney size do not predict differential renal function in kidney transplant donors, prior transplantation.

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Purpose: The Revised British Transplantation Society (BTS) Guidelines on living donor renal transplantation (3rd/ed.2011) recommend 1) renal ultrasound (US) for initial donor evaluation 2) If US identifies a 2cm size discrepancy radioisotope scan should be performed for assessment of differential renal function and 3) DRF $> 10\%$ may be significant and donation of the kidney contributing lower proportion of total function is appropriate, irrespective of vascular anatomy. Since June 2016 modified BTS ($\geq 1\text{cm}$ size disparity) were introduced locally by the Sussex Kidney Unit, Brighton. The aim of this study was to investigate the importance of performing functional imaging with differential function in all potential live kidney donors irrespective of disparity in kidney size. **Method:** One hundred forty three potential donors reviewed at the Sussex Kidney Unit (07/2009-05/2016) underwent renal US and MAG-3 scintigraphy regardless of disparity in size. Kidney size and DRF were compared. GFR Cr51-EDTA was performed in all patients and 116/143 (81%) had CT angiogram. **Results:** Size: One hundred ten/143 (77%) patients had $< 1\text{cm}$ difference in size between their kidneys. Twenty eight/143 (20%) had a difference between 1-2 cm and 4/143 (3%) had a difference $\geq 2\text{cm}$. DRF: Seventeen/143 (12%) donors had $> 10\%$ difference in DRF. In this group only 1/17 (6%) had

size disparity ≥ 2 cm and 8/17 (47%) had 1–2 cm. All patients with $DRF > 10\%$ had acceptable GFR values by donor age for donation. Sixteen/17 with $DRF > 10\%$ had CT angiogram performed. Only 1/16 showed discrepancy in size of 1–2 cm, which was not shown on US. If revised BTS guidelines were applied (≥ 2 cm disparity in size) we would proceed to nuclear renal functional imaging in only 4/143 (3%) potential donors. This means significant reduction in scans. However, only 1/17 (6%) potential donor would have been identified with more than 10% difference in function. Therefore 16/143 (11%) donors could have had kidney with better function removed. If modified BTS guidelines were applied, only 9/17 (53%) donors would have been identified with $DRF > 10\%$. Therefore 9/143 (6%) could have had kidney with better function removed. **Conclusion:** This study emphasizes the value of DRF in the assessment of potential donors. Size disparity at ultrasound or CT does not accurately predict DRF measured using MAG-3. If BTS guidelines were applied 11% donors would be at risk to donate the kidney with better function. If modified BTS guidelines were applied 6% would be at risk to donate the kidney with better function.

OP-473

Renal output efficiency and normalized residual activity examined by technetium-99m-DTPA renography has by far greater specificity as compared to conventional diagnosis of renal obstructive disease

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Introduction: Diuretic renography is a non-invasive test for the assessment of equivocally obstructed upper urinary tract. Reduced renal function and dilated collecting system can make it difficult to distinguish between obstructed and unobstructed kidney. One of methods proposed for overcoming these problems is calculation of output efficiency (OE) and normalized residual activity (NORA). The use of these parameters has been reported in several studies, mainly using ^{99m}Tc-MAG₃. **Objectives** of this study were: a) to calculate OE and NORA for the ^{99m}Tc DTPA diuretic renogram in normal kidneys and kidneys with suspected urine outflow obstruction b) to validate diagnostic accuracy of the above two parameters against the final diagnosis of obstruction and c) to assess their utility in reducing the number of indeterminate or false positive findings of ^{99m}Tc DTPA diuretic renography. **Subjects and Methods:** 143 patients with suspicion of upper urinary tract obstruction and 48 kidney donors were investigated. Control group consisted of 96 normal kidneys, group A of 73 obstructed kidneys and group B of 80 kidneys with dilated, but unobstructed upper urinary tract. The division into patients' groups was made on the basis of the status of urinary tract at final diagnosis. A 40min acquisition with 240 of 10sec images was applied. Furosemide was administered after 20min (F+20). Post-void image was acquired at 50min. OE was calculated at the end of the furosemide test (OE_{40}) and

NORA on the post-micturition acquisition ($NORA_{PM}$). The comparison was made with the result of conventional interpretation of renogram and against final diagnosis to determine sensitivity/specificity of OE and NORA. **Results:** Both the above parameters had high sensitivity (92% and 97%), specificity (99%) and accuracy (95% and 98%) in differentiating between obstructed and unobstructed kidneys. Our tests correctly reclassified 39 out of 41 indeterminate/false positive renograms. Cut-off values of the best predicting obstruction were 80% and 0.23 for OE_{40} and $NORA_{PM}$ respectively. **Conclusion:** For the ^{99m}Tc-DTPA diuretic renography (F+20, t=40), normal values of OE_{20} are higher than 82%, OE_{40} is higher than 90%, $NORA_{20}$ is less than 0.91 and $NORA_{PM}$ less than 0.12. Obstructed kidneys present with OE_{40} less than 80% and $NORA_{PM}$ higher than 0.22. In comparison to final diagnosis, the above two parameters have high sensitivity and specificity for detecting obstruction. They remarkably reduce the number of indeterminate response to furosemide. Calculation of $NORA_{PM}$ upgrades the information obtained by the OE_{40} and further improves the accuracy of diuretic test.

OP-474

In-vivo determination of renal glucose analogue effects in case of diabetes type 2 with PET/MRI

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Aims: Diabetes type 2 is a widespread, in recent years increasingly occurring metabolic disease, where patients suffer from an insulin resistance leading to an increased blood glucose level. A new generation of anti-diabetic drugs follows the approach to inhibit SGLT2 in the kidneys, a transporter in charge of renal glucose re-absorption. Thus, a reduced glucose re-absorption causes an increased glucose excretion and therefore a decreasing blood glucose level. The aim is to quantify non-invasively the renal effects of diabetes and SGLT2-inhibition, leading to a deeper understanding of the glucose re-absorption process. **Materials and methods:** In 2017, we started a study with 20 male and 20 female diabetes type-2 patients at the Medical University of Vienna. With a combined positron emission and magnetic resonance tomography (PET/MRI), the abdomen of all subjects was scanned twice: immediately before as well as one or two weeks after SGLT2-inhibitor therapy. To study renal glucose effects, for 20 patients (with an equal distribution of male and female subjects) the barely re-absorbed glucose analogue 2-[18F]Fluor-2-deoxy-D-glucose (FDG) is used. The other 20 subjects are investigated with α -methyl-4-deoxy-4-[18F]FDG (Me4), a similar tracer mainly re-absorbed via SGLT2. From the dynamic scans, the tracer concentration curves from the total kidney volume as well as the renal cortex were extracted and analyzed with deconvolution, integral and Patlak analysis. Results were compared between diabetic patients before and after therapy start, as well as to the results of a recently finished similar study with 25 healthy subjects. **Results:** So far, 15 patients who obtained PET/MRI scans with FDG have been evaluated. The preliminary results of the total kidney integral analysis showed that the renal uptake within the first three minutes is higher by 9 % ($p = 0.03$) after SGLT2-inhibitor therapy. The cortical mean transit

time and the Patlak plot slope were lowered by 67 % ($p = 0.04$) and 6 % ($p = 0.02$), respectively, after therapy start. In comparison with healthy subjects, the Patlak plot slope is higher in case of healthy subjects by 15 % ($p < 0.0001$) compared to diabetes patients before therapy start. **Conclusion:** We expect that with these results, so far solely obtained with FDG, the controversially discussed contribution of SGLT2 to the renal processes of FDG and Me4 can be clarified with state-of-the-art in-vivo methods. The results may also help to predict SGLT2-inhibitor therapy response in diabetic patients.

1110 Tuesday, October 16, 2018, 08:00 - 09:00, Hall 28

Cardiovascular: Myocardial Imaging with SPECT and PET

OP-475

Multimodal imaging using FDG PET / MR and adenosine stress NH₃ PET in patients with hypertrophic cardiomyopathy

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Background: In hypertrophic cardiomyopathy (HCM), FDG PET could explain the inflammatory process preceded by myocardial fibrosis, but FDG PET studies about HCM are lacking. We aimed to compare regional inflammation by FDG uptake, fibrosis by LGE MRI and, microvascular dysfunction by adenosine stress NH₃ PET in patients with HCM. **Method:** From Jan 2016 to Apr 2018, 25 patients were included in the retrospective study. FDG and MRI were simultaneously acquired by integrated PET/MR scanner. To the suppression of physiologic myocardial uptake, patients were prepared with a low carbohydrate diet. FDG PET and LGE were analyzed by a 17 - segment (sg) model, and myocardial flow was analyzed by commercial software (4DM) and compared with FDG PET and LGE. **Result:** Four patients were excluded (improper physiologic myocardial suppression ($n=1$) and combined ischemic heart disease ($n=3$)), 21 patients (59 ± 15 y-o, 16 males) were enrolled, finally. All 21 patients showed abnormal FDG uptake (6.8 ± 3.7 sg) and 20 patients showed LGE (5.7 ± 3.1 sg), and mean stress myocardial blood flow was 1.89 ± 0.59 mL/min/g. FDG uptake and LGE were observed in hypertrophic myocardium and in some patients also had in non-hypertrophic myocardium. Hypertrophic myocardium showed decreased stress myocardial flow compared with non-hypertrophic portion. Increased FDG uptake was related with LGE ($\rho=0.805$, $p<0.001$). Of the total 357 sg, 83.8% were matched results (102 sg were both positive and 197 sg were both negative). And increased FDG uptake was related to decreased stress flow ($\rho=-0.512$, $p=0.043$). **Conclusion:** Evaluation of HCM with FDG PET/MR and stress NH₃ PET was useful in evaluating inflammatory changes, fibrosis, and ischemic severity, to explain pathophysiology and to understand disease status. We also newly found that FDG PET has a correlation with LGE and ischemia, which are known as poor prognostic factors.

OP-476

Prognostic significance of combined analysis of myocardial flow reserve and maximal myocardial blood flow using pharmacological stress N13-Ammonia PET in dialysis-dependent end stage renal disease patients

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Purpose: We investigated the prognostic significance of combined analysis of myocardial flow reserve (MFR) and maximal myocardial blood flow (MBF) derived from pharmacological stress N13-ammonia PET myocardial perfusion imaging (MPI) in the dialysis dependent end stage renal disease (dd-ESRD) patients. **Methods:** 438 consecutive dd-ESRD patients (median 68 years), who were performed ammonia PET-MPI for the evaluation of suspected ischemic heart disease, were enrolled in this investigation. Patients were divided into four groups based on the median value of MFR (2.0) and maximal MBF (2.0); low MFR and low maximal MBF (L-L) group: $n=162$, low MFR and high maximal MBF (L-H): $n=57$, high MFR and low maximal MBF (H-L): $n=57$, and high MFR and high maximal MBF (H-H): $n=162$. The incidence of all-cause death and cardiovascular death were compared between each group. **Results:** L-L group had a worst prognosis group among all groups in all-cause death and cardiovascular death. In low CFR group, low maximum MBF group had worse prognosis than high maximum MBF group in all-cause mortality ($p=0.046$) and cardiovascular death ($p=0.045$). However, in high CFR group, there were no significant differences in any prognosis between high and low maximum MBF groups. **Conclusions:** Combination analysis of MFR and maximal MBF predicts poor prognosis in the dd-ESRD patients.

OP-477

Impact of left bundle branch block on myocardial perfusion and metabolism in patients with non-ischemic dilated cardiomyopathy prior to cardiac resynchronization therapy

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Aim: Left bundle branch block (LBBB) induces inhomogeneous activation of the left ventricle resulting in redistribution of regional myocardial work. In general, LBBB is associated with reduced glucose uptake in the septum compared to the lateral wall, however data on myocardial perfusion changes are conflicting. Here we aim to evaluate myocardial perfusion-metabo-

lism patterns using $^{13}\text{N-NH}_3$ and $^{18}\text{F-FDG}$ PET/CT in patients with LBBB and non-ischemic dilated cardiomyopathy (DCM) who are eligible for cardiac resynchronization therapy (CRT). **Materials and methods:** 24 consecutive non-ischemic DCM patients with LBBB underwent resting $^{13}\text{N-NH}_3$ and $^{18}\text{F-FDG}$ PET/CT using a hyperinsulinemic euglycemic clamping method 1 week before CRT implantation. Static PET images were semi-quantitatively analyzed using a 17 segment model (segment 17 (apex) was excluded for further analysis). In each segment $^{13}\text{N-NH}_3$ and $^{18}\text{F-FDG}$ uptake were expressed as percentage of the segment with highest $^{13}\text{N-NH}_3$ activity. Additionally, perfusion and metabolism in the septal and lateral wall were calculated by averaging tracer uptake in the corresponding segments. Segmental “reverse mismatch” and “mismatch” patterns between perfusion and metabolism were defined as $^{13}\text{N-NH}_3$ / $^{18}\text{F-FDG}$ uptake ratio larger than 1.2 and lower than 0.8, respectively. **Results:** Overall, segmental analysis of the perfusion-metabolism relation revealed “mismatch” and “reverse mismatch” patterns in 88 (23%) and 114 (30%) segments, respectively. In all other segments myocardial $^{13}\text{N-NH}_3$ uptake matched $^{18}\text{F-FDG}$ uptake. A perfusion-metabolism “mismatch” pattern was present in the septum and lateral wall in respectively 5 (6%) and 62 (70%) segments while a “reverse mismatch” pattern was present in 64 (56%) and 1 (1%) segments, respectively. This is also reflected in an overall higher $^{13}\text{N-NH}_3$ / $^{18}\text{F-FDG}$ ratio in the septum compared to the lateral wall (1.49 ± 0.54 vs 0.78 ± 0.20 , $p < 0.0001$). “Mismatch” and “reverse mismatch” patterns are explained by a significantly lower $^{18}\text{F-FDG}$ uptake in the septum compared to the lateral wall (mean septal-to-lateral uptake ratio (SLR) 0.55 ± 0.2). In contrast, $^{13}\text{N-NH}_3$ activity was homogeneously distributed between septum and lateral wall (mean SLR 0.99 ± 0.18). In 2 patients, a homogeneous $^{18}\text{F-FDG}$ distribution with higher septal $^{13}\text{N-NH}_3$ uptake was observed. **Conclusion:** Patients with non-ischemic DCM and LBBB prior to CRT implantation demonstrate a lower septal glucose uptake without a reduced $^{13}\text{N-NH}_3$ uptake. Absolute quantification of myocardial perfusion is currently ongoing to evaluate absolute perfusion in relation to late $^{13}\text{N-NH}_3$ uptake. Our study confirms regional differences in metabolism that are most likely associated with differences in myocardial workload. Whether these patterns may predict CRT response needs to be clarified in further studies.

OP-478

Diagnostic impact of blood ketone body level for predicting effect of dietary preparation for myocardial physiological accumulation suppression in FDG-PET/CT

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Objectives: ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) is a useful method for diagnosing cardiac sarcoidosis (CS). However, in cases with obstructive FDG physiological accumulation in the myocardium, cardiac sarcoidosis lesions could be concealed

and misdiagnosed. While several dietary preparations, such as long-term low-carbohydrate diet, to suppress myocardial physiological accumulation have been introduced, reliable indices for predicting the effect of the procedures have not been specified. The purpose of this study was to assess the diagnostic value of blood ketone body level for predicting the effect of long-term low-carbohydrate diet for FDG-PET/CT for patients with cardiac sarcoidosis. **Materials and Methods:** A total of 48 consecutive cardiac sarcoidosis patients (12 men and 36 women, 62 ± 12 y) who underwent FDG-PET/CT using low-carbohydrate diet for over 24 h (glucose intake < 10 g) were included in this study. FDG-PET images were acquired 60 min and 120 min after the administration of FDG 4 MBq/kg. Blood ketone body level was measured simultaneously with the FDG administration. In order to evaluate myocardial physiological accumulation, myocardial uptake was interpreted visually by two nuclear cardiologists and categorized using a 4-point grading system (0, lower than blood pool; 1, similar to blood pool; 2, higher than blood pool and lower than liver; 3, higher than liver). Grade 0 was determined as relevant suppression. For quantitative analyses, regions of interests were drawn on the unaffected left-ventricular myocardium and the left-ventricular cavity in the transaxial FDG-PET images. Myocardium to background ratio (MBR) was then calculated by dividing SUVmax in the myocardium by SUVmax in the left ventricular cavity. Based on the previous report on the physiological myocardial accumulation suppression, MBR less than 0.93 was defined as relevant suppression. **Results:** In all 48 patients, blood ketone body level was 0.55 (0.32–0.86) mmol/l, 21 patients (44%) were categorized as grade 0, and MBR was 1.01 (0.83–1.24). The area under the curve in the ROC analyses for visual analysis and quantitative analysis were 0.77 and 0.78, respectively. Cut-off values for blood ketone body level for relevant myocardial physiological suppression in both analyses were identically 0.60 mmol/l. Under the derived cut-off values, the sensitivity and specificity were 93% and 62% in the visual analysis, and 100% and 58% in the quantitative analysis, respectively. **Conclusion:** Blood ketone body level may have a high diagnostic performance for predicting myocardial physiological accumulation suppression in FDG-PET/CT under long-term low-carbohydrate diet preparation.

OP-479

Prevalence of transthyretin amyloidosis in the elderly and its relationship to heart failure

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Introduction: Cardiac scintigraphy with diphosphonate has emerged recently as a highly sensitive and specific diagnostic tool in the detection of cardiac transthyretin amyloid deposits. Cardiac ATTR amyloidosis has been suggested to be a prevalent cause of heart failure in the elderly, whose real is unknown and probably underdiagnosed. **Purpose:** The aim of our inves-

tigation is to study prevalence of cardiac ATTR amyloidosis and its relationship to heart failure, according to the myocardial diphosphonate uptake grades 2 and 3, and heart failure hospitalizations. **Subjects and methods:** We revised retrospectively 1509 whole body scans with bone agents, that performed in our department between 2010 and 2016 to 1114 patients ≥ 75 years (80.5 ± 4.1 years, 65% males), without previous suspicion of cardiac amyloidosis. Myocardial uptake was graded according to a visual score compared with the adjacent bone uptake intensity, grade 1 less than the bone uptake, grade equal to bone and grade 3 greater than the bone uptake. Scans were interpreted independently by two experienced nuclear cardiologists from two different centers, blinded to patient data and discrepancies were resolved by consensus. Heart failure hospitalizations according to regional administrative databases were investigated and the estimated prevalence for Murcia and the European standard population ≥ 75 years were calculated. **Results:** Thirty-one Of 114 patients (2.78%) showed cardiac uptake: 9 patients grade 2 (0.81%) and 22 patients grade 3 (1.97%). The prevalence of myocardial uptake was 3.88% in males and 0.77% in females in the whole studied population, 11% in patients > 85 years (13.9% in males). Heart failure hospitalizations rates were 14% in patients without uptake and 29% in those with cardiac uptake ($p=0.034$). Myocardial uptake was associated with a higher risk of HF hospitalization (OR 2.60, 95%CI 1.09–5.74, $p=0.022$) after adjusting for age and gender. **Conclusions:** The prevalence of cardiac ATTR amyloidosis is 2.8% in subjects ≥ 75 years, it is more prevalent among males 3.8% and increases with age, reaching 11% in males ≥ 85 years. Myocardial uptake grade 2 and 3 in diphosphonate scintigraphy is associated with a higher risk of heart failure hospitalization. Our results obtained in a large population of elderly subjects suggest that cardiac ATTRwt amyloidosis, is related to aging and affects mainly males, one in ten males ≥ 85 years. Furthermore, it is associated with an increased risk of heart failure hospitalization.

OP-480

Evaluation of Myocardial Sympathetic Denervation in Advanced Parkinson Disease Patients with Autonomic dysfunction using 18F-FDOPA PET-CT

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Objective: We evaluated myocardial sympathetic denervation using L-3,4-dihydroxy-6-F-18fluorodihydroxyphenylalanine (18F-FDOPA) PET-CT in advanced Idiopathic Parkinson's disease (IPD) patients with autonomic dysfunction. **Materials and methods:** This prospective study was approved by the institutional review board and informed consent was obtained from all subjects. Twelve patients of advanced IPD with autonomic dysfunction underwent 18F-FDOPA cardiac PET-CT study. The clinical diagnosis of advanced IPD with autonomic dysfunction was based on Unified Parkinson disease rating scale (UPDRS) & Hoehn and Yahr (H&Y) scale. Autonomic dysfunction was assessed by autonomic function tests (AFT) which included head-up tilt test, Valsalva maneuver, deep-breathing test, handgrip

test and Cold Pressor test to evaluate neurocirculatory failure. Nineteen age matched subjects who had undergone 18F-FDOPA PET-CT for indications other than Parkinsonism and had no history of coronary artery disease or coronary risk factors, were recruited as controls. All the 12 patients and 19 controls underwent 18F-FDOPA cardiac PET-CT study. Cardiac images were interpreted visually and semi-quantitatively using SUVmax value. We derived global myocardium to liver ratio (MLR) and myocardium to mediastinal vessel ratio (MMR). For myocardial regional analysis, these ratios were calculated separately for septum, apex, anterior wall, inferior wall and lateral wall of the left ventricle. The values of MMR and MLR derived from controls were compared with those of IPD patient group using unpaired T test.

Results: 18F-FDOPA cardiac PET-CT studies of twelve patients of advanced IPD with autonomic dysfunction (UPDRS = 54.3 ± 7.2 ; range 44–72 and H&Y = 2.0 – 4.0 , disease duration = 6.6 ± 3.2 yrs; range 4–14 yrs) were analyzed and compared with the control group. Global MLR in advanced IPD group (0.68 ± 0.15) was significantly decreased compared to control group (1.25 ± 0.19) ($p < 0.05$). Similarly, the global MMR in the patients group (1.49 ± 0.21) was significantly less compared to control group (1.83 ± 0.22) ($p < 0.05$). Also, regional MMR and MLR values for septum, apex, anterior wall, inferior wall and lateral wall were significantly reduced in patient group compared to controls ($p < 0.05$ for all). **Conclusion:** 18F-FDOPA PET-CT can be used to evaluate myocardial sympathetic denervation in patients of advanced IPD with autonomic dysfunction.

OP-481

Simultaneous cardiac 18F-FDG PET/MR for the assessment of different stages of cardiac impairment in patients with Anderson-Fabry disease

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Background: Anderson-Fabry disease (AFD) is an X-linked lysosomal storage disorder associated with severe multi-organ dysfunction. While native myocardial T1 mapping by magnetic resonance (MR) may allow non-invasive measurement of myocyte sphingolipid accumulation both positron emission tomography (PET) and MR are able to identify different pathological patterns of disease progression. **Aim:** We investigated the potential relationship between T1 mapping and ¹⁸F-FDG PET by cardiac simultaneous PET/MR imaging in AFD female patients. **Methods:** 17 AFD female patients without cardiac symptoms and with normal left ventricular (LV) function underwent simultaneous cardiac PET/MR (Biograph mMR; Siemens Healthcare, Erlangen, Germany) imaging after administration of ¹⁸F-FDG and contrast agent injection (gadolinium-DPTA) for assessment of late gadolinium enhancement (LGE). In all patients and in 7 female controls T1 mapping was performed using native pre-contrast T1 Modified Look-Locker Inversion-recovery (MOLLI) proto-

type sequences. For the T1 mapping quantification, LV apical, mid-ventricular and basal short-axis slices were considered. Mean T1 values were measured by drawing a 6-pixel size region of interest in the septal and lateral segments of each slice. Cardiac FDG uptake was quantified by measuring the standardized uptake value in 17 myocardial segments in each subject. The coefficient of variation (COV, i.e. the standard deviation divided by the average) of the uptake of the 17 segments was calculated as an index of heterogeneity in the heart and values >0.17 were considered abnormal. **Results:** 5 patients showed focal LGE indicating intra-myocardial fibrosis and were excluded from the final analysis. Compared with controls, mean T1 values of AFD female patients were significantly lower (1238 ± 51.1 vs. 1334.32 ± 26.6 , $p < 0.001$). At PET analysis, 7 out of the remaining 12 patients showed abnormal COV values suggesting inflammation pattern and the other 5 patients demonstrated normal COV values (0.32 ± 0.1 vs. 0.12 ± 0.03 , $p < 0.005$) with homogeneous FDG uptake. Interestingly, patients with abnormal COV showed higher mean T1 values of lateral segments of the mid-LV wall (1219.16 ± 23.4 vs. 1154 ± 62.1 , $p < 0.05$), suggesting a potential relationship between progressive myocyte sphingolipid accumulation and inflammation. **Conclusion:** This study highlights the role of ^{18}F -FDG PET/MR imaging in the early detection of cardiac involvement in AFD patients allowing to identify different stages of disease progression. In particular, myocardial inflammation with pseudo-normalization of abnormal T1 mapping values, associated with abnormal COV values, may represent an intermediate stage before the development of myocardial fibrosis.

OP-482

Phase I/II study of $^{99\text{m}}\text{Tc}$ -Annexin A5-128: safety, biodistribution, dosimetry and preliminary results in infective endocarditis

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Introduction: $^{99\text{m}}\text{Tc}$ -Anx128 is a radiopharmaceutical targeting phosphatidylserine. Our group showed that $^{99\text{m}}\text{Tc}$ -Anx128 SPECT was able to detect vegetations in a rat model of infective endocarditis (IE). The aim of this phase I/II study was to evaluate the safety of $^{99\text{m}}\text{Tc}$ -Anx128 in humans and to perform a preliminary assessment of its sensitivity in the diagnosis of IE (NCT02459613). **Methods:** For the first phase of the study, 10 patients with possible or definite IE according to Duke-Li criteria were included (mean age: 62 y [51–79], all were males).

Blood sampling was performed at baseline and iteratively after $^{99\text{m}}\text{Tc}$ -Anx128 administration (up to 4 weeks for immunogenicity). Urines were collected during the first 24 hours. Whole body planar acquisitions were performed 30 min, 1, 3, 6, and 24h after intravenous injection of 339 MBq [320–370] $^{99\text{m}}\text{Tc}$ -Anx128 using a dual-head gamma camera equipped with a low-energy, high resolution collimators Symbia T2 (Siemens). SPECT/CT centered on the chest was acquired 2h after injection. Images were reconstructed with Flash3D iterative algorithm. Absorbed and effective dose were calculated using OLINDA V2.0 software. The final diagnosis of IE was based upon the Duke-Li criteria at the end of follow-up. **Results:** No significant out-of-range clinical or biological values were identified with all safety assessments, including immunogenicity. No adverse events were considered to be attributable to the tracer. The highest tracer uptake was present in the kidneys, the liver and the spleen. Kidneys had the highest absorbed dose ($76 \mu\text{Gy}/\text{MBq}$). Total effective dose estimate was $5.1 \pm 0.3 \mu\text{Sv}/\text{MBq}$, twice lower than that reported with $^{99\text{m}}\text{Tc}$ -HYNIC-Annexin. The decrease rate of blood-pool activity was mainly related to serum creatinine level. Out of 6 patients with a final diagnosis of definite IE, $^{99\text{m}}\text{Tc}$ -Anx128 scintigraphy was positive in the cardiac area in 5. One patient with a 10-day antibiotic therapy before imaging and 6-mm vegetation was a false negative. $^{99\text{m}}\text{Tc}$ -Anx128 scintigraphy was negative in 4 patients with a final diagnosis of rejected ($n=2$) or possible IE ($n=2$). One intense uptake focus on a tibial artery was associated with vascular septic emboli. FDG-PET/CT scan performed in 7 patients was abnormal in the cardiac area in 2 cases, both matching with $^{99\text{m}}\text{Tc}$ -Anx128 uptake. One patient with $^{99\text{m}}\text{Tc}$ -Anx128 positive uptake on a native valve was negative with FDG-PET/CT. **Conclusion:** the study suggests that $^{99\text{m}}\text{Tc}$ -Anx128 is well tolerated. Preliminary results are promising regarding the detection of IE. The assessment of the diagnostic value of $^{99\text{m}}\text{Tc}$ -Anx128 in a larger population is ongoing.

1201/1204 Tuesday, October 16, 2018, 10:00 - 11:15, Plenary Hall
Plenary 3: The Fascinating World of Molecules

OP-483

The Fascinating World of Molecules

B. L. Feringa; University of Groningen, Faculty of Science and Engineering, Groningen, NETHERLANDS.

OP-484

Coronary Flow for Assessment of Myocardial Ischemia – The ‘Hot’ Topic in Cardiology

J. Piek; University of Amsterdam, AMC Heart Center, Amsterdam, NETHERLANDS.

OP-485

PET to Evaluate Response to Therapy – Theranostic and Beyond

N. Aide; Service de Médecine Nucléaire, Centre Régional de lutte contre le cancer François Baclesse, Caen, FRANCE.

1301 Tuesday, October 16, 2018, 11:30 - 13:00, Plenary Hall

CME 10 - Interactive: Bone & Joint: How Much Radiology Do We Need in Bone and Joint Multi-Modality Imaging?

OP-486

How Much CT is Needed for Bone & Joint SPECT/CT?

K. Strobel; Radiology and Nuclear Medicine, Cantonal Hospital Lucerne, Lucerne, SWITZERLAND.

OP-487

How to Settle Anatomic and Functional Discrepancies in SPECT/CT and PET/CT?

F. Paycha; Service de Medecine Nucleaire, Hopital Lariboisiere, Paris, FRANCE.

OP-488

The Role of PET/MR in MSK Imaging

L. Stegger; Klinik für Nuklearmedizin, Universitätsklinikum Münster, Münster, GERMANY.

1302 Tuesday, October 16, 2018, 11:30 - 13:00, Hall 2

Joint Symposium 19 - Neuroimaging / EANO: Meningioma

OP-489

Imaging Meningioma

I. Law; Rigshospitalet, Dept of Clinical Physiology, Nuclear Medicine and PET, Copenhagen, DENMARK.

OP-490

The State-of-the Art Surgical Management of Meningiomas

J. C. Tonn; Ludwig-Maximilians-Universität, Dept. Neurosurgery, Munich, GERMANY.

OP-491

Radiation and Chemotherapeutical Treatment of Meningiomas

F. Dhermain; Gustave Roussy University Hospital, Villejuif France, Dept of Oncology, Paris, FRANCE.

1303 Tuesday, October 16, 2018, 11:30 - 13:00, Hall 3

Joint Symposium 20 - Cardiovascular / EACVI: Quantification of Myocardial Blood Flow

OP-492

How do I Quantify MBF?

S. Nekolla; Klinikum rechts der Isar, Department of Nuclear Medicine, Munich, GERMANY.

OP-493

How do I Interpretate MBF?

J. Knuuti; Turku University Hospital, Turku PET Centre, Turku, FINLAND.

OP-494

FFR, MFR, Ischemia: Is it All the Same?

H. Verberne; Academic Medical Center, Department of Nuclear Medicine, Amsterdam, NETHERLANDS.

OP-495

Clinical Applications for MBF

P. Knaapen; VU University Medical Center, Department of Cardiology, Amsterdam, NETHERLANDS.

1304 Tuesday, October 16, 2018, 11:30 - 13:00, Hall 5

Technologist Oral Presentations 3

OP-496

Optimized non-conventional radioisotopes production with industrial mid-energy cyclotron

S. Bertrand¹, *J. Geets¹*, *E. Kral¹*, *C. Gameiro¹*, *B. Nactergal¹*, *F. Devillet¹*, *F. Alves²*, *J. Comor³*, *S. de Neuter¹*, *A. Abrunhosa²*, *V. Alves²*; ¹IBA, Louvain-la-neuve, BELGIUM, ²University of Coimbra, Coimbra, PORTUGAL, ³ELEX Commerce, Novi Beograd, SERBIA.

Objectives: This paper presents the solutions developed in order to facilitate and increase the productions of non-conventional PET radioisotopes (such as ⁶⁴Cu, ⁸⁹Zr, ⁴⁴Sc and ⁶⁸Ga) on an industrial mid-energy cyclotron. **Methods:** A proton only optimized cyclotron with fixed energy was designed using internal ion sources, negative ions acceleration and stripping extraction [1;2]. **Dual energy:** Standard extraction energy on the 8 exit ports is 18 MeV, which is ideal energy for high yield production of ¹⁸F and ^{99m}Tc. However, some radioisotopes require lower energy in order to limit the co-production of impurities. Usual method for lowering energy consists in using degrading foils, but the cooling capacity of such degrader will limit the current on target. The industrial cyclotron proposes one or two exit ports that can be operated at lower energy (typically between 13 MeV and 15 MeV) [3]. This helps overcoming the current limitation of the degrader foils and allows safely increasing the current on target. **High power solid target:** With solid targets, production rates are limited by low intrinsic reaction yield. Consequently, target current must be increased to reach higher production levels. A new universal solid target was designed, allowing irradiation of slanted targets. The larger irradiated surface reduces the power density and allows increasing the current up to 150µA or 300µA, depending on the target material considered. **Liquid target technology:** Many recent developments in the production of radiometals with liquid targets have been published [4]. Productions rates and purity levels reached for ⁶⁸Ga show that this technology [5] is a perfect viable alternative to the ⁶⁸Ge/⁶⁸Ga generators. This same process has been transferred to other metallic radioisotopes. An IBA Conical target is used to irradiate a nickel solution for the production of ⁶⁴Cu and ⁶¹Cu [6]. **Results:** The dual energy feature has been successfully tested in factory. Two beam exit ports can be modified to accommodate lower proton energy on target for more effective non-conventional radioisotope productions. Consequently, the energy degraders

can be removed and current can be safely risen on liquid or solid targets. The liquid target technology has now proven records and benefits from an increasing popularity. **Conclusions:** Combining the cyclotron, its dedicated features, the target technologies and the chemistry solutions, a whole range of possibilities are given to easily produce non-conventional radioisotopes. These integrated attractive solutions can be implemented on a PET radiopharmacy without compromising the productions of conventional PET radioisotopes.

OP-497

Quantitative assessment of differences in physiological uptake of [⁶⁸Ga]-DOTANOC and [⁶⁸Ga]-DOTATATE

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The knowledge of the physiological distribution of the radio-tracer is crucial for the proper interpretation of images. This issue is of particular importance if the subsequent exams performed with radiopharmaceuticals of the similar but not identical structure are compared. The study aimed to assess the differences in physiological uptake of two octreotide-based PET radiotracers [⁶⁸Ga]-DOTANOC and [⁶⁸Ga]-DOTATATE. **Material and methods:** The study included 47 patients (26 females and 21 males), aged 28–88 years, evaluated for suspected or confirmed neuroendocrine neoplasia, in whom PET/CT with both [⁶⁸Ga]-DOTANOC and [⁶⁸Ga]-DOTATATE was performed. GE Discovery V690 PET/CT hybrid system was used for images acquisition. The uptake of the tracers was assessed quantitatively as SUVmax values for following organs: pituitary gland, parotid and submandibular salivary glands, thyroid, liver, spleen, right and left adrenal glands and uncinate process of the pancreas. The differences in SUVmax values (Δ SUVmax) between two evaluated tracers were correlated with potentially confounding factors: the length of the period between two exams, the difference in time from tracer injection to images acquisition, the difference in injected activity, and patients' age. Statistical analysis was performed with Statistica 13 and IBM SPSS software. **Results:** The mean period between two exams was 885 $\pm$ 434 days. There was no significant difference in mean injected activity between the tracers (119 $\pm$ 32.9 MBq for [⁶⁸Ga]-DOTANOC, and 130 $\pm$ 33.2 MBq for [⁶⁸Ga]-DOTATATE). The SUVmax values for every investigated organ were significantly higher for [⁶⁸Ga]-DOTATATE than for [⁶⁸Ga]-DOTANOC (the Wilcoxon paired test). There was no significant correlation (Spearman rho correlation) between Δ SUVmax for every investigated organ and patients' age. The period between both exams correlated significantly with Δ SUVmax for right parotid salivary gland only (rho coefficient -0.331, p=0.025); and differences in injected activity with Δ SUVmax for left lobe of thyroid (rho coefficient 0.377, p=0.021). The difference in time from tracer injection to

image acquisition correlated significantly with Δ SUVmax for right parotid salivary gland (rho coefficient -0.343, p=0.018), right (rho coefficient -0.3871, p=0.008) and left submandibular salivary gland (rho coefficient -0.377, p=0.010), spleen (rho coefficient -0.388, p=0.013), right (rho coefficient -0.399, p=0.007) and left adrenal gland (rho coefficient -0.389, p=0.007). **Conclusions:** The obtained differences in [⁶⁸Ga]-DOTANOC and [⁶⁸Ga]-DOTATATE uptake in investigated organs are consistent with differences in the tracers affinity to somatostatin receptor subtypes and are mostly independent of investigated confounding factors. Images obtained with those two radiotracers should be compared with caution.

OP-498

A Retrospective Comparison of two PSMA Ligands Ga-68-HBED-PSMA -11 & Ga-68-THP-PSMA

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Purpose: A number of ligands are available for Ga-68-PSMA imaging. The purpose of this study was to retrospectively compare the results of imaging with synthesizer-produced Ga-68-HBED-CC PSMA to imaging with kit-based Ga-68-THP-PSMA following a cross over from external provision of the former to in-house production of the latter. Specifically we investigated the frequency of any perivesical photopenic artefacts observed with respect to each tracer. Furthermore we reviewed the proportion of negative findings in case matched cohorts across both groups of patients. **Methods:** 102 patients (mean age 67.8, range 47–84 years) were scanned across our two sites using a Siemens Biograph mCT 128 or a Philips Gemini TF 16. In the first set of comparisons, patient data were retrospectively evaluated (THP n=48; HBED n=54) for perivesical halo artefact frequency, bladder activity, bladder SUVmean & max, & background SUVmean & max. For the second set of comparisons, matched cohorts of patients (n=37 THP, n=37 HBED) with biochemical recurrence were identified to compare overall detection rates, PSA-stratified detection rates and number of scans deemed equivocal or containing technical limitations. **Results:** Ga-68-THP-PSMA showed a higher frequency of the perivesical halo artefact (72.9% vs. 14.8%). Halo artefacts were associated with higher bladder activity. In the matched cohort comparison, Ga-68-THP-PSMA exhibited lower detection rates when compared to Ga-68- HBED -PSMA-11 (36.11% vs 67.6%), with similar PSA values (3.05 and 3.26 ng/mL, respectively). As compared to Ga-HBED-PSMA-11, the Ga-68-THP-PSMA cohort also demonstrated higher levels of equivocal findings i.e. subtle low grade activity (8.1% vs 5.4%, respectively) and had more scans indicating technical limitations i.e. intense physiological bladder activity or low tracer count (32.4% vs 0, respectively). **Conclusion:** Ga-68-THP-PSMA provides the opportunity for in-house production without the need for a synthesizer. However, as compared to synthesizer-produced Ga-68- HBED -PSMA-11, Ga-68-THP-PSMA imaging was associated with higher rates of the perivesical "halo artefact", lower detection rates and higher percentages of scans with technical limitations and equivocal findings.

OP-499

Standard protocol compared to a novel protocol for ^{68}Ga -PSMA-PET/CT in patients with recurrent prostate cancer - which one is superior?

L. Dijkstra, F. Haupt, M. Viscione, V. Fech, T. Krause, A. Rominger, A. Afshar-Oromieh; Inselspital Bern, Bern, SWITZERLAND.

Purpose / Introduction: Since the clinical introduction of PET-imaging with ^{68}Ga -PSMA-11, this diagnostic tool has spread worldwide and is regarded as a breakthrough in the diagnosis of recurrent prostate cancer (PC). According to its first described clinical set-up, ^{68}Ga -PSMA-11 PET/CT is conducted at 1h post injection (p.i.). However, further publications demonstrated that later imaging (e.g. at 3h p.i.) show the majority of PC lesions with higher contrast. In 2017, we conducted scans at 1h p.i.. However, in 2018, we changed our protocol to later imaging timing. The aim of this evaluation was to compare the standard protocol of ^{68}Ga -PSMA-11 PET/CT with a novel protocol described below.

Subjects & Methods: We retrospectively compared two patient cohorts scanned with ^{68}Ga -PSMA-11 PET/CT in 2017 (n=94 patients) and 2018 (n=75 patients). In 2017, the scanning protocol was as follows: acquisition at 1h p.i. (targeted activity: 200 MBq) with 2 min per bed position, neither hydration nor forced diuresis. In 2018, the scans were conducted at 1.5h p.i. (also 2min per bed position and targeted activity of 200 MBq). In addition, the patients started to drink 1L of water at 0.5h p.i. and were injected with 20mg of furosemide at 1h p.i.. Rates of pathologic scans, maximum standardized uptake values (SUVmax) of tumor lesions (n=164 in 2017 and n=127 in 2018), average standardized uptake values (SUVmean) of urinary bladder as well as tumor contrast (SUVmax-tumor/SUVmean gluteal musculature) were measured in all patients. **Results:** Average tumor contrast was significantly ($p=0.0451$) higher in 2018 compared to 2017 (59.0 vs. 46.1). Average SUVmean of the urinary bladder was significantly ($p<0.0001$) lower in 2018 (SUVmean 7.6 ± 24.6) compared to 2017 (SUVmean 35.3 ± 7.6). Also the background activity was significantly ($p<0.0001$) lower in 2018. No relevant differences were detected for SUVmax of tumor and the rate of pathologic scans (2017: 80.9%; 2018: 80%; both numbers for $\text{PSA} \leq 3.0$ ng/ml). **Discussion / Conclusion:** Despite highly promising results of the novel protocol including significantly higher tumor contrast and lower urinary activity which enable the assessment of tumor lesions and local recurrent PC, respectively, no higher rate of PET-positive patients were observed in the relatively low patient cohorts. However, we expect that with increasing scan numbers, more tumor lesions and more pathologic scans will be detected in a few percent of patients referred to PSMA-PET/CT thereby changing their therapeutic procedure.

OP-500

SUVmax behavior in metformin-treated patients with pulmonary disease

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Purpose: the aim of this study was to evaluate the difference of SUVmax of the primary or secondary lung cancer in diabetic

patients undergoing metformin therapy. In particular the SUVmax behavior between patients who assumed and those who stopped metformin 48h prior FDG PET examination was made.

Materials and methods: from a monocentric database, 518 patients with primary or secondary pulmonary disease undergoing FDG PET/CT were collected. Seventy-four patients were affected by diabetes mellitus and 29 were under treatment with metformin. The value of SUVmax for the pulmonary lesion was calculated for each patients and thereafter compared in accordance with the assumption of metformin before PET examination. T-student test was used for comparing continuous variables. **Results:** Metformin was withdrawn 48h before the examination in 15/29 patients. The median age of patients was 72 years (range 52-85). The median level of sugar in the blood was 128 mg/dL (range 76-199) before the FDG injection. The median value of SUVmax was 4.48 (0-23.39). PET/CT was positive in 15 subjects. The value of SUVmax in patients who stopped metformin 48h prior PET was 5.75 ± 5.82 while in those who did not discontinue metformin, the value was 6.75 ± 7.94 ($p = \text{NS}$). The glycemic value and the value of the administered dose of FDG between the two groups was similar (127 ± 21 vs. 130 ± 35 mg/dL and 232 ± 52 vs. 219 ± 47 MBq, respectively in patients without and with metformin suspension; $p = \text{NS}$). **Conclusions:** our preliminary analysis shows that the metformin withdrawn for at least 48h prior PET scan does not alter the metabolic behavior of the lung lesions in cancer patients. Therefore, the anti-cancer activity of metformin would appear to be present even in the event of short suspensions.

OP-501

Diagnostic impact of Dual-Time-Point ^{18}F -FDG PET/CT in detection of liver metastasis

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Aim: to evaluate the utility of dual-time imaging with ^{18}F -FDG-PET/CT in the detection of liver metastasis by analysis of differences between standard and delayed acquisition. **Methods:** we evaluated 87 cancer pts who underwent, from Jan 2015 to Dec 2017 PET/CT performing the delayed acquisition. We compared the results of the whole-body scan (PET1) with the delayed scan (PET2) performed by two fields of view (FOV) of the abdomen. Both studies were evaluated qualitatively analysing standardized uptake value (SUV) of lesions. We divided the patients in according to the pathology. PET results were then confirmed by radiological/histological data when available, or follow up. **Results:** we study 87 pts (male 50) who underwent PET1 one hour after FDG injection and PET2 about a mean time of 60 minutes after PET1. Pts were clinically: 29 colorectal, 19 breast, 7 lung, 28 different type and 4 pts with 2 different tumours. At PET1 62/87 pts had one or more lesions for a total number of 106, 25/87 pts had no lesions at liver; at PET2 64/87 pts had one or more lesions for a total number of 122, 23/87 patients had no lesions at liver. Evaluating number of lesions, in 51/87 pts there were no differences between the two acquisition, in PET2 we found an increase in the number of liver lesions in 14/87 pts and a decrease in 10/87. Specifically, in 7 cases lesions disappeared

at PET2 showing that lesions at PET1 were referred to superimposed aspecific intestinal activity (false positive at PET1), in 6 pts lesions compared only at PET2 showing at PET1 only a disomogeneous uptake (false negative at PET1). Evaluating SUV, at PET2 we found an increase in SUV value in 98 lesions, a decrease in 21 and no differences in 3 lesions. Between pts with no differences in lesions number 22/51 were negative at both scans (19/22 were true negative, 3/22 were false negative). Between the 29/51 pts positive for hepatic lesions, 27/29 showed an increase in SUV value at PET2. Pts who benefit from delayed scan were colorectal (33%) and breast cancer (19%), even if at now is not possible to establish a correlation with specific pathology; the absence of delayed acquisition would have underestimated the pathology, with diagnostic delay. **Conclusions:** in a significative number of patients delayed PET scan was useful in detecting the real number of liver metastasis, changing the TNM stadium or the therapeutic approach.

OP-502

Dynamic curve patterns based on First-Pass Breast dynamic 18F-FDG PET/CT: a step further in breast cancer diagnostic

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Purpose: The purpose of this study was to evaluate a quantitative method to shape the pattern of enhancement kinetic curve on the different histological subtypes of breast tumors through a dynamic first-pass 18F-FDG PET-CT. **Methods and Materials:** A retrospective study based on prone dynamic first-pass F18-FDG PET-CT studies performed on sixty-eight patients (51,9 ± 11,8 years old) covering the breast region and the armpits, and a whole body FDG PET-CT 60-70 min after injection were performed. Distribution coefficients and glucose metabolism were quantified by ROIs and analyzed in both acquisitions. For quantitative assessment, the slope of persistently enhancing, plateau, or washout curve was calculated and evaluated. Results were correlated with biopsy findings realized prior PET-CT and tumor histology reports after surgeries. Follow up of patients clinical history from 2012 to 2018 was realized. **Results:** 136 FDG-avid lesions were identified by dynamic breast first-pass PET-CT, in comparison with 109 in whole-body PET-CT 60-70 min after injection. Despite only 94 were analyzed by pathologists which 60 were reported as invasive ductal carcinoma (IDC), 5 in situ ductal carcinoma (DCIS), 13 invasive lobular carcinomas (ILC), 4 papillary carcinomas (PC), 2 mucinous carcinoma (MC) and 5 benign lesions (fibroma and adenosis). Mean values based on the PET-CT ROIs were 4.34±2,86 (standardized uptake value), 0.63±0.35 ml·g⁻¹ (distribution coefficient) and 6.5±3.2 mg·min⁻¹·100g⁻¹ (glucose metabolism). The SUVmax measured on delayed PET images correlated strongly and positively with the expression of Ki67 (r= +0.72; P<0.0001) reported. Different dynamic curve patterns of uptake were observed during this research according to the subtypes of breast cancer diagnosed: IDC pattern curve has a persistently enhancing without plateau or washout and has usually a higher final SUV(20-30%); ILC pattern curve has a

final plateau from 3-4 min since 10 min and no washout; benign pattern curve has a low enhancing and a quick plateau with or without washout; only healthy tissue has a regular enhancing a minimal plateau and a constant washout. Sensitivity and negative predictive values were 80% and 52%, respectively for PET-CT studies and 89% and 71.5% for dynamic breast first-pass PET-CT. **Conclusion:** Tumor uptake quantification by dynamic first-pass on 18F-FDG PET/CT is significantly associated with tumor angiogenesis. We are able to differentiate normal breast tissue and breast cancer, and classify it by histological subtypes. These preliminary results have shown that we can improve breast cancer diagnosis and shorten treatment times in breast cancer.

OP-503

Correlational descriptive study of PET/CT versus 4DCT in Radiotherapy planning of Non-Small Cell Lung Carcinoma: Systematic Literature Review

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Introduction and Aim: Lung cancer is the most common cause of death from cancer. Radiotherapy plays an important role in the curative treatment of Non-Small Cell Lung Carcinoma (NSCLC), with CT being the basis for radiotherapy planning, but it does not always allow accurate target volume definition. The purpose of this study is to understand which of the techniques, 4DCT or PET/CT, more benefit the definition of the target volume in the radiotherapy planning for NSCLC, and whether the use of these techniques may be associated with a greater local control of the disease. **Material and Methods:** This work consists in a systematic literature review. It was used scientific articles from 2006 to 2018. The literature search was performed using the databases Pubmed, B-on, NCCN, ScienceDirect and Elsevier. In the search, the Boolean logic used was "PET/CT and 4DCT in NSCLC", "PET/CT in planning radiotherapy for NSCLC" and "PET/CT or 4DCT in NSCLC". In this study, inclusion parameters were articles or books related to NSCLC, 4DCT and PET/CT for radiotherapy planning. Exclusion parameters were the sample size of the articles being small (below twelve), websites, blogs, PET/CT and 4DCT for diagnosis. **Results:** PET/CT and 4DCT influence the definition of target volume in different ways. In the PET/CT, the definition depends on the radiopharmaceutical used, in the case of ¹⁸F-FDG it is possible to determine hypermetabolic areas, ¹⁸F-FMISO evaluates the hypoxia in the tumour lesion, ¹⁸F-FLT evaluates tumour cell proliferation and ⁶⁸Ga-MAA evaluates the pulmonary perfusion. PET/CT or CT can't identify the movement that the tumour lesion suffers due to respiratory movements. 4DCT provides information about the changes that tumour undergoes during the respiratory cycle and allows to decrease the artefacts in the images caused by the respiratory movements, leading to a reduction of the PTV. It is still possible for PET/CT to include a respiratory gated, allowing a 4D-PET/CT acquisition. **Conclusion:** This study demonstrated that both PET/CT and 4DCT are important for RT planning because they influence the definition of the target volume, but in different ways. The PET/

CT allows to evaluate the need to boost the dose and to identify the limits with more precision of the GTV, normally leading to a reduction of the same, the 4DCT allows to evaluate the movements of the lesion, which leads in most cases to a reduction of the margins given in the PTV.

OP-504

Respiratory motion management in PET/CT: how to help technologists in choosing the best tailored technique

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Introduction: Breathing movement can introduce heavy bias in both image quality and quantification in PET/CT studies. Currently, many tools are available to manage respiratory motion, any of them, with pros and cons, able to help the technologist to optimize the choice of the motion management protocol in order to improve image quality and quantification, increasing compliance. **Aim:** Comparing different motion management techniques in terms of quantification (SUV_{max}) and proposing a flow chart to select the best approach and acquisition modality.

Material and Methods: 18F-FDG PET/CT WB-3D scans (1.5 min/FOV) with an integrated 9 minutes 4D-FOV on thorax/upper-abdomen, by using a high sensitivity 5-rings PET/CT scanner (Discovery-IQ, GE Healthcare, Milwaukee, WI-US) were performed in 15 patients (male 9, mean age 69 yrs) with 21 target lesions analyzed. 4D-data PET acquired in List Mode were reconstructed using different regularized reconstruction (QClear-GE) and Beta factors (factor modulating T/BKG ratio) as follows: 1) standard ungated 1.5 min/FOV, beta 350 (WB), 2) 4D-images, 6 phases, 1.5 min/phase, beta 350 (4D-QC350), 3) 4D-images, 6 phases, 30 sec/phase, beta 450 (4D-QC450), 4) 3D-image, 1.5 min/FOV obtained by an End Expiration Quiescent Phase technique (EEQP named Q.Static-GE), beta 350 (WB-EE). In any dataset, SUV_{max} values of target lesions (n=21) were calculated and compared (paired t-test). Advantages and limitations of different available approaches were described. The technologist approaches to patients were evaluated considering patient health conditions and compliance for gating acquisition. **Results:** The mean values [range] of SUV_{max} resulted: 7.45 [1,98-16,85] for WB; 9.11 [2,86-20,54] for 4D-QC350; 9.14 [2,91-21,8] for 4D-QC450; 8.29 [2,48-19,5] for WB-EE. SUV_{max} 4D-techniques resulted significantly higher than WB and WB-EE ($p < 0.01$), however the main disadvantage of respiratory gating resides in the cineCT additional dose. SUV_{max} values obtained from WB-EE resulted higher than those of standard WB ($p < 0.01$), but the technique requires high patient compliance. Finally, the SUV difference between 4D-QC350 (30 sec/phase) and 4D-QC450 (1.5 min/phase) was not statistically significant, suggesting the possibility to reduce acquisition time for 4D-scan. A flow-chart was defined in order to help technologists in choosing the best acquisition approach (mainly evaluating patients characteristics and clinical indication). **Conclusion:** Amongst respiratory motion management techniques, 4D-protocols provided the highest SUVs; also EEQP improved SUVs respect to standard imaging. The knowledge of advantages (better quantification, image quality) and disadvantages

(acquisition time, dosimetry) of different motion management methods can help technologists in the workflow improving better imaging results.

1305

Tuesday, October 16, 2018, 11:30 - 12:45, Hall X

M2M: Therapy Effects - α Emitters and PDT

OP-505

Photodynamic Therapy of Ovarian Cancer with EpCAM-Targeting DARPins

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Introduction: Epithelial ovarian cancer (EOC) is the most lethal gynaecological malignancy. The current treatment for advanced stage disease consists of cytoreductive surgery in combination with chemotherapy. However, complete tumor removal is often impossible, resulting in relapses, because of remaining (micro) metastases in the abdominal cavity. Since these metastases are often fatal, new treatment strategies are required. Over 90% of these lesions express epithelial cell adhesion molecule (EpCAM) (1,2), allowing treatment with EpCAM-targeted photodynamic therapy (PDT). Designed ankyrin repeat proteins (DARPins) are antibody-mimicking engineered proteins with a small size (15 kDa) and high affinity and specificity for their target. Here, we used EpCAM-targeted DARPins-photosensitizer (PS) conjugates, and evaluated potency for eradication of EpCAM positive ovarian cancer cells *in vitro*. **Methods:** A DARPins with subnanomolar affinity for EpCAM and a control DARPins were functionalized site-specifically with the PS IRDye700DX. Adherent cell cultures and spheroids of EpCAM expressing ovarian carcinoma cell lines OV90 and OVCAR3, and EpCAM-negative control cell line E98 were incubated with different concentrations of DARPins-PS conjugates and illuminated with 60 J/cm² near infrared (NIR) light. 18 hours after illumination, cell viability of adherent cells was determined with the resazurin assay, and in spheroids with the acid phosphatase assay. In order to analyze penetration of DARPins into 3D structures, the DARPins were site-specifically functionalized with AlexaFluor680. Spheroids were incubated with DARPins-AlexaFluor680 conjugates and penetration was assessed by confocal microscopy. Furthermore, fresh metastatic tissue from patients undergoing cytoreductive surgery were sliced into 300 μ m thick sections and incubated with DARPins-AlexaFluor680. Colocalisation of DARPins with EpCAM expressing cells was assessed with immunohistochemistry. **Results:** We show that upon illumination with NIR light, DARPins-PS conjugates induce cell death of EpCAM expressing ovarian carcinoma cell lines OV90 and OVCAR3 in both adherent cell cultures

(with IC₅₀ values of 24.72 nM and 48.02 nM, respectively) and in spheroids. No cell death was observed in the control conditions or in the control cell line E98. Furthermore the DARPin rapidly and completely penetrate into spheroids and bind specifically to EpCAM-expressing cells in patient-derived tumor tissue. **Conclusion:** From this work we conclude that DARPin-PS conjugates efficiently induce EpCAM-dependent phototoxicity upon illumination *in vitro*. Furthermore, they are able to penetrate into tissue and bind to target expressing cells, indicating potential for the *in vivo* use of these molecules for treatment of metastasized EOC. 1.Bellone S, et al. Int J Gynecol Cancer. 2009;19(5):860-6. 2.Spizzo G, et al. J Clin Pathol. 2011;64(5):415-20

OP-506

Targeted photodynamic therapy of GLP-1R positive lesions with exendin-IRDye700DX

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Background: Insulinoma and focal lesions in congenital hyperinsulinism (CHI) are GLP-1R positive lesions that are characterized by excessive insulin production and thereby causing severe hypoglycaemia. The therapy of choice is surgery, however, these surgical procedures are challenging because of the necessity to preserve as much healthy pancreatic tissue as possible and in some cases due to the localization of lesions near the ducts or large vessels. Targeted photodynamic therapy (tPDT) could provide selective destruction of tumour tissue without causing damage to surrounding tissues. The glucagon-like peptide-1 (GLP-1) analogue exendin specifically binds the GLP-1R expressed on pancreatic beta cells. GLP-1R imaging using [⁶⁸Ga]Ga-labelled exendin is a successful pre-operative imaging technique for insulinoma and is under investigation in CHI. We hypothesize that tPDT using exendin labelled with the near-infrared (NIR) sensitive photosensitizer IRDye700DX enables specific destruction of GLP-1R positive cells. **Methods:** Exendin-IRDye700DX was characterized *in vitro* and *in vivo*. A competitive binding assay was performed using CHL-cells transfected with the GLP-1R. The feasibility of inducing specific cell death was assessed by incubating different cell-types (CHL-GLP-1R cells, INS-1 cells and PANC-1 cells) with 300 nM exendin-IRDye700DX and exposing them to various intensities of NIR LED light. Cell viability was measured using a cell titer glo assay. Tracer biodistribution was determined in BALB/c nude mice bearing subcutaneous GLP-1R positive tumours. To determine therapy response, tumours of 2 groups of mice (N=8 per group, 1 group injected with 20 µg exendin-IRDye700DX and 1 control group injected with PBS) were exposed to 120 J/cm² of NIR LED light of 690 nm. Mice were sacrificed when tumours reached a size of 1000 cm³. **Results:** Exendin-IRDye700DX has a high affinity for the GLP-1R with an IC₅₀ value of 6.3nM, which is comparable to unlabeled exendin. In CHL-GLP1R cells as well as INS-1 cells, NIR light reduced cell viability in a dose-dependent manner with 0% viability reached at 175 J/cm². PANC-1 cells, which do not express the GLP-1R remained 100% viable with this tracer dose and light-intensity. Injection of 0.3 µg exendin-IRDye700DX resulted in an *in vivo*

tumour uptake of 12.8 ± 6.4 %ID/g, which decreased with increasing peptide doses. The survival of mice treated by PDT with exendin-IRDye700DX was significantly increased compared to control mice (p<0.05). **Conclusions:** These data show *in vitro* as well as *in vivo* evidence for the efficacy of tPDT using exendin-IRDye700DX. This could be a promising new therapeutic option for GLP-1R positive lesions.

OP-507

Single dose efficacy of FPI-1434, a radioimmunoconjugate targeting human IGF-1R, in preclinical models of human cancer

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Objectives: Insulin-like growth factor-1 receptor (IGF-1R) is an oncogenic protein and has been shown to overexpressed in multiple cancer types. IGF-1R targeted therapeutics have not demonstrated clinical efficacy for treating cancers either as standalone agents or in combination with other therapies. Despite this, targeted alpha therapeutic agents (TAT) may be ideal for treating IGF-1R expressing cancers due to their high potency and lower protein mass dose. Herein we describe the preclinical efficacy of FPI-1434. **Methods:** FPI-1434 was produced by conjugating with a lysine directed bifunctional chelated to AVE1642 and radiolabeled with Ac-225. Single dose radiotherapeutic efficacy studies were carried out using Colo-205 (colorectal), A549 (radioresistant lung), or LNCaP (prostate) xenograft bearing athymic nude mice. Animals received singled doses ranging from 0.05 µCi to 0.4 µCi with a corresponding dose of total protein typically less than 10 µg (0.5 mg/kg). Study endpoints included tumor volume measurement and/or impact to animal health status. **Results:** Colo-205 xenograft bearing mice received single doses of FPI-1434 at 0.05, 0.2, and 0.4 µCi or vehicle and radiotherapeutic efficacy was followed for 178 days. FPI-1434 caused suppression of tumor growth at the 0.05 µCi dose and the 0.2 and 0.4 µCi doses caused durable tumor regression (shrinkage) lasting the study. Median survival for the vehicle, 0.05, and 0.4 µCi dose groups was 42, 66 and 151 days and remained undefined in the 0.2 µCi group at study termination. In addition; FPI-1434 caused regression in large Colo-205 tumors grown to a volume of greater than 400 mm³ prior to dosing. FPI-1434 was also efficacious in the LNCaP and A549 models following single doses of radioimmunoconjugate. The antibody control had no efficacy in the Colo-205 and A549 models at doses >100-fold higher than the mass given in FPI-1434. **Conclusion:** Single doses of FPI-1434 as a standalone agent in pre-clinical models demonstrate a high degree of durable anti-tumor efficacy in multiple tumor xenograft types including large tumors and cell lines resistant to ionizing radiation (e.g. A549). These results strongly support the use of FPI-1434 in IGF-1R overexpressing cancers.

OP-508

Efficacy of Astatine-211 radioimmunotherapy of Multiple Myeloma using an anti-mCD138 monoclonal antibody in a syngeneic murine model.

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Aim: Multiple myeloma is a B-cell malignancy of terminally differentiated plasma cells within the bone marrow. In spite of a very active search for new treatments, cure is almost never achieved. Alpha-radioimmunotherapy (RIT) is a new cancer treatment modality with tumour specific antibodies coupled to alpha particle-emitting radionuclides. CD138 (Syndecan-1) is found mainly in epithelial cells, but was shown to be expressed by most myeloma cells, both in human and in the mouse. The aim of the study was to evaluate the biodistribution, toxicity and efficacy of a rat Astatin-211-labelled anti-mouse CD138 antibody (²¹¹At-9E7.4) in a syngeneic mouse myeloma model. **Materials and methods:** C57BL/KaLwRij mice were grafted with 10⁶ 5T33 cells (murine myeloma cell line). Biodistribution was studied 15 min, 1h, 4h, 7h, 14h and 21h post-administration of ²¹¹At-9E7.4 mAb. Toxicity (animal weight, blood cell counts and transaminase) and RIT efficacy were studied after a dose escalation using 370, 555, 740 and 1110 kBq of ²¹¹At-9E7.4 and two control groups ²¹¹At-IgG2a isotype control at 555 kBq or no treatment, 10 days after tumour engraftment. **Results:** Studies demonstrated a highly statistical survival benefit for the mice treated with ²¹¹At-9E7.4 at 555 kBq (p=0,0006) and 740 kBq (p<0,0001). At 555 kBq, the survival median was increase by 34 days and at 740 kBq 65% of the mice survived 160 days after engraftment. For treatments with 370 kBq with ²¹¹At-9E7.4 or ²¹¹At-isotype control at 555 kBq no significant benefit was observed. The higher activity with 1110 kBq of ²¹¹At-9E7.4 was clearly radio-toxic since mice were euthanized after a lost more than 30% of baseline weight 14 days after radiopharmaceutical injection. For the other groups, except transient decreases of leukocytes and red cells, no other toxicity could be demonstrated, especially on liver function, which does not seem to be affected. Concerning red blood cells, the effect is much weaker than that observed with the use of Bismuth-213 at an injected activity of 3.7 MBq. **Conclusions:** RIT of MM using Astatine-211 coupled to monoclonal antibody directed against murine CD138 is effective. The activity in astatine-211 which allows 60% survival corresponds to an activity injected in Bismuth-213 located between 3.7 and 7.4 MBq, which seems to reflect the influence of the half life of the two radionuclides. In addition, the upper half-life of astatine appears to be a benefit, particularly because of the lower toxicity observed in this syngeneic model of MM.

OP-509

Enhancing targeted α -therapy for treatment of metastatic breast cancer

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Background: Metastatic cancer remains the major cause of mortality in cancer patients, including breast cancer patients. Breast cancer patients with metastatic disease have a significantly lower five-year survival rate (26%) compared to a patient with localized cancer (99%). Breast cancer patients that have an overexpression of human growth factor receptor-2 (HER2) are associated with a poorer prognosis including a higher potential to metastasize and a higher likelihood to have disease recurrence. Previously, in a lung metastasis mouse model of breast cancer our lab demonstrated that an anti-HER2 antibody labeled with ²²⁵Ac, ²²⁵Ac-DOTA-anti-7.16.4, was able to eradicate metastatic disease in 67% of mice while mice having disseminated disease showed only a significant increase in survival. The aim of this study is to investigate biological response modifiers (BRMs) that will reduce the proliferation rate of HER2 (17-AAG), decrease double stranded break repair (Nu7441), or increase the permeability of targeted tumors (TNF- α) to potentially augment targeted alpha therapy. **Methods:** The ability of ²²⁵Ac-DOTA-7.16.4 to kill HER2-positive tumor cells in combination with 17-AAG, Nu7441, or TNF- α was investigated both *in vitro* (except TNF- α) and *in vivo*. Therapeutic efficacy of ²²⁵Ac-DOTA-7.16.4 was determined by colony formation assays (17-AAG and Nu7741) and survival studies in mouse models of metastatic breast cancer. ¹¹¹In-DTPA-7.16.4 was utilized to investigate tumor uptake in mice bearing NT2.5 tumors with and without TNF- α . **Results:** Colony formation assays demonstrated that the combination of ²²⁵Ac-DOTA-7.16.4 with 17-AAG or Nu7441 increased the tumor cell kill as compared to ²²⁵Ac-DOTA-7.16.4 alone; the ²²⁵Ac-DOTA-7.16.4 + Nu7441 had a greater impact on tumor cell kill than when combined with 17-AAG. *In vivo* the combination of ²²⁵Ac-DOTA-7.16.4 + 17-AAG led to no difference in tumor growth (subcutaneous tumor model) or survival (lung metastasis model). The combination of ²²⁵Ac-DOTA-7.16.4 + Nu7441 led to improved survival in mice with disseminated disease compared to ²²⁵Ac-DOTA-7.16.4 alone. The combination of ¹¹¹In-DTPA-7.16.4 + TNF- α demonstrated increased accumulation of the labeled 7.16.4 antibody within the targeted tumor site. **Conclusion:** The combination of ²²⁵Ac-DOTA-7.16.4 with the BRMs Nu7441 and TNF- α resulted in improved therapeutic efficacy and tumor uptake. These combinations have the potential to augment targeted alpha therapy and improve the long-term survival in patients with metastatic breast cancer.

1306 Tuesday, October 16, 2018, 11:30 - 12:45, Hall Y

Do.MoRe - Rapid Fire Session: Quantification & Data Analysis

OP-510

Interventional Real-Time Quantification of ⁹⁰Y-Microspheres Distribution in Selective Internal Radiotherapy

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Purpose: Selective internal radiotherapy (SIRT) is a treatment option for disseminated malignant liver lesions. Further optimization in patient's outcome might be achievable by highly selective dose implantation and/or tumor-orientated dose escalation. We propose a new workflow for real-time quantification of the ⁹⁰Y-microspheres distribution. The methodology is based on planar ⁹⁰Y-Bremsstrahlung imaging and is intended for future online monitoring during angiographic application. Emission data are compared against Monte Carlo (MC) simulated data representing predefined ⁹⁰Y-accumulation pattern. We present two cases demonstrating the proposed workflow.

Material and Methods: Two male patients (both 74 yr., Patient 1: 15 ml metastasis of colorectal cancer in segment IV, and Patient 2: hepatocellular carcinoma lesion of 1055 ml in the right lobe) were treated by SIRT. Planar Bremsstrahlung imaging (energy window: 130 ± 30 keV, imaging duration: 5 minutes) was performed after SIRT with a declipse[®]SPECT system (SurgicEye GmbH, Munich, Germany) extended by four CZT-based detectors (CrystalCam, CrystalPhotonics GmbH, Berlin, Germany). Detectors were arranged in a 2x2 matrix. In parallel, a patient-specific database of MC simulated projection data (GATE, OpenGATE collaboration) was generated. For this purpose we used the pre-therapeutic ^{99m}Tc-MAA SPECT/CT to simulate the initial distribution of ⁹⁰Y accumulation in the lesion(s) and healthy liver tissue. Furthermore, the corresponding low-dose CT was used for MC simulation of scatter and attenuation. Best fit of measured projections and MC simulated images was estimated by a k-Nearest Neighbors model trained on parameters resulting from the fitting of a multivariate t-distribution with a baseline component. The activity distribution used for simulating the best fitting MC projection represents the result of the quantification workflow. Standard of truth was the uptake pattern obtained by post-therapeutic ⁹⁰Y-PET/CT. Uptake values were calculated for the tumor lesion(s) and liver tissue. **Results:** In Pat.1, the tumour uptake was highly underestimated (Simulation (S): 950, PET: 2800 kBq/ml). Better accordance was found for background liver tissue (S: 620, PET: 647 kBq/ml). In contrast, the approach revealed adequate values for the tumor in Pat.2 (S: 1013, PET: 1100 kBq/ml). However, the liver background within the FOV was overestimated (S: 636, PET: 350 kBq/ml). **Conclusion:** Rapid in-silico quantification of intra-hepatic ⁹⁰Y accumulation pattern from planar Bremsstrahlung imaging is feasible by a MC based framework. Activity quantification in large volumes is more precise than in small volumes. Potentially, scatter and anisotropic Bremsstrahlung generation degrade simulation results. MC framework will be refined and tested accordingly.

OP-511

Investigation of maximum likelihood scatter scaling for high contrast PETCT

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Scatter correction in PETCT imaging is essential in order to obtain quantitative estimates of the PET activity distribution. Currently, an image based single-scatter simulation (SSS) and a tail fitting outside the emission support to compute plane-by-plane scatter scaling factors (TFSS) estimates the total scatter. While this approach produces robust scatter correction for most clinical studies, there are cases where it can fail such as in high image contrast producing PETCT studies. We present a method to estimate scatter scaling factors simultaneously with image activity and SSS scatter shape estimations with evaluation for high contrast PETCT studies. Poisson maximum likelihood based solution for nested scatter scales estimation and activity image update was used to compute scatter scaling factors referred to as the maximum likelihood scatter scaling approach (MLSS). A GEANT4 simulation of the image quality (IQ) phantom was performed to compare the scatter shape estimated with MLSS and TFSS approach to the simulated scatter. In addition, experimental phantom studies were performed using a 37 cm diameter uniform cylinder, a high contrast bladder phantom and IQ phantoms filled with F-18 and Ga-68. Uniformity in the axial and trans-axial profiles and hot sphere contrasts were used as figures of merit for phantom studies. Whole-body Ga-68 PSMA clinical studies (N = 11) with challenging high contrast tracer distribution were also assessed. Analysis of clinical data was based on computing relative difference in SUVs in low and high contrast regions using MLSS and TFSS methods for scatter correction. For the GEANT4 simulation, the axial scatter profile obtained with MLSS approach was closer to the simulated scatter (~4% error) compared to TFSS approach (~5% error) mainly in the end planes. Axial profiles for uniform cylinder showed less variability with MLSS (~0.06%) compared to TFSS (~2%) approach. IQ phantom with Ga-68 showed scatter under-correction trans-axially with TFSS approach due to the use of prompt gamma correction. For the high contrast phantom, TFSS resulted in scatter over-correction close to the high activity object while MLSS gave a more uniform background activity. For clinical studies, low contrast regions SUVs were similar (~2% difference) with MLSS and TFSS approach while higher with MLSS compared to TFSS near high contrast regions (~523% difference). The proposed MLSS approach helps obtain more accurate scatter estimates with potential to improve image quality particularly in the case of high contrast PETCT.

OP-512

Validation of SiPM-based PET imaging for left ventricular volumes measurements in preclinical imaging: comparison with simultaneously-acquired cardiac magnetic resonance at 7T.

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Aim: PET has been proposed as a technique allowing the measurement of left ventricular volumes in small animals. Unfortunately, it has been difficult to provide a reference method obtained at comparable level of anaesthesia, heart rate, blood pressure and body temperature. Integrated PET/MR imaging offers the unique opportunity to compare PET and MR measurements (considered as the gold standard), both in exactly the same physiological state. The purpose of this work was to compare end-diastolic volume (EDV), end-systolic volume (ESV) and left ventricular ejection fractions (LVEF) obtained either with PET or with MR in an integrated micro-PET/MR imaging system.

Materials and Methods: Seven Wistar rats were injected with 18F-FDG (15.8 ± 2.3 MBq) and imaged using a SiPM-based PET integrated inside a 7T preclinical magnet. Acquisitions were respiratory- and cardiac- gated using a pneumatic cushion and subcutaneous needles. Twelve phases per cardiac cycle were simultaneously acquired 30 min post-injection. PET was acquired in list-mode during 30 min and reconstructed using 3D OSEM. For MR, a FLASH cine sequence was used. The accuracy of MR volumes measurement was assessed using a 3D-printed phantom. Following baseline acquisitions, 4 rats were treated with doxorubicin and 3 with vehicles and were imaged at 2 and 4 weeks. MR volumes were determined by manually delineating the endocardial contour on short axis slices. PET endocardium was delineated using 2 different semi-automatic processing methods: 3D Laplacian (LAP) and region growing image segmentation (RGS). **Results:** At baseline, CMR yielded ESV, EDV and LVEF values (mean $\pm$ SD) of 81 ± 10 μ L, 270 ± 39 μ L and 70 ± 3 %, respectively. LVEF computed from RGS (58 ± 6 %) was significantly lower (Friedman test and Dunn's post-test, $p < 0.05$) than CMR or LAP (71 ± 4 %). Including repeated measurements over time ($n=21$), modified Bland-Altman analysis showed that the difference (mean ± 1.96 SD), between LAP and CMR measurements of ESV, EDV and LVEF was -0.3 ± 36.8 μ L, 7.2 ± 50.8 μ L and -0.3 ± 17.4 %. RGS exhibited much larger differences with CMR, overestimating ESV and underestimating LVEF. **Conclusion:** Similar left ventricular volumes were found using PET (LAP) and MR. These preliminary results suggest that volumetric and functional parameters can be used interchangeably in an integrated micro-PET/MR imaging system. Moreover, integrated PET/MR appears as the ideal technique to validate measurements done with the same PET scanner but used as a standalone imager.

OP-513

Assessment of Ejection Fraction in Myocardial Perfusion SPECT Imaging in Finland: A Multicenter Phantom Study

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Helsinki University Hospital, Helsinki, FINLAND, ⁵Department of Physics, University of Helsinki, Helsinki, FINLAND.

Aim: The aim of this study was to compare the accuracy of gated myocardial SPECT for estimating the left ventricular ejection fraction (LVEF). **Materials and methods:** All public nuclear medicine laboratories in Finland that routinely perform myocardial perfusion imaging (MPI) participated in the study. The Initial results of 22 gamma cameras are presented. A commercial gated heart phantom was used to produce repeatable end-diastolic (EDV) and end-systolic (ESV) volumes for determining ejection fraction (EF) at a fixed heart rate of 60 beats per minute. The phantom's performance has been verified previously by comparing the set EF values to those measured from a gated multi-slice X-ray computed tomography scan. The phantom was set to an EF of 50% and was imaged twice: 1) with a routinely applied clinical (LEHR/IQ-SPECT) stress protocol (CLINICAL) and 2) with a standardized higher count-statistic protocol (STANDARD). The STANDARD imaging protocol allowed for comparisons of gamma camera performance across laboratories. Reconstructions and subsequent analyzes were performed as 1) routinely and 2) in a centralized manner. **Results:** CLINICAL and STANDARD protocols with routine clinical analyses yielded slightly high estimates (mean $\pm$ SD) for the EF (56 ± 7 % and 57 ± 5 %, respectively), whereas estimates for ESV (22 ± 5 ml and 22 ± 5 ml, respectively) and EDV (46 ± 5 ml and 48 ± 6 ml, respectively) were approximately 1/3 too low. The centralized analyzes yielded better estimates for the EF from CLINICAL and STANDARD protocols with lower deviations (51 ± 5 % and 53 ± 4 %, respectively), but similarly underestimated ESV and EDV. Two acquisitions made with IQ-SPECT (cardio-focal collimation) had poorer results (EF > 60 %) than most of the systems that had LEHR collimators. **Conclusions:** Based on the current study, gated MPI may overestimate the EF, due to underestimating the ESV and EDV volumes. This observation is consistent with a previous study that utilized the same phantom but only investigated LEHR and IQ-SPECT acquisition protocols in the same laboratory. The reasons for volume underestimation are multifactorial, and can include poor resolution (i.e., collimators), bad choice of reconstruction parameters (i.e., iterations), too strong post-filtering of the images or even insufficient patient dose and imaging time (i.e., count-statistics). Even though the volumes were underestimated, the EF estimates were generally close to the set value of 50%. However, absolute errors larger than 10% were reported in 5 laboratories, when the clinical imaging and analysis routines were used.

OP-514

Quantification of hepatic and extrahepatic OATP function using whole-body dynamic¹¹C-glyburide PET imaging

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Aim: Organic Anion-Transporting Polypeptides (OATP) transporters expressed by hepatocytes are major determinants of the liver uptake and further hepatobiliary elimination of many drugs. Some OATPs are expressed by other blood-tissue interfaces such as the myocardium suggesting a so far unpredict-

ed role in the tissue distribution of drugs. Metabolically stable probes are thus needed to reveal and quantify the importance of OATP function for the tissue kinetics of its substrate drugs. ^{11}C -glyburide is a radiolabeled substrate of several OATPs including liver-specific (OATP1B1 and 1B3) and pleiotropic (OATP1A2 and OATP2B1) members. This study aimed at validating a clinically achievable method for the quantification of OATP function at the blood-tissue interface using ^{11}C -glyburide PET imaging. **Materials and methods:** Two baboons underwent 3 consecutive ^{11}C -glyburide PET-CT scans (266 ± 36 MBq, 60 min). Repeated whole-body scans were performed and reconstructed to provide whole-body dynamic PET images (2.5 to 5 min per frame). In each animal, the PET kinetics obtained in baseline conditions were compared with those obtained after OATP inhibition using rifampicin (RIF, 8.6mg/kg) and cyclosporin A (CsA, 15mg/kg/h). ^{11}C -glyburide metabolism and arterial input function were assessed during PET acquisition. The uptake of the radioactivity in each tissue type was estimated using the area under the time-activity curve (AUC) relative to plasma ($\text{AUC}_R = \text{AUC}_{\text{tissue}} / \text{AUC}_{\text{plasma}}$). The transfer of ^{11}C -glyburide from plasma to tissues (k_{uptake}) was estimated from 0 to 12 min (linear part) using an integration plot analysis. Response to inhibition was estimated in each animal as the percentage change in AUC_R and k_{uptake} induced by RIF and CsA. **Results:** ^{11}C -glyburide was slowly metabolized and parent ^{11}C -glyburide accounted for >90% of the plasma radioactivity from 0 to 15 min in all tested conditions. AUC_R was therefore calculated from 0 to 15 min. OATP inhibition resulted in a pronounced decrease in AUC_R in the liver (RIF=88–90%; CsA=94–90%), kidney cortex (RIF=52–71%; CsA=76–71%) and myocardium (RIF=28–60%; CsA=18–69%) but not in the brain and lungs. A decrease in k_{uptake} was consistently observed in the liver (RIF=93–93%; CsA=96–94%), kidney cortex (RIF=53–71%; CsA=87–81%) and myocardium (RIF=10–20%; CsA=60–40%). k_{uptake} could not be estimated (negative slopes) in the brain and lungs. **Conclusion:** ^{11}C -glyburide is metabolically stable in the uptake phase, regardless of the presence of OATP inhibition. Whole-body acquisition, with limited time-resolution, did not allow for accurate estimation of k_{uptake} in organs with low baseline uptake. AUC_R can be used to simultaneously quantify and compare OATP function in different organs of the body.

OP-515

Derivation and Validation of a General Motion Resolution Model for Data-Driven Respiratory Gating in PET

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Purpose/Introduction: Data-driven gating (DDG) methods are promising alternatives to conventional hardware-based respiratory gating methods. However, their motion resolution success is directly dependent on the statistical quality of the PET raw data. We therefore investigated the relation between PET raw data statistics and the success of motion resolution in a study comprising PET/CT and PET/MRI list mode datasets using a DDG approach. **Subjects and Methods:** High-quality single bed position PET list mode data (5 - 10 minutes duration, free breath-

ing) of 19 [^{18}F]FDG PET/CT and PET/MRI scans of patients with at least one organ/lesion of high tracer uptake were retrospectively analysed. A centre-of-mass-based DDG approach was used on the original raw data to calculate gating signals; additionally, only every 2nd, 4th, ..., 128th, and 256th prompt event was used to calculate alternative gating signals. The signal-to-noise ratio **SNR** of every thus determined raw signal was calculated, and every curve was used to perform gated reconstructions of end-expiration and end-inspiration. The respiratory shift vectors **d** of the organs/lesions were determined from the images, and a general motion resolution model relating **d** and **SNR** was derived. This was then validated in additional 25 [^{18}F]FDG PET/MRI datasets with the help of continuously acquired fast sagittal MR slices synchronised to the PET list mode data, giving ground truth internal motion information for additional PET gating. **Results:** All 19 high-quality PET list mode datasets demonstrated highly similar behaviour in terms of motion resolution when reducing the amount of data for signal calculation. The measured respiratory shifts **d** of PET-active organs or lesions could be modelled by $d/d_{\text{max}} = 1 - \exp(-1.5 \cdot \sqrt{\text{SNR}-1})$, with d_{max} as the actual respiratory shift. This general motion resolution model was used to approximate d_{max} in the 25 PET/MRI datasets. Measured DDG shifts were significantly smaller than the MR-based shifts d_{MR} , while there was no significant difference between the extrapolated values d_{max} from the general model and the d_{MR} . Angles between the shift vectors d_{max} and d_{MR} were small, especially for larger vectors. **Discussions/Conclusion:** The **SNR** value of the DDG raw curve was demonstrated to be an objective metric to determine the success of motion resolution. The general motion resolution model allows a reasonable estimate of the actual respiratory shift value even in cases of limited raw data statistics. This might be of interest for personalised high-precision radiotherapy treatment planning of moving targets.

OP-516

Evaluation of Positron Range in the Fibrotic Lung

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Introduction: When a positron is emitted in PET, it travels a short distance before annihilation with an electron. Consequently the detected photons identify the point of annihilation rather than the point of emission. The positron range depends on the energy of the radionuclide used to label the tracer, but also on the density of the surrounding tissue, and is rarely considered in PET image reconstruction of human data. It is well-known that positron range is larger in the normal lung, but rarely studied in diseased lung. Here we concentrate on fibrosis as this disease causes local changes in the density. This work aims at evaluating the influence of positron range on the measured activity in lungs that include localised fibrotic regions for two widely used radionuclides: ^{18}F and ^{68}Ga (maximal positron energies: 0.635MeV and 1.899MeV, respectively). **Methods:** Positron range in the lungs was evaluated using GATE Monte Carlo simulation software. After validating the positron range in homogeneous materials, a high resolution CT image was used to conduct a realistic simulation of the fibrotic lung. The image was cropped and segmented into 14 regions,

according to local density. Each region was assigned a different GATE material, resulting in a spatially-variant composition. A range of materials from normal lung to severe fibrotic lung was used. Activity was assumed to be homogeneously distributed in the lung. Two volume-of-interest (VOI) sizes were used - small ($3 \times 3 \times 3 \text{ mm}^3$) and medium-sized ($9 \times 9 \times 9 \text{ mm}^3$) - at 10 locations: 5 predominantly normal lung and 5 predominantly fibrotic lung (20 VOIs in total). **Results:** Events corresponding to annihilations outside of the phantom were discarded. The “apparent activity”, defined as the mean of regional annihilation events as a percentage of the true positron emission events, was calculated: - 5 small “normal” VOIs (mean HU: -762 ± 32): $96.8\% \pm 1.9\%$ for ^{18}F and $82.7\% \pm 1.8\%$ for ^{68}Ga . - 5 medium-sized “normal” VOIs (mean HU: -718 ± 34): $98.8\% \pm 0.7\%$ for ^{18}F and $90.7\% \pm 3.5\%$ for ^{68}Ga . - 5 small “fibrotic” VOIs (mean HU: -285 ± 74): $107.0\% \pm 2.5\%$ for ^{18}F and $132.8\% \pm 11.2\%$ for ^{68}Ga . - 5 medium-sized “fibrotic” VOIs (mean HU: -495 ± 35): $101.4\% \pm 0.6\%$ for ^{18}F and $107.4\% \pm 2.8\%$ for ^{68}Ga . **Conclusion:** Positron range resulted in bias, especially for ^{68}Ga due to its high-energy positron emission. This may lead to mis-interpretation of clinical studies with artificially-induced contrast between normal and fibrotic regions.

1307 Tuesday, October 16, 2018, 11:30 - 13:00, Hall 1

Pitfalls & Artefacts 6 - Interactive Clinical Cases: Translational Molecular Imaging & Therapy: Is this Uptake Pathological or is it Due to Excretion?

OP-517

CT Findings of the Excretory System

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OP-518

Excretory System and Radiopharmaceuticals

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OP-519

Pitfalls from Liver and Bowel

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OP-520

Pitfalls from Nephro-Urinary System

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1308 Tuesday, October 16, 2018, 11:30 - 13:00, Hall 4

Clinical Oncology - Rapid Fire Session: Lung! Lung! Lung!

OP-521

Hot-to-Global Volume Ratio (HGVR): To predict PD-L1 tumoral expression, its correlation to necrosis and

outcome in NSCLC patients treated with checkpoint inhibitors using standard FDG PET/CT

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Purpose: Humanized anti-PD-L1 or anti-PD-1 IgG1 monoclonal antibody can restore tumor-specific T-cell immunity by inhibiting the binding of PD-L1 to PD-1. It is considered as an emerging therapy in non-small cell lung cancer (NSCLC). Herein, we investigate the correlation of known and new metabolic markers on ^{18}F -FDG-PET/CT with tumoral tissue expression of PD-L1, tumor necrosis (TN) and radiological outcome using iRECIST in patients under checkpoint inhibitor treatment. **Materials and methods:** All patients with confirmed NSCLC who were investigated by immunohistochemistry (IHC) for PD-L1 on biopsy sample or on resection specimen and who had an FDG-PET prior to surgery or biopsy, were retrospectively included in the study. From January 2016 to March 2017, 50 patients were investigated. Sampled surgical and biopsy tumor specimens were analyzed by immunohistochemistry (IHC) for PD-L1 tumor expression and TN. ^{18}F -FDG-PET images were analyzed for SUVmax, SUVmean, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) with a threshold of 42% of the maximum SUV signal intensity for the biopsied or resected tumor lesion. Metabolic information on ^{18}F -FDG-PET/CT was correlated using Spearman rank correlation with the positivity of expression of PD-L1 in corresponding tissue and TN. Finally, the ratio of morphologic and metabolic lesion volumes (HGVR) was calculated and correlated to PD-L1 expression of the respective lesion and all obtained imaging variables of FDG-PET were correlated to radiological outcomes on follow-up after targeted anti-PD-1/PD-L1 therapy by iRECIST criteria using Spearman's rank correlation. **Results:** 25/49 adenocarcinomas (ADC) and 24/49 squamous cell carcinomas (SCC) were analyzed. All tumors showed metabolic FDG-PET uptake with mean SUVmax 13.3 g/ml (range:3.3-28.1), SUVmean 7.4 g/ml (range:1.9-16.3), MTV 50.3 cm³ (range:1.2-456) and TLG 284 g·cm³/mL (range:5.0-2,233). We found a statistically significant correlation analysis only for the proposed HGVR ($R=0.618$, $p<0.005$) -but not MTV ($R=-0.042$, $p=0.773$), TLG ($R=0.139$, $p=0.34$), morphologic tumoral volume ($R=0.21$, $p=0.15$), SUVmax ($R=0.171$, $p=0.24$) and SUVmean ($R=0.119$, $p=0.42$) - and PD-L1 tumor expression. PD-L1 expression was significantly higher in patients with TN ($p=0.48$) and correlated to percent of necrosis ($R=0.438$, $p=0.032$). Only PD-L1 expression and HGVR were significantly correlated to radiological outcome using iRECIST criteria ($p=0.017$ and $p=0.042$, respectively). **Conclusion:** This study shows a positive correlation between PD-L1 expression and TN. HGVR, a novel imaging marker evaluating FDG avid versus non-FDG avid necrotic tumor lesions, is significantly correlated with tumoral PD-L1 expression and radiological outcome by iRECIST in NSCLC patients under checkpoint inhibitor treatment.

OP-522

Predictive And Prognostic Role Of Metabolic Response In Patients With Non-Small Cell Lung Carcinoma (NSCLC) Treated With Neo-adjuvant Chemotherapy

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Introduction: NSCLC is still a challenging disease to treat, since recurrences are common even in the earliest stages. Our study aimed to assess the predictive and prognostic role of metabolic response measured by 18F-FDG PET/CT in NSCLC after neoadjuvant therapy. **Methods:** Overall, 75 NSCLC patients treated with neoadjuvant regimen were retrospectively identified. Patients performed an 18F-FDG PET/CT scan before and after three cycles of chemotherapy. PET data were analyzed for the following parameters: SUVmax, SUVmean, MTV, and TLG, as well as the relative changes during treatment, both on primary tumor (T) and regional lymph nodes (N). The association between PET parameters and pathologic response was analyzed in 45 (60%) patients submitted to surgery. Cox proportional hazards regression models were used to evaluate clinical variables and PET parameters as predictors of PFS and OS. **Results:** We found a significant positive correlation between T status and SUVmax ($\rho=0.40$, $p=0.001$), SUVmean ($\rho=0.41$, $p<0.001$), MTV ($\rho=0.47$, $p<0.001$), and TLG ($\rho=0.48$, $p<0.001$) after neoadjuvant therapy. In resected NSCLC patients, persistent pathologic N+ was present in 51% (23 out of 45), while PET N- status was demonstrated in 53% (24 out of 45). The sensitivity, specificity, and accuracy of post-neoadjuvant chemotherapy PET for N status were 65%, 73%, and 69%, respectively. Median survival was 11 months. Univariate analysis showed that stage, %change of MTV and TLG for T were significant parameters for PFS ($p=0.003$, $p=0.004$, respectively). Likewise, post-neoadjuvant PET parameters on N status for PFS: SUVmax ($p=0.006$), SUVmean ($p=0.004$), MTV ($p<0.001$), and TLG ($p<0.001$). On the other hand, univariate analysis for OS demonstrated %change of N status, SUVmax, MTV and TLG being significant prognostic factors, while no association for T status was found. Multivariate stepwise analysis showed that stage (HR=9.7; 95% CI, 2.0 to 46.9; $p=0.005$), %change of MTV (HR=1.012; 95% CI, 1.003 to 1.020; $p=0.008$) for T status and %change of TLG (HR=1.009; 95% CI, 1.003 to 1.016; $p=0.003$) for N status were predictors for PFS. Multivariate analysis for OS showed that MTV for N status, both as absolute value or %change, was a significant prognostic factor (HR=1.065; 95% CI, 1.018 to 1.113; $p=0.006$ and HR=1.003; 95% CI, 1.000 to 1.006; $p=0.021$, respectively). **Conclusions:** Metabolic response after neoadjuvant chemotherapy is associated with pathologic response of T and N disease. Additionally, PET parameters of primary tumor and regional lymph nodes results predictors of PFS, whereas only MTV for lymph nodes resulted a prognostic factor for OS.

OP-523

Phase 0/1 of Positron Emission Tomography (PET) imaging agent [18F]-ODS2004436 as a marker of EGFR mutation in patients with non-small cell lung cancer (NSCLC)

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Background: Multiple EGFR tyrosine kinase inhibitors (TKIs) are approved for treatment of NSCLC harboring EGFR activating mutations or secondary TKIs resistant mutation. Our objective is to evaluate the sensitivity and specificity of a new PET radiotracer targeting specifically activated EGFR in a phase 0/1 clinical trial (NCT02847377) to be used as dynamic imaging biomarker in order to predict responsiveness to EGFR TKI in patients with NSCLC. **Methods:** This trial is divided into 3 steps according to the genetic profile of primary tumours. Step 1: inclusion of 8 patients harboring EGFR activating mutation. PET/CT with [18F]-ODS2004436 was performed at baseline (before treatment), and 7 days after beginning of treatment by EGFR TKI in order to calculate changes in the tumour radiotracer uptake. A significant tumour uptake on at least 6 patients with EGFR mutation is required (sensitivity > 75%). Step 2: enrollment of 6 patients without EGFR mutation (wild type). PET is performed only at baseline. Step 3: enrollment of 4 others patients with EGFR mutation. The primary endpoint is to obtain data on sensitivity and specificity of [18F]-ODS2004436 regarding EGFR activating mutations. The Secondary objectives are to validate the binding competition of [18F]-ODS2004436 in mutated patient treated by TKI, and to evaluate dosimetry and safety. Comparison with standard clinical FDG PET/CT before inclusion is planned. **Results:** Currently 8 patients have been included in step 1 and 5 in step 2. All patients in step 1 (EGFR mutation) exhibited significant uptake in primary tumours and metastases (median SUV_{ratio} between tumour and background=2.6; range 1.6 to 4.2), and reduced uptake after one week of TKI treatment (Median ΔSUV_{ratio} = -56%, range -78 to -32). In 2 patients this radiotracer allowed the observation of brain metastases that were not detected with FDG PET/CT. Concerning step 2 (EGFR WT), all patients except one showed absence of uptake in primary tumour and metastases (median SUV_{ratio} = 1.16, range 1.03-1.3). For the one patient exhibiting significant tumour uptake despite EGFR wild type (SUV_{ratio} = 3.6), TKI treatment was introduced during only one week and a second [18F]-ODS2004436 PET/CT, performed immediately after, showed significant reduction of tumour uptake (ΔSUV_{ratio} = -46%), suggesting presence of targets for TKI. **Conclusion:** This first in man study of [18F]-ODS2004436 proves the high sensitivity and specificity of this novel PET radiotracer and drives the clinical positioning for the next clinical trial as a companion biomarker to identify patients responder or resistant to EGFR TKI.

OP-524

¹⁸F-FLT PET/CT imaging of inositol trisphosphate receptor type 3-mediated enhancement of EGFR and MET co-targeting efficacy in non-small cell lung cancer

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Purpose: Co-targeting of EGFR and MET receptors in patients with oncogene-driven non-small cell lung cancer (NSCLC) is a strategy currently adopted in clinical trials to potentially improve therapeutic benefit and to prevent the overcoming of resistance. Here we tested whether imaging with ^{18}F -fluorothymidine (^{18}F -FLT) PET/CT was able to detect the combined effects of EGFR and MET inhibitors in resistant NSCLC and investigated the mechanisms underlying the enhanced efficacy of drug combination. **Methods:** NSCLC H1993 cells bearing high level of MET amplification were treated with EGFR and MET inhibitors either alone or in combination and then tested for cell viability and inhibition of signaling pathways. Nude mice bearing H1993 tumors underwent ^{18}F -FLT PET/CT scan before and after treatment with erlotinib and crizotinib alone or in combination (1:1 ratio) and post-treatment changes of ^{18}F -FLT uptake in tumors were determined. The role of inositol trisphosphate receptor type 3 (IP3R3) in mediating the combined action of EGFR and MET inhibitors was tested by transfecting NSCLC cells with IP3R3-targeted siRNA. **Results:** Imaging studies showed a significant reduction of ^{18}F -FLT uptake in response to combined treatment with EGFR and MET inhibitors that was higher than that obtained with single agents (ANOVA, F ratio=6.215, $p=0.001$). Imaging findings were confirmed by analysis of surgically excised tumors. Since levels of IP3R3 were drastically reduced in both cells and tumors after treatment with crizotinib, H1993 cells transfected with IP3R3-targeted siRNA were treated with erlotinib and crizotinib and both agents caused a reduction of K-Ras levels, indicating that both drugs were able to modulate K-Ras when IP3R3 is downregulated. Finally, immunoprecipitation of untreated and treated samples showed that erlotinib was able to reduce the interaction of IP3R3 with K-Ras mainly through dephosphorylation of serine residues of K-Ras. **Conclusion:** Our findings indicate that ^{18}F -FLT PET/CT is able to detect the enhanced efficacy of EGFR and MET inhibitors in oncogene-driven NSCLC and that such enhancement is mediated by IP3R3 through its interaction with K-Ras.

OP-525

Solitary Pulmonary Nodule (SPN) and pre-test likelihood of malignancy: the role of FDG-PET/CT in the Italian Tailored Assessment of Lung Indeterminate Accidental Nodule (ITALIAN) trial

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Purpose: No data exists on the spread of the disease at SPN presentation correlated with pre-test cancer-risk. The aim of the study was to assess the role of FDG-PET/CT in patients with SPN who were stratified by the pre-test risk. **Materials and Methods:** Scans for the characterization of SPN in 502 consecutive patients of thirteen Italian centers were retrospectively collected. Staging of lung cancer were excluded. Patients were stratified in low (<5%), intermediate (5%–65%) and high (>65%) risk category using the Brock model. FDG uptake in SPN was visually assessed by a 4-point scoring system. Final diagnosis was established by histopathology or follow-up. Data were evaluated by chi-square and logistic analysis. **Results:** Mean±SD age of study population (60% male) was 67±12 years. Based on standard of reference, 180 (36%) patients had malignant, 175 (35%) benign and 147 (29%) indeterminate disease. Patients were in low, intermediate and high category risk in 15%, 77% and 8%, respectively. The FDG uptake in SPN increased progressively from low to high risk patients ($p<0.0001$). Overall, 436 patients (87%) did not have metastases, 66 (13%) had thoracic metastases (47 only lymph node), and 13 (3%) had extra-thoracic lesions. None of patients at low pre-test risk had an extra-thoracic disease; however, it was present in patients at intermediate (3%) and high (5%) pre-test risk. Patients with extra-thoracic lesions had a significantly higher Brock risk (29 vs 46, $p<0.01$). All patients with extra-thoracic lesions had both FDG uptake in SPN equal to 4 and thoracic lymph node involvement (negative predictive value equal to 100%). By excluding patients with indeterminate SPN, 71% of subjects at low pre-test risk and a negative PET/CT scan, showed a benign SPN; conversely 95% of patients at intermediate-high pre-test risk and with a positive FDG PET/CT had a malignant SPN. **Conclusions:** ITALIAN, the largest PET/CT trial in SPN clinical presentation, highlights the role of assessment of risk before diagnostic imaging. None of patient in low-risk category had extra-thoracic lesions. All patients with distant lesions, had both a high FDG uptake in SPN and a thoracic lymph node involvement. These data make it conceivable an initial limited chest PET/CT strategy in low-risk patients.

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The role of 18F-FDG PET/CT over clinical data in patients with single pulmonary nodule (SPN): results from the Italian Tailored Assessment of Lung Indeterminate Accidental Nodule (ITALIAN) multicenter trial

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Purpose: This study assessed the additional role of ¹⁸F-FDG PET/CT over clinical/morphological data in the definition of likelihood of malignancy in patients with SPN. **Material and Methods:** The study population included 355 consecutive patients with one or more SPN previously identified by CT images, defined as lung nodule with a size ≤ 3 cm who were sent to ¹⁸F-FDG PET/CT for the characterization of the nodule/nodules. Patients with prior cancer history and those candidates to ¹⁸F-FDG PET/CT for the staging of lung cancer were excluded. SPN malignancy risk was calculated by using the Brock University cancer prediction equation (as pre-PET probability of malignancy) and the Herder Solitary Pulmonary Nodule Malignancy Risk Calculator (as post-PET probability of malignancy). According to the pre-PET and post-PET likelihood of SPN malignancy, patients were classified into low-likelihood (<5%), intermediate-likelihood (5%–65%), and high-likelihood (>65%) subsets. The difference between correct and incorrect reclassification according to patient outcome was defined as the net reclassification improvement (NRI). Final diagnosis of SPN was established by histopathology and/or by other imaging data at follow-up. Assuming independence between individuals with benign or malignant SPN and following McNemar's logic for significance testing in correlated proportions, a simple asymptotic test for the null hypothesis of NRI=0 was used (z test). **Results:** According to the pre-PET likelihood of malignancy, 47 (13.2%) patients were at low, 277 (78%) at intermediate and 31 (8.8%) at high risk of malignant SPN. Conversely, based on the post-PET likelihood of malignancy, 85 (23.9%) were at low, 123 (34.6%) at intermediate and 147 (41.5%) at high likelihood of malignant SPN. Based on the standard of reference, 175 patients had a benign and 180 a malignant SPN. In overall patients, the NRI was 78% ($z=10.0$; $p<0.0001$). Out of 126 patients at intermediate pre-PET likelihood of malignancy who had a benign SPN, 47 (37%) shifted in the low post-PET likelihood. Moreover, out of the 151 patients at intermediate pre-PET likelihood of malignancy who had a malignant SPN, 111 (73.5%) shifted in the high post-PET likelihood. **Conclusions:** This study demonstrates that patients with a malignant SPN are better stratified by an algorithm including ¹⁸F-FDG PET/CT imaging than using only clinical/morphological variables. In fact, a substantial number of patients considered at intermediate pre-PET likelihood of malignancy are re-classified as at high or low risk, based on the PET findings.

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Detection of small pulmonary nodules with respiratory-gated PET/MR

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Purpose: To assess diagnostic sensitivity of MR sequences (STIR, FIESTA, LAVA FLEX, DWI) and FDG-PET for detection of pulmonary nodules (PN) using a respiratory gated simultaneous PET/MR system, taking FDG-PET/CT and CT lung imaging as a reference. **Subjects & Methods:** 20 cancer patients and PN, were studied using FDG-PET/CT and CT thorax scans followed by PET/MR imaging including PET_{gated}, STIR_{gated}, LAVA FLEX, FIESTA, SSFSE and DWI. Two reviewers identified nodules and performed measurements on both CT and MR images. The presence of nodules and FDG avidity were also evaluated on PET/CT and PET/MR images. The sensitivity of PET_{gated} and MR for PN detection was compared with PET/CT imaging. Maximum Standardized Uptake Value (SUV_{max}) in pulmonary nodules was also measured for the two systems. **Results:** A total of 69 nodules were detected with CT, mean nodule diameter $\pm$ standard deviation was 5.95 ± 2.95 (range, 1.8–15.8mm). Sensitivity for PN detection in MR sequences (S_{NP-MR}) for STIR_{gated}, LAVA FLEX, FIESTA, SSFSE were: in PN greater than 8mm ($n=16$) a $S_{NP-MR mean} = 94.95\%$ and PN between 4–8mm ($n=32$) an $S_{NP-MR mean} = 76.22\%$. For PN smaller than 4 mm ($n=19$) the $S_{NP-MR} = 63.15\%$ for STIR_{gated} sequence, being the minimum detected size 2.5mm. The PN sizes between MR and CT showed a Pearson correlation of 0.88 with $p < 0.0001$. From PET images, 35 avid FDG nodules were detected in PET/CT versus 51 PN in PET/MR triggered, an average sensitivity of PET/CT versus PET/MR ($S_{PETCT/PETMR} = 69\%$). For PN smaller than 4mm the $S_{PETCT/PETMR} = 45\%$, PN 4mm–6mm $S_{PETCT/PETMR} = 81\%$ and PN larger than 8mm $S_{PETCT/PETMR} = 93\%$. The smallest avid size was 3.1 mm in the PET/MR system. **Conclusions:** A respiratory-gated PET/MRI scan protocol shows great potential for detecting micro-nodular metastatic lesions, as well as small primary lung tumors in oncological patients. A large percentage of those lesions would be missed in ordinary routine PET/MR scans. The performance of the STIR sequence for PN below 4mm is highlighted by detecting 2.5mm nodules and providing reliable measurements of PN size. The minimum size detected for a metabolic PN by triggered PET/MRI is approximately 3.1 mm.

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Prognostic Significance of 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Derived Metabolic Parameters in Surgically Resected Clinical N0 Non-Small-Cell Lung Cancer

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Purpose: Although surgical resection remains the choice of treatment for early-stage non-small-cell lung cancer (NSCLC), recurrence, death rate of patients with stage I–II NSCLC with-in postoperative 5 years is reported to be high. Heterogeneous prognosis of NSCLC requires consideration of individual clinicopathological, tumor-specific factors for choosing the best treat-

ment, follow-up planning. We evaluated the significance of metabolic PET parameters for the prediction of occult mediastinal lymph node metastasis (OLM) and recurrence in patients with clinical-N0 NSCLC after curative surgical resection, lymph node dissection. **Subjects & Methods:** We evaluated 98 patients with NSCLC; 52 adenocarcinoma (ADC), 46 squamous-cell carcinoma (SQCC) who had undergone initial FDG PET/CT. Eligibility criteria for participation were clinically staged as N0, no FDG uptake in mediastinal lymph nodes on preoperative 18F-FDG PET/CT, surgically treated, properly followed-up more than 2 years. Clinicopathological characteristics, diagnosis of recurrence were retrieved from the Department of Thoracic Surgery records. Metabolic parameters were determined on initial FDG PET/CT. Association of metabolic parameters with OLM, recurrence was assessed. **Results:** OLM was found in 26 (26.53 %) of patients. T stage, central location, lymphovascular invasion were associated with OLM (respectively, $p = 0.007$, $p = 0.011$, $p < 0.001$). None of the metabolic parameters were associated with OLM. Metabolic parameters (SUVmax, SUVmean, MTV, and TLG) of the tumor were significantly higher in patients with recurrence when the cohort was evaluated as a whole ($p = 0.002$, 0.005 , 0.016 , 0.004 , respectively). In particular evaluation; A significant association between recurrence and tumor size, histological grade, TNM stage, MTV ($p < 0.001$), TLG ($p < 0.001$) was detected in ADC. We could not determine this kind of association in SQCC. Multivariate Cox proportional hazards analysis determined that only MTV was an independent prognostic factor for recurrence in ADC (hazard ratio=1.4, 95% confidence interval=1.054–1.906, $p = 0.021$). The optimal cutoff value was determined as 4.99 for MTV with 93.7% sensitivity, 85.7% specificity (AUC: 0.876). Kaplan-Mayer survival analysis determined that disease free survival (DFS) in ≤ 4.99 cm³ MTV group was significantly higher than > 4.99 cm³ MTV group (69.79 ± 2.16 vs. 27.04 ± 5.24 months, $p < 0.001$). **Conclusions:** Metabolic parameters of primary tumor on preoperative F-18 FDG PET/CT cannot predict OLM in patients with clinical-N0 NSCLC. MTV is an independent risk factor for recurrence in ADC and associated with DFS, but this association is not substantial for SQCC. Our results suggest that MTV is a promising independent parameter associated with prognosis in clinical-N0 surgically resected ADC.

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Correlation of endobronchial ultrasound with new predictor variables on positron emission tomography in lung cancer. Preliminary analysis

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Introduction: In the diagnosis and staging of non-small cell lung cancer (NSCLC), positron emission tomography (PET) is usually performed prior to endobronchial ultrasound (EBUS).

The low specificity of PET can lead to unnecessary tests. Alternative variables have been postulated. Aim: to correlate EBUS and PET results to search new variables. **Subjects & Methods:** Patients undergoing EBUS in the NSCLC management were prospectively included from December-2017 to March-2018. Patients with other diagnoses (other tumors, sarcoidosis) were excluded. A descriptive analysis was carried out, sensitivity (Se), specificity (Sp), positive (VPP) and negative predictive values (VPN) were calculated. Kruskal-Wallis test was used to compare, as well as ROC curves. **Results:** Forty-two patients were included. Samples from 117 lymph node stations were taken with the following maximum standard uptake values for adenopathies (SUV_A): 4R (n = 19, SUV_A = 4.67 ± 3.79), 4L (n = 14, SUV_A = 3.15 ± 2.16), 7 (n = 29, SUV_A = 4.38 ± 3.74), 10R (n = 5, SUV_A = 2.70 ± 0.46), 10L (n = 3, SUV_A = 9.53 ± 8.44), 11R (n = 23, SUV_A = 5.01 ± 4.06), 11L (n = 21, SUV_A = 4.77 ± 2.39) and 12R (N = 3, SUV_A = 5.88 ± 0). The SUVmax of tumors (SUV_T) was 14.62 ± 8.18 and the SUVmax of the mediastinum (SUV_M) 2.29 ± 0.45 . Taking a SUV_A > 2.5 as a cut-off for malignancy, the Se = 94%, Sp = 25%, PPV = 23% and NPV = 94%. New variables have been postulated like the ratio of SUV_A to SUV_T (SUV_{A/T}) or SUV_M (SUV_{A/M}). When we use a published cut-off (SUV_{A/T} > 0.4) then Se = 91%, while there is an increase in Sp = 69%, VPP = 48% and NPV = 96%. SUV_A values are clearly higher in stations with positive result in EBUS, however there were not found statistically significant differences (3.46 ± 1.61 vs 9.89 ± 5.39). Neither when using SUV_{A/T} (0.34 ± 0.28 vs 1.26 ± 1.07) or SUV_{A/M} (1.67 ± 0.91 vs 4.99 ± 2.45). When performing a ROC curve, the values of the area under the curve were 0.86 for the SUV_A, 0.83 for the SUV_{A/T} y 0.85 for the SUV_{A/M}. **Conclusions:** 1. New variables such as SUV_{A/T} > 0.4 could help optimize PET results and decrease false positives, mainly in the low values of SUV_A. 2. However, a larger sample is needed to achieve statistical significance and to use it in clinical practice.

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Mediastinal lymph node staging in suspected lung cancer: preliminary comparison of positron emission tomography with F-18-fluorodeoxyglucose and specific EBUS sonographic characteristics

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Aim: Accurate staging of mediastinal and hilar lymph nodes is essential for determining operability in patients with non-small cell lung cancer (NSCLC). Positron emission tomography using 2-[18F] fluoro-2-deoxy-D-glucose (FDG-PET) is widely reported as being effective in detecting tumor involvement but suffers from lack of specificity in lymph nodes undergoing reactive changes in response to inflammatory or immune reactions. More recently the individual sonographic features of lymph nodes assessed by endobronchial ultrasound (EBUS) have hypothesized to be a useful tool in differentiating malignant from benign lymph nodes, but its accuracy has still to be established. The present work was devised with an aim of comparing the

metabolic and ultrasonographic features of mediastinal and hilar lymphadenopathy in the thoracic lymph node staging of NSCLC. **Materials and methods:** In the present pilot study 26 patients (age 52+/-9 years) with suspected NSCLC were included and underwent both FDG-PET and EBUS preoperative scanning. Surgical staging was performed within 6 weeks after the imaging procedures. Evaluation of lymph node stations was performed for EBUS accessible thoracic level (2L/R, 4L/R, 7 and 11L/R) in both modalities using a semiquantitative scoring system. FDG-PET total body emission scans were acquired 64 +/- 13 minutes after injection of 385 +/- 30 MBq of fluorodeoxyglucose. FDG-Scoring was based on visual interpretation of FDG-Uptake using mediastinal blood pool and liver as the two reference scaling organs in a five-point scale for FDG-avidity. The EBUS-Scoring used also a semiquantitative four-point visual scale based on sonographic features including size, shape, calcification, hilar structure, necrosis sign, margins, echogenicity and vascular patterns. The sonographic and FDG-PET findings were confirmed by the final pathology results and clinical follow-up. The diagnostic performance of both imaging techniques was analyzed using a ROC surface assessment. **Results:** Of the 26 patients, 11 had confirmed lymph node metastasis on histopathology. ROC-Analysis of EBUS-scores generated an area under the curve (AUC) of 0.994. Estimation of AUC for the FDG-data was 0.904. The statistical comparison of the two ROC-curve estimates from paired datasets showed a good correlation between EBUS and FDG-PET scores ($p = 0.017$). **Conclusion:** Semi-quantitative scores based on sonographic features of the EBUS images or FDG-uptake surely helps predict intrathoracic lymph nodes metastasis in lung cancer patients. Combined multimodal scores may further help differentiate metastatic from reactive lymph nodes. Ongoing clinical follow-up as well as further inclusions are needed to reduce sampling errors.

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Correlation of immunohistochemical parameters, apparent diffusion coefficient (ADC) and standardized uptake value (SUV) in lung cancer using hybrid PET/MRI

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Purpose: To correlate various prognostically relevant immunohistochemical parameters of primary lung cancer with simultaneously acquired standardized uptake values (SUV) and apparent diffusion coefficient (ADC) derived from hybrid PET/MRI. **Material and methods:** 55 consecutive patients with histologically proven lung cancer (mean age 62.5±9.1 years) underwent PET/MRI using 18F-fluorodeoxyglucose (18F-FDG) as radiotracer. As part of the diagnostic imaging protocol, diffusion-weighted imaging (DWI, b values: 0, 500, 1000 s/mm²) was performed simultaneously with PET acquisition. A region of interest (ROI) encompassing the entire primary tumor was

drawn into each patient's PET/MR images to determine the glucose metabolism represented by maximum and mean SUV and also into ADC maps to assess tumor cellularity represented by mean and minimum ADC values. Histopathological tumor grading was available in 43/55 patients. In 15/55 patients, additional prognostically relevant immunohistochemical markers, i.e. phospho-AKT Ser473 (pAKTS473), phosphorylated extracellular signal-regulated kinase (pERK), phosphatase and tensin homolog (PTEN), and human epidermal growth factor receptor 2 (erbB2) were determined. Pearson's correlation coefficients were calculated to compare SUV and ADC values, while Spearman's correlation coefficients were used for the immunohistochemical markers. **Results:** The average SUVmax, SUVmean, ADCmin, and ADCmean in lung cancer primaries was 12.6±5.9, 7.7±4.6, 569.9±96.1 s/mm², and 825.8±93.2 s/mm², respectively. We found a significant inverse correlation between the ADCmin and SUVmax ($r=-0.58$, $p<0.001$) as well as between the ADCmin and SUVmean ($r=-0.44$, $p<0.001$). Tumor grading showed a significant positive correlation with SUVmax and SUVmean ($r=0.34$ and $r=0.31$, both $p<0.05$) and a significant inverse correlation with ADCmin and ADCmean ($r=-0.30$ and $r=-0.40$, both $p<0.05$). In addition, erbB2 showed a significant inverse correlation with SUVmax and SUVmean ($r=-0.50$ and $r=-0.49$, both $p<0.05$). There was no significant correlation with other immunohistochemical markers. **Conclusion:** The present data show a correlation between increased glucose-metabolism, cellularity, degree of differentiation as well as erbB2 expression of lung cancer primaries. 18F-FDG-PET and DWI from hybrid PET/MRI may offer complementary information for evaluation of lung cancer aggressiveness in initial staging and treatment response.

OP-532

Application of Convolutional Neural Networks is promising in the definition of T-stage in lung cancer

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Convolutional neural networks (CNNs) are machine learning algorithms relying on convolution and pooling operations, that identify relevant features on the images that allow them to classify an input object. They have been applied in medical imaging for lesion detection, segmentation and diagnostic tasks. The aim of the present study was to develop an algorithm, based on a CNN, for the classification of lung cancer lesions as T1-T2 or T3-T4 on staging FDG-PET/CT images. **Methods:** A cohort of 632 patients submitted to FDG-PET/CT, over a 6-year period, for the purpose of staging a suspected lung cancer, within 60 days before biopsy or surgery, was retrospectively selected. TNM classification system 7th edition was used as reference. Staging was pathological and clinical in 390 and 242 cases, respectively. Four hundred thirty-two and 200 patients resulted to be T1-T2 and T3-T4, respectively. To develop the algorithm a 5-fold cross-validation was used. For the final model the entire cohort was randomly divided in training ($n=405$), validation ($n=101$) and test ($n=126$) sets. Post-acquisition processing and data augmenta-

tion were performed. The input of the CNN were two bounding boxes, on PET and CT images, cropped around the lesion centre. The results were classified as Correct (concordance between reference and prediction), and Incorrect (discordance between reference and prediction). Accuracy (Correct/[Correct+Incorrect]), recall (Correctly predicted T3-T4/[all T3-T4]), and specificity (Correctly predicted T1-T2/[all T1-T2]), as commonly defined in deep learning models, were used to evaluate algorithm performance. **Results:** We developed an algorithm composed of two networks: a “feature extractor” (CNN) and a “classifier”. The mean cross-validation accuracy resulted 83% and 77% in the training and validation sets, respectively. The final model algorithm achieved an accuracy of 84%, 76% and 70% in the training, validation and test set, respectively. The recall resulted 79%, 62% and 62% in the training, validation and test set, respectively; specificity resulted 86%, 83% and 73% in the training, validation and test set, respectively, for the classification as T1-T2 or T3-T4 of lung cancer lesions. **Conclusion:** We obtained proof of concept that CNNs can be used as tools to assist lung cancer staging. The development of an algorithm based on CNNs able to automatically stage and perform risk assessment of the patient, on FDG-PET/CT, will allow more reproducible use of imaging data and to guide treatment. Moreover, improvement in risk stratification is expected with the incorporation of clinical data in the neural network algorithm.

1309 Tuesday, October 16, 2018, 11:30 - 12:45, Hall 6

Thyroid - Featured Session: Thyroid Scintigraphy - An Evergreen

OP-533

Thyroid Scintigraphy, Basis, Image Quantification - Current Role and Perspectives

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Value of 20-Minute Tc-99m Per technetate Uptake in Predicting Biochemical Response in Patients with Graves Disease Treated with Radioiodine

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Aim: Tc-99m per technetate scan is routine practice in evaluation of patients with hyperthyroidism. In our ongoing retrospective study with long-term follow-up, we present preliminary findings and evaluate the role of Tc-99m per technetate uptake in patients treated with radioiodine for Graves disease. **Material and methodology:** After applying stringent inclusion criteria, 67 patients (mean±SD, 38±11.5 years, 46 females) were included in this preliminary analysis. Multiple factors like age, duration of symptoms, antithyroid drug (ATD) intake, radiotracer uptake modality used (per technetate uptake at 20 minute and I-131 uptake at 4, 24 and 48 hours) were considered. Normally distributed data was represented as mean±SD; otherwise as median and range. Achievement of biochemical hypothyroidism/euthy-

roidism were chosen as target outcomes. ROC and regression analyses were used to identify predictors of outcome. P value < 0.05 was considered statistically significant. **Results:** Median follow-up duration was 28 months (range 3 - 145 months). Median serum TSH was 0.56 µIU/mL (range 0 - 14.8). Fifty one patients were biochemically thyrotoxic, 14 were euthyroid and 2 were hypothyroid at the time of radioiodine treatment. Median ATD intake duration was 3 years (range 2 months - 14 years). All patients underwent either Tc-99m per technetate uptake or I-131 radioiodine uptake prior to radioiodine therapy. Median first therapeutic dosage of radioiodine was 8.45 mCi (range 4.5 - 17 mCi). During follow-up, fifteen patients needed retreatment (mean cumulative dosage 21.6±8.68 mCi). Three patients were excluded from analysis due to refractory thyrotoxicosis during follow-up. Out of remaining 64 patients, 16 patients underwent I-131 uptake (RAIU) while 48 underwent Tc-99m uptake for pre-treatment evaluation. In RAIU group, clinical effect was completed in shorter duration (median 6 months, range 3 - 51 months) compared to Tc-99m uptake group (median 9 months, range 3 - 31 months). Proportion of biochemical euthyroidism to hypothyroidism was identical in both groups (75% hypothyroid, 25% euthyroid). On ROC analysis, 24-hour and 48-hour RAIU values were equally reliable (AUC 0.854) and marginally better than 4-hour (AUC 0.833) values in predicting hypothyroidism; Tc-99m uptake was a poor predictor (AUC 0.397). However linear regression analysis revealed that combination of Tc-99m uptake and first therapeutic dosage of I-131 predicted the duration to achieve biochemical euthyroidism/hypothyroidism (p = 0.038). **Conclusion:** Tc-99m per technetate uptake underperforms in predicting biochemical hypothyroidism in patients treated for Graves disease with radioiodine. However, regression analysis shows that in conjunction with first therapeutic dosage of radioiodine, it predicts the duration to achieve biochemical euthyroidism/hypothyroidism.

OP-535

Technetium thyroid scintigraphy predicts the outcome in Graves disease patients on antithyroid medications

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Background: Technetium thyroid scintigraphy (TcO4) is routinely used in hyperthyroidism to characterise the disease etiology and decide on low dose I 131 therapy. Literature search fails to provide insight whether TcO4 thyroid scintigraphy can predict remission/relapse in Graves disease (GD) pts on drug therapy.

Aim: To establish if TcO4 scintigraphy has a role in predicting remission and relapse in documented Graves disease pts on antithyroid medications (ATD). **Materials & Methods:** 174 pts with a) confirmed hyperthyroidism biochemically with scintigraphic evidence of GD b) remitters at least 1½ years followup after achieving remission c) pts more than 12 yrs of age were included. Records of 174 GD pts who presented to our hospital from Jan 2006 to 14 were analyzed. Variables included Age, gender, smoking history, goiter at presentation and 1 year after initiating therapy, treatment duration before scintigraphy, uptake, free T4 at diagnosis, total treatment duration, maximum dose

of ATDs used, duration of maximum dose of ATD, time taken for normalization of TFT after ATD initiation, time to normalization of TFT multiplied by the dose used for same, time taken to reach the minimum dose of ATD, remission, relapse at < 1 yr & after 1 yr, low dose I 131 therapy, presence of ophthalmopathy, dermopathy. Data compared between remitters & non- remitters. Mann-Whitney Utest and Chisquare tests used to compare the groups statistically. **Results:** 57/174 (32.7%) pts attained remission after at least 1 year of thionamide therapy. Of these, 11 (19.2%) pts relapsed within 1 year. Age, gender, goiter and presence of extrathyroidal manifestations were not associated with remission. Time to achieving normal thyroid function & composite dose studied. Time scores were significantly associated with remission (P 0.05 and P 0.01, respectively). Pts with lower free T4 at presentation had higher chance of remission (P 0.01). Those who remitted had faster normalization of thyroid function. Relapse rates were lower than previously reported in literature in our population. Pts with relapse (12.4% vs. 5.9%) had higher thyroid trapping function (P 0.009). **Conclusion:** Prognostic factors associated with remission in GD in this Indian study differ from Western reports and were lower. TcO4 thyroid scintigraphy has a new additional and incremental role in identifying pts who are likely to undergo remission & thus predict outcome of Graves' disease in pts on ATD.

OP-536

Ultrasound classification of autonomously functioning thyroid nodules

C. Braun, M. Luster, F. Verburg; University Hospital Marburg, Marburg, GERMANY.

Introduction: Several risk stratification systems for the ultrasound risk stratification of thyroid nodules, like TIRADS, ATA, EU-TIRADS and Korean-TIRADS, exist in parallel. These systems have largely been developed and validated in countries with iodine sufficiency. Autonomously functioning thyroid nodules (AFTN) cannot be identified with thyroid ultrasound as they are indistinguishable from other nodular lesions. Although benign, on cytological examination they may appear as follicular lesions of undetermined significance, which as a consequence would result in the indication for unnecessary surgery. The aim of this study is the assessment of the ultrasound classification of AFTN using the above-mentioned risk stratification systems. **Patients & Methods:** Retrospective study of 93 patients who received I-131 therapy for AFTN at the Department of Nuclear Medicine of our University Hospital between January 2014 and May 2017. The ultrasound images of the thyroid nodules as acquired with high-resolution (18 MHz) ultrasound machine were classified by two observers based on consensus reading. **Results:** 63/93 (69%; ATA), 83/93 (89%; TIRADS), 65/93 (70%; EU-TIRADS) and 60/93 (65%, KOREAN-TIRADS) of the patients with AFTN were classified in categories of intermediate or high suspicion which by definition should be examined further cytologically. **Conclusion:** 65-90% of the observed functionally relevant AFTN were rated as nodules with a non-negligible risk of malignancy. In these patients, without scintigraphy the next diagnostic procedure would be to perform fine needle biopsy, almost inevitably

leading to (unnecessary) surgery. Hence, at least in iodine deficient areas, scintigraphy should be mandatory before performing a fine needle biopsy for cytological examination of a thyroid nodule.

OP-537

Scintigraphic Patterns in Subclinical Hyperthyroidism

P. Gouveia, R. Teixeira, R. Brito, I. Amorim, R. Castro; Centro Hospitalar do Porto, Porto, PORTUGAL.

Aim: Defined as suppressed thyroid stimulating hormone (TSH) levels with normal serum thyroid hormone (T3 and T4) levels, subclinical hyperthyroidism (SBH) has come to clinical attention over the past few years. There are only few studies that characterize the scintigraphic pattern in SBH. The purpose of this study was to evaluate this entity using the standard method of radionuclide thyroid imaging with (99m)Tc-pertechnetate ((99m)TcO₄⁻). **Materials and Methods:** One hundred and eight patients (18 males and 90 females) with suppressed serum TSH levels and normal fT3 and fT4 levels, who were referred to our Nuclear Medicine department, between January 2008 and March 2016, for thyroid scintigraphy were retrospectively included in the study. Any thyroid or non-thyroidal medication that could have interfered with the exam or previous thyroid surgery constituted the main exclusion criteria. Thyroid scintigraphy was performed 20 min after the i.v. injection of 111 - 185 MBq (99m)TcO₄⁻ using a pinhole collimator. **Results:** Patients showed five different scintigraphic patterns in their thyroid scintigrams: multinodular goiters, 59.2%; solitary hyperactive nodular glands, 30.6%; solitary hypoactive nodular glands, 4.6%; diffuse hyperactive glands, 3.7%, and normal glands, 1.9%. **Conclusion:** Most patients with SBH had thyroid glands with at least one nodule (multinodular goiter = 59.2%; solitary nodules = 35.2%), while only 5.6% had normal or diffusely enlarged glands. These results are in consistency with the few reported in the literature.

1401 Tuesday, October 16, 2018, 14:30 - 16:00, Plenary Hall

CME 11 - Oncology: Update on PET/MR in Oncology

OP-539

Update on PET/MR Technical Developments

H. Quick; University Hospital Essen, High-Field and Hybrid MR Imaging & Erwin L. Hahn Institute for MR Imaging, University of Duisburg-Essen, Essen, GERMANY.

OP-540

Update on PET/MR in Paediatric Oncology

J. Schaefer; University Hospital Tuebingen, Dept. of Diagnostic Radiology, Tübingen, GERMANY.

OP-541

Update on PET/MR in Abdominal Oncological Diseases

P. Veit-Haibach; University Health Network, Toronto Joint Department Medical Imaging, Toronto, CANADA.

OP-542**Update on PET/MR in Thoracic Oncological Diseases**

G. Johnson; Division of Nuclear Medicine, Department of Radiology, Mayo Clinic, Rochester, UNITED STATES OF AMERICA.

1402**Tuesday, October 16, 2018, 14:30 - 16:00, Hall 2**

Joint Symposium 21 - Translational Molecular Imaging & Therapy / AHA: Imaging Early Remodelling in Cardiomyopathies - From Preclinical to Clinical

OP-544**Clinical Challenges in Cardiomyopathies**

M. Salerno; University of Virginia School of Medicine, Departments of Cardiology, Radiology and Biomedical Engineering, Charlottesville, UNITED STATES OF AMERICA.

OP-545**New Concepts, New Targets**

A. Saraste; Heart Center and PET Centre, University of Turku, Turku, FINLAND.

OP-546**Imaging Perfusion, Metabolism and Innervation**

F. Caobelli; Clinic of Nuclear Medicine and Radiology, Department of Nuclear Medicine, University Hospital Basel, Basel, SWITZERLAND.

OP-547**New Imaging Approaches in Cardiomyopathies**

J. T. Thackeray; Department of Nuclear Medicine, Hannover Medical School, Hannover, GERMANY.

1403**Tuesday, October 16, 2018, 14:30 - 16:00, Hall 3**

Joint Symposium 22 - Thyroid / ETA / EUGOGO: Treatment of Graves' Disease (GD) in the Presence of Graves' Ophthalmopathy (GO)

OP-549**Non-Radioiodine, Optimal Therapeutic Choices for the Hyperthyroidism Associated with GD in the Presence of GO**

T. H. Brix; Department of Endocrinology and Metabolism, Odense University Hospital, Odense, DENMARK.

OP-550**Radioiodine Treatment of GD in the Presence of Ophthalmopathy**

M. Hoffmann; Radiology Center, Nuclear Medicine, Vienna, AUSTRIA.

OP-551**Orbital Surgery in the Treatment of Graves' Orbitopathy**

D. Morris; Cardiff Eye Unit, University Hospital of Wales, Cardiff, UNITED KINGDOM.

1404**Tuesday, October 16, 2018, 14:30 - 16:00, Hall 5**

CTE 5 - Technologists/ESTRO: PET/CT Radiotherapy Planning in Head & Neck Malignancies

OP-552**The Contribution of PET/CT for Head and Neck Tumours - From Diagnose to Radiotherapy Planning**

W. Vogel; The Netherlands Cancer Institute - NKI, Amsterdam, NETHERLANDS.

OP-553**Head & Neck Radiotherapy - The Contribution of PET/CT for Radiotherapy Planning**

P. Cegla; Greater Poland Cancer Centre, Poznan, POLAND.

OP-554**Hadron Therapy in Head & Neck Tumours - A Technologist's Perspective**

F. Raimondi; Centro Nazionale di Adroterapia Oncologica - CNAO, Pavia, ITALY.

1406**Tuesday, October 16, 2018, 14:30 - 16:00, Hall Y**

Do.MoRe: Dosimetry Methodologies - From Images to Absorbed Dose

OP-555**MIRDcalc internal dosimetry software - initial development and validation**

A. L. Kesner¹, E. Olguin², P. Zanzonico¹, D. Lafontaine¹, W. E. Bolch²; ¹Memorial Sloan Kettering Cancer Center, New York, NY, UNITED STATES OF AMERICA, ²University of Florida, Gainesville, FL, UNITED STATES OF AMERICA.

Purpose/introduction: The MIRDcalc internal dose calculation software has been developed as a community tool for calculating organ-level radiopharmaceutical dosimetry. The software enables biodistribution-to-dosimetry calculations using the MIRD schema and incorporates calculation-specific details for 333 isotopes (ICRP Publication 107) and a family of 12 ICRP reference phantoms with 79 source organs/regions and 43 target organ/regions. MIRDcalc offers several innovations over existing tools, including error propagation, phantom interpolation, dynamic remainder values, quality control checks, documentation standardization, and optional command line execution. MIRDcalc is based on the familiar EXCEL platform and provides all input fields and output on a single, intuitively organized screen. The MIRDcalc project has been endorsed by the SNMMI MIRD committee, and the software is projected to be ready, to be freely distributed, in Fall 2018. **Subjects & methods:** In this work, we assessed the usability of MIRDcalc and performed an initial validation by comparing dosimetry estimates published in ICRP Publication 128 with estimates derived from MIRDcalc, given the input biodistributions provided in ICRP Publication 128. Comparisons were performed for four phantom/isotope

cases. **Results:** The global average percent difference and standard deviation between ICRP and MIRDCalc organ doses, for measured organs, across measured pharmaceuticals was 8% and 20%, respectively. The ratio of effective doses calculated for C-11 acetate, F-18 FDG, Xe-133 gas, and Rb-82 chloride were 1.13, 1.18, 1.07, 1.13, respectively. With respect to workflow, dose calculations were rapidly attained via MIRDCalc software, requiring approximately 20 seconds operator interaction given a defined biodistribution. Automatic reprocessing of input data was performed for all cases, demonstrating software's ability to be integrated with external workflows. **Discussion/conclusion:** The MIRDCalc software allows for fast/easy calculation of organ absorbed dose and whole body effective dose. Initial testing demonstrated MIRDCalc can provide dosimetry estimates similar to previous ICRP calculated values, but with advanced anatomically realistic reference phantoms and improved radiation transport of electrons and beta particles. The MIRDCalc software presents a new, accessible, standardized tool that can be used to calculate organ-level dosimetry. This tool will serve as a platform for future innovation. This work comprises initial testing, further, more comprehensive testing will be performed before release.

OP-556

A French multicenter comparative study of 3D dosimetry software used in therapeutic Nuclear Medicine

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Introduction: The internal radiotherapy has been growing significantly in recent years, favored by the emergence of new specific radiotracers and advanced imaging techniques. In this context, the development of dosimetric tools dedicated to nuclear medicine is attracting increasing interest from industrials. There are already several commercialized solutions but it is difficult to judge their quality without being able to compare them objectively. The French federation of anticancer Centers (named UNICANCER) proposes a comparative study of the dosimetry software performances currently marketed for nuclear medicine. In particular, it will be evaluated if the dosimetric result differs according to the choice of the software. **Material and Methods:** Six commercially available 3D dosimetry software have been evaluated in this study. Their evaluation and comparison were conducted in clinical situation for two types of most common treatment: SIRT by yttrium 90 encapsulated in microspheres and the neuroendocrine tumors (NET) treatment by lutetium 177. The dosimetry plans of five patients per treatment (SIRT and NET) have been realized with each soft-

ware. For each patient, the same set of data (SPECT/CT images, segmented volumes, calibration factor) was used for dosimetric planning whatever software. For SIRT dosimetry, following volumes have been segmented: whole liver, perfused liver, healthy liver and tumor. For NET dosimetry, liver, kidneys, spleen and bone marrow L2 to L4 were segmented. For each patient, the minimum, maximum and mean doses of each segmented volume thus that the doses encompassing at least 95% (noted D95) of the tumor volume were computed and then compared between software. **Results:** A prior performances comparison was obtained from a detailed technical questionnaire which highlighted several differences between the software such as: images registration methods, segmentation tools, list of available isotopic, dose calculation algorithm, dosimetric analyze tools, etc. First dosimetric results for SIRT patients show mean deviation of 23% for mean dose at non-tumor volumes and 18% for the D95 of tumors. Dosimetric results for NET patients are in progress. **Conclusion:** This study makes the state of the art of marketed 3D dosimetry software. The methodology used gives an objective evaluation and comparison of these tools. The six commercial software tested offer different technical performances levels and the first dosimetric results show relatively large differences.

OP-557

Comparison between PLANET®Dose and OLINDA/EXM V2.0 in organ-based absorbed doses estimations for patients treated with Lutathera®

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Introduction: Lutathera® is used to treat patients with neuroendocrine tumors. Absorbed dose calculation participates to the optimization of the treatment. Several commercial solutions are now available to perform dosimetry of targeted radionuclide therapy. The local deposition method (LDM) implemented in PLANET®Dose (PDose) from DOSISOFT, considers β -particles as non-penetrating radiation. The new version of OLINDA/EXM V2.0 (OLINDA) within HERMES workstation estimates absorbed doses based-on S-Values computed for ICRP-89-derived NURBS models. The goal of this work is to compare organ absorbed dose estimations obtained with PDose and OLINDA. **Methods:** Two patients (1M, 1F) who benefited from Lutathera® were injected with approximately 7.4GBq of [¹⁷⁷Lu-DOTA⁰Tyr³]-octreotate. Four SPECT/CT's were performed with the GE-Discovery NM/CT 670 at 4h, 24h, 72h and 168h. Organs studied were liver, spleen, left and right kidneys. For each organ, segmentation on the first CT image was done. For each organ, rigid registration

based-on CT images were performed, taking the first time-point as a reference. The volume of each organ/tissue of interest was therefore kept constant, and was used to estimate organ mass. PDose provides a bio-kinetics analysis tool, in which SPECT/CT calibration factors can be entered. Fitting functions were used to derive cumulated activities. PDose then computed the mean absorbed dose by LDM, with correction for tissue density. Residence times were calculated from cumulated activity and entered into OLINDA, in order to compute absorbed doses. Mass corrected absorbed doses obtained with OLINDA (taken as reference) were then compared with PDose results. **Results:** Masses of liver, spleen, left and right kidney were respectively: 1639g, 99g, 145g and 126g for 1F; 1366g, 234g, 203g and 206g for 1M. Residence times were: 45.25h, 0.67h, 0.80h, 0.83h for 1F; 2.72h, 1.50h, 0.83h, 0.84h for 1M. For liver, spleen and averaged kidneys absorbed dose estimations using PDose were: 16.9Gy, 4.3Gy, 3.7Gy for 1F; 1.2Gy, 3.9Gy, 2.5Gy for 1M. For liver, spleen and kidneys absorbed dose estimations using OLINDA were: 17.8Gy, 3.8Gy, 3.6Gy for 1F; 1.1Gy, 4.5Gy, 2.7Gy for 1M. Relative differences ranged from -9.3% to +15%. **Conclusions:** Results obtained with PDose using the LDM hypothesis are consistent, with mass corrected OLINDA results within $\pm 15\%$ for a selected group of organs. For organ mean absorbed dose calculations and for ^{177}Lu , LDM seems to be a reasonable assumption, especially in conditions where cross-absorbed dose contribution is low or negligible. However, work is in progress to evaluate absorbed dose gradients within each target organ.

OP-558

Definition of a source region for the lacrimal glands based on the ICRP adult reference voxel phantoms for use in internal dosimetry

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Objectives: The lacrimal gland is an exocrine gland, which releases its secretions directly into the eyeball. Lacrimal glands play an essential role in maintaining the normal anatomy and function of the eye and are an important part of the lacrimal system. Dacryoscintigraphy or lacrimal scintigraphy is a nuclear medicine procedure to image the lacrimal system to diagnose abnormalities that cause epiphora (pathological overflow of tear). It has also been shown that diagnostic examinations with ^{67}Ga -citrate have an increased lacrimal gland uptake also in patients without ocular pathology. Other radiopharmaceuticals that have been reported to show lacrimal gland uptake are ^{68}Ga -PSMA and $^{99\text{m}}\text{Tc}$ -HMPAO as well as sodium iodide and pertechnetate. The lacrimal glands have not been considered to be a radiosensitive organ for stochastic effects and thus it has not been included as a source or target region in the ICRP/ICRU adult reference voxel phantoms. To be able to estimate the absorbed dose contribution from the lacrimal glands to other organs and tissues, a computer program was developed. The purpose of the computer program was to create a source region for the lacrimal glands in the adult reference phantoms to facilitate absorbed dose estimations from specific uptake in the lacrimal

glands. **Methods:** A computer program was developed for the adult male and female reference voxel phantoms where each transaxial slice was shown in color. The lacrimal glands were created based on the information given by Bingham *et al.* (*Ophthalmol Plast Reconstr Surg* 29, 157-159, 2013). The data was saved as a source file in the Monte Carlo simulation program MCNP, allowing a uniform distribution of activity within the lacrimal glands. The lacrimal glands were just created as a source region without changing the anatomy of the reference phantoms. Specific absorbed fractions were generated for photons, electrons and alpha particles enabling the use for arbitrary radionuclides. **Results:** For gallium-68 the absorbed dose was estimated for 30 different organs and tissues from homogeneously distributed decays in the lacrimal glands. The organ and tissue which received the highest absorbed doses was extrathoracic region, lenses of the eyes, oral mucosa, brain, red bone marrow and salivary glands, respectively. **Conclusion:** A source region for the lacrimal glands was developed to estimate the absorbed doses to other organs and tissues. Creating a source region for the lacrimal glands based on the adult reference phantoms enables more realistic absorbed dose estimations than before.

OP-559

Prototype for a Mesh-based Radiation Transport Model for Bone Marrow Dosimetry using GATE

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Aim: In molecular radiotherapies, the necessity to improve the correlation between bone marrow hematotoxicity and absorbed dose in the bone marrow compartments (hematopoietic and fat tissue, trabecular bone), has led to the development of radiation transport models, which reproduce this microscopic mixture of soft tissue and bone. The aim of this study is to develop a radiation transport model using GATE (Geant4 Application for Emission Tomography) to study the energy deposition in the hematopoietic tissue (active bone marrow), considering different fractions of fat tissue (inactive bone marrow) in conjunction with a 3D trabecular bone geometry. **Materials and Methods:** This model is based on two 3D structures: 1 -trabecular bone and 2- inactive bone marrow, contained in a volume of 8 mm³. The trabecular bone structure is based on a 3D mesh rendering of micro-CT images of a human vertebrae. The inactive bone marrow compartment is represented by a 3D mesh microstructure of adipocytes, which was created by randomly distributed spheres (adipocytes) in a volume of 1 mm³. The adipocytes microstructure was reproduced and merged to cover the whole simulation volume (8 mm³). Both structures were located in the simulation volume containing a uniformly distributed Lu-177 source in soft tissue representing the active bone marrow compartment. Using GATE, four different fat fractions (fraction of the volume occupied by adipocytes) were simulated (0%, 22.4%, 51.6% and 80.3%), each one with 10⁶ particles. The diameter of the spheres was obtained from published histological data of the bone marrow. The energy deposition in each

compartment was scored; in addition S-values were calculated for each compartment. **Results:** The S-values for the respective simulated fat fraction in each compartment were: active bone marrow: 2.80 mGy/MBq-s, 3.56 mGy/MBq-s, 5.47 mGy/MBq-s and 13.07 mGy/MBq-s; inactive bone marrow: 0.0 mGy/MBq-s, 0.06 mGy/MBq-s, 0.38 mGy/MBq-s and 1.45 mGy/MBq-s; trabecular bone: 0.95 mGy/MBq-s, 0.89 mGy/MBq-s, 0.79 mGy/MBq-s and 0.78 mGy/MBq-s. **Conclusion:** For this small-size prototype, an inversely proportional correlation between fat fraction and S-Values of the active bone marrow is observed. Nevertheless, the results indicate that the use of such full 3D mesh geometries will enable a more accurate quantification of deposited energy in bone marrow for different fat fractions and radionuclides after molecular radiotherapies.

OP-560

The effect of target shape, size, and Partial Volume Correction on voxel dosimetry for Molecular Radiotherapy

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Molecular Radiotherapy (MRT) is an increasingly common therapy for a range of cancers. Accurate absorbed dose calculations for lesions require dosimetry to be performed at the voxel-level. Typically, voxel dosimetry is performed by obtaining a set of SPECT images, converting the counts to activity, and applying a voxel S-factor to the resultant distribution. The calculated dose distribution is degraded by a number of limitations associated with SPECT imaging, including attenuation, scatter, and the partial volume effect. A library of 3D printed tumour representative inserts has been created to investigate the effect shape and size has on the absorbed dose calculations derived from SPECT scans. Tumours were modelled as spheroids and the ratio between the two radii, λ , was varied to include prolate ($\lambda < 1$) and oblate ($\lambda > 1$) spheroids, as well as spheres ($\lambda = 1$). The volume of the inserts was varied from 16 ml to 100 ml and, for comparison, realistic tumours derived from patient CT scans were also modelled and printed. The printed inserts were filled with ¹⁷⁷Lu and imaged on a clinical SPECT scanner. Calibration factors were calculated for each insert and voxel dosimetry was calculated for each reconstructed image and compared to Monte Carlo simulations of the same setup. Algorithms from the PETPVC partial volume correction toolbox[1] were applied to the SPECT images and dose calculations were repeated, resulting in a significant increase to the calculated dose in each insert depending on the size and shape of the insert, and provided a better match to the Monte Carlo simulated dose distributions. [1] BA Thomas, V Cuplov, A Bousse, A Mendes, K Thielemans, BF Hutton, K Erlandsson *PETPVC: a toolbox for performing partial volume correction techniques in positron emission tomography*. Physics in Medicine and Biology 61(22), 7975 (2016).

OP-561

How Partial-Volume Effects Influence SPECT/CT-Based Organ Dose Estimates

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Aim: The SPECT/CT-based estimation of organ doses is among the most challenging calculations required in internal dosimetry for radionuclide therapies. Therefore, the aim of this study was to investigate the influence of partial-volume effects on the dose estimation based on a set of 3D-printed phantoms. Additionally, the potential of an open-source partial-volume correction tool ("PETPVC"[1]) for SPECT-based organ dosimetry was investigated. **Materials and Methods:** Phantoms: 3D-printed 2-compartment kidney (hot 100mL cortex, cold 50mL medulla), 1-compartment ellipsoid and sphere (both 100mL) with ¹⁷⁷Lu solution (1.05MBq/mL) inside water-filled NEMA body phantom [2]. Acquisition: Siemens Intevo Bold SPECT/CT, medium-energy collimator, 60 views of 30s continuous, non-circular orbit. Reconstruction: xSPECT Quant (voxel-size: 2mm, output: Bq/mL). "Standard" preset: 16 iterations, 1 subset, 20.8mm Gaussian post-filtering. In-house: 48 iterations, 1 subset, no post-filtering. CT-based attenuation correction, triple-energy-window scatter correction. Partial-Volume Correction (PVC): Interpolation of VOIs to SPECT resolution, application of PETPVC with iterative Young and predetermined SPECT resolutions of 12.0mm (In-house) and 24.8mm (Standard). Absorbed Dose Distributions: Convolution of SPECT/CT images [MBq/mL] with a Monte-Carlo-based, pre-tabulated Lu-177 dose kernel [mGy/MBq/s] [3]. Multiplication with voxel volume [mL] and time-integrated activity coefficient (assuming 51h tissue-specific kidney half-life [4]) yields absorbed dose [Gy] in each voxel. Total Absorbed Doses: Sum over dose distribution (masked to >1% of maximum) divided by number of voxels of CT-based VOI [5]. Two kidney VOIs: 1) Cortical contour. 2) Entire kidney. Nominal Absorbed Doses D_{NOMINAL}: Calculation based on a uniform activity distribution in a voxel representation of the 3D printing designs (dose-calibrator-based activity concentration). **Results:** Absorbed Dose Distributions: Mean of 6.2±0.1Gy over all geometries. A dose shift towards smaller values occurred for unfiltered SPECT/CT (In-house→3.6±0.9Gy) which was even stronger with post-filtering (standard→0.5±0.1Gy). Although higher doses were re-established by PETPVC (In-house→7.0±0.7Gy, standard→6.9±0.6Gy), the distribution remained wider. Total Absorbed Doses: Volume determination had a major impact on the organ dose (~36% difference between cortex-only and entire-kidney). PETPVC led to an increased error for ellipsoid and sphere (3%→13%). **Conclusion:** Lu-177 quantitative SPECT/CT imaging leads to spatial dose distributions largely differing from the underlying anatomy. Despite large errors in the absorbed voxel doses, total absorbed doses can be determined with an average difference of 2% to the nominal value by means of well-calibrated SPECT/CT imaging in combination with well-defined VOIs. While the PETPVC clearly improved the voxel dose distributions, it increased the error in total absorbed dose by about 10%. **References:** [1]Thomas;Phys-MedBiol;2016;61(22). [2]Tran-Gia;JNuclMed;2016;59(4). [3]Kletting;ZMedPhys;2015;25(3). [4]Hänscheid;JNuclMed;2018;59(1). [5]Fedorov;MagnResonImaging;2012;30(9).

1407 Tuesday, October 16, 2018, 14:30 - 16:00, Hall 1

Teaching Session 5 - Interactive Clinical Cases:: Radiopharmacy: Nanomedicine and Radiopharmaceuticals

OP-563

Nanomedicine for Tumour Targeting - Concepts and Clinical Translation

T. Lammers; RWTH Aachen University Clinic, Institute for Experimental Molecular Imaging, Dept. of Nanomedicine and Theranostics, Aachen, GERMANY.

OP-564

Integrating Nuclear Imaging into Nanomedicine - Preclinical and Clinical Applications

R. T. M. de Rosales; School of Biomedical Engineering & Imaging Sciences, St. Thomas' Hospital, King's College London, London, UNITED KINGDOM.

OP-565

Lung Administration of NPs - Developing New Drugs to Combat Antibiotic-Resistant Infections

J. Llop Roig; CIC biomaGUNE, Radiochemistry and Nuclear Imaging, San Sebastian, SPAIN.

1408 Tuesday, October 16, 2018, 14:30 - 16:00, Hall 4

Clinical Oncology: Radioligand Therapy of Neuroendocrine Tumours - Safety & Toxicity

OP-567

Prescribing Tumour Dose in Molecular Radiotherapy using a PBPK Model-based Algorithm for Individualised Treatment Planning

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Introduction: An important advantage of external beam radiotherapy (EBRT) over molecular radiotherapy (MRT) is the possibility of prescribing absorbed dose to individual tumour lesions within controlled dose ranges for the organs at risk (OARs). This has influenced radio-oncologists to more frequently use EBRT even in cases in which MRT may produce better outcomes (e.g. in patients with multiple metastases). Therefore, the aim of this work was to develop a treatment planning algorithm for MRT to reduce the gap between EBRT and MRT. **Methods:** An algorithm for treatment planning in MRT was developed, which allows to individually prescribe tumour absorbed doses and that considers maximum tolerated biological effective doses (BEDs) for multiple OARs and a maximum achievable specific activity. The algorithm uses physiologically-based pharmacokinetic (PBPK) models to perform simulations of biokinetics. This algorithm delivers the combination of amount and activity which maximises the number

of killed tumour cells in the considered lesions. The optimal activity is subsequently scaled down to achieve at least the prescribed absorbed dose in all lesions. An *in silico* clinical trial with nine virtual patients (showing 15 lesions) was conducted for ¹⁷⁷Lu-DOTATATE. Simulations of biokinetics were performed increasing the amount of ¹⁷⁷Lu-DOTATATE from 2 nmol to 2048 nmol. Maximum tolerated BEDs of 10 Gy_{2.5} and 0.5 Gy₁₅ per cycle (total of four cycles) were defined for the kidneys and the red marrow (potentially dose-limiting organs), respectively. A prescribed tumour absorbed dose of 12.5 Gy per cycle (50 Gy cumulative) was assumed for each lesion. A maximum specific activity of 420 MBq/nmol was assumed. The developed algorithm was used to determine optimal amounts and activities to achieve the tumour prescription dose within the defined constraints. **Results:** In 5 out of 9 virtual patients (9 out of 15 lesions) the prescribed tumour dose for the considered lesions was achieved within the defined constraints. For virtual patients in which the prescribed dose was not achieved, the plan was selected which maximises the number of killed tumour cells. The amount of ¹⁷⁷Lu-DOTATATE ranged from 24 nmol to 512 nmol and the activity from 1 GBq to 30 GBq. Kidney and red marrow BEDs ranged from 0.7 Gy_{2.5} to 10 Gy_{2.5} and from 0.06 Gy to 0.49 Gy₁₅, respectively. **Conclusions:** The developed algorithm can be used for individualised treatment planning in MRT to prescribe tumour dose within safe dose ranges for the OARs. Thus, it reduces the gap between MRT and EBRT.

OP-568

Survival and safety analysis of intra-arterial PRRT of SSTR-expressing tumors in over 50 patients: targeting NEN and beyond

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Introduction: Peptide receptor radionuclide therapy (PRRT) of gastroenteropancreatic neuroendocrine neoplasms (GEP-NEN) has proven efficacious following the NETTER-1 trial. However, limited reports are published on intra-arterial (i.a.) PRRT. We present a retrospective analysis of survival and safety following i.a. PRRT of large and inoperable liver metastases from NEN and of other SSTR-expressing tumors. **Subjects and Methods:** Fifty-five patients (M 31, F 24; mean age 52 years) with SSTR-expressing tumors received 77 applications of i.a. Y-90 and/or Lu-177 PRRT. Of which, 2 patients received Tandem-PPRT. Mean administered activity of Y-90 and Lu-177 was 4.2 and 7.2 GBq, respectively. Staging and restaging with the assessment of molecular response were performed using Ga-68 SSTR PET/CT according to European Organization Research and Treatment of Cancer (EORTC) criteria, and the objective response was determined by CT/MRI according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1). Kaplan-Meier survival analysis was performed for determination of median progression-free survival (PFS) and median overall survival (OS), defined from the start of PRRT and a follow-up time of at least 3 months after i.a. PRRT. Safety analysis was performed by applying CTCAE (v4.03) to the laboratory values obtained for complete blood counts,

renal and liver function tests at baseline, before each PRRT, and at each restaging. Additionally, MAG3 renogram based tubular extraction rates (TER) were calculated and assessed using scatter-plot analysis. **Results:** Primary tumor entities treated with i.a. PRRT included GEP-NEN (n=49; 41 P-NEN, 6 SI-NEN), CUP-NEN (n=2), pheochromocytoma/paraganglioma (n=3), glomus tumor (n=2), and meningioma (n=1). Overall median PFS and median OS were 29.9 and 70.0 months, respectively. Thirty-four (56.4%) patients died at a median follow-up of 94.6 months (range 4.0–156.2 months). Safety analysis demonstrated anemia (G1, n=31; G2, n=9; G3, n=1), leukocytopenia (G2, n=6), thrombocytopenia (G1, n=14; G3, n=1), and clinically insignificant renal dysfunction (G1, n=6; G2, n=3) after i.a. PRRT. No G3/G4 liver dysfunction was observed in any patient. There was no severe deterioration of MAG3 TER at end of the analysis. **Conclusion:** Intra-arterial PRRT of large and inoperable liver metastases from NEN and of other SSTR-expressing tumors with Y-90 and/or Lu-177 is effective and prolongs median OS and PFS. It is well-tolerated and safe with a very low rate of severe hematotoxicity, and no severe nephro- or hepatotoxicity. Standalone or combination (Duo-PRRT / Tandem-PRRT) can be recommended in carefully selected patients. Prospective studies are warranted to verify these results.

OP-569

Preliminary safety evaluation of ^{177}Lu -DOTA-EB-TATE radionuclide therapy in patients with advanced metastatic neuroendocrine tumors

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Purpose: ^{177}Lu -DOTA-EB-TATE, a novel radiolabeled somatostatin analogue using Evans blue to bind serum albumin as a reversible carrier to increase the binding to somatostatin receptors, was used to treat advanced metastatic neuroendocrine tumors in 4 patients. This study was performed to evaluate the safety of ^{177}Lu -DOTA-EB-TATE after a single dose of approximately 1.85GBq (50 mCi) in the patients. **Methods:** After obtaining the approval from the Institutional Review Board and informed consent, we enrolled 4 advanced metastatic neuroendocrine tumor patients (3 men, 1 woman; 42–62 y) who were positive on diagnostic ^{68}Ga -DOTATATE PET/CT scans. For kidney protection, a solution containing 25 g arginine diluted in 1 L of normal saline was infused over 4 h, starting from 60 min before ^{177}Lu -DOTA-EB-TATE injection. The mean administered radioactivity was 1.79 ± 0.22 GBq (48.38 ± 5.94 mCi). Clinical symptoms, hematological indexes, renal function and liver function indicators were obtained at baseline, 1 week and 4 weeks after the therapy. **Results:** ^{177}Lu -DOTA-EB-TATE is safe, well tolerated without any side effects such as irritating pain, nausea, vomiting, allergy or fever throughout the observation period. Hemoglobin level dropped slightly from 124.75 ± 4.79 g/L at baseline to 119.00 ± 6.98 g/L at week 1 ($P = 0.041$), but recovered to 124.75 ± 9.07 g/L at week 4. No significant change

was observed in white blood counts ($P = 0.738$), neutrophils counts ($P = 0.522$) and platelet counts ($P = 0.561$). In hepatotoxicity evaluation, some indicators were abnormal at baseline in some patients due to the disease including liver metastasis. Alanine aminotransferase (ALT) showed a significant drop from 46.75 ± 15.54 U/L at baseline to 31.25 ± 13.45 U/L at week 4 ($P = 0.016$), indicating a recovery of diseases but not toxicity. No significant change was observed in aspartate transferase ($P = 0.129$), glutamyl transpeptidase ($P = 0.874$), and total bilirubin ($P = 0.059$). In nephrotoxicity evaluation, no significant change was found in serum creatinine ($P = 0.364$) and urea ($P = 0.239$). **Conclusion:** ^{177}Lu -DOTA-EB-TATE therapy seems to be safe for a dose of approximately 1.85 GBq (50 mCi) in the treatment of advanced metastatic neuroendocrine tumor patients. The results merit further clinical translation of ^{177}Lu -DOTA-EB-TATE for peptide receptor radionuclide therapy at similar or even higher doses.

OP-570

Long-term Nephrotoxicity After PRRT: Fact or Fiction?

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Objectives: Kidneys are considered as the dose-limiting organ for peptide receptor radionuclide therapy (PRRT) and consequently are of primary concern. The aim of this retrospective analysis with prospective documentation and long-term follow up was to assess nephrotoxicity of PRRT in a large cohort of patients with neuroendocrine neoplasms (NEN) treated over 20 years in our institution. **Methods:** 1361 patients with NEN (male 767, female 594; mean age 60.0 ± 11.8 y), treated with 1–10 cycles of ^{177}Lu - or ^{90}Y -DOTATATE/-TOC or both were prospectively documented in a structured database (comprising >250 items/patient) and retrospectively analyzed. Kidney function was evaluated prior to each PRRT cycle and in follow up (restaging at 6-months intervals until death) by determination of creatinine, BUN, cGFR, electrolytes and quantified by measuring the tubular extraction rate using $^{99\text{m}}\text{Tc}$ -MAG3 renal scintigraphy and the glomerular function (GFR) using $^{99\text{m}}\text{Tc}$ -DT-PA. Treatment-related adverse events were graded according to CTCAE v5.0. **Results:** Between 1998 and 2018, 4048 cycles of PRRT were administered to 1361 NEN patients; in addition, 4052 records were available for restaging. The median overall survival was 70.1 months (median follow-up 91.8 months). Baseline creatinine was normal in 82% of subjects, grade 1 (G1) renal insufficiency (RI) was present prior to PRRT in 16.2%, G2 in 1.7%, and G3 in 0.1%, respectively. After treatment, renal function was normal in 78.2%, 18.9% had G1, and 1.9% had G2 RI. CTC grade 3 events were recorded in only four patients (0.3%), two with recurrent urinary tract infections and two had already GTC-3 at baseline. No CTC-4 or 5 nephrotoxicity was observed. For those patients who received 1–4 and 5–10 cycles of PRRT, CTCAE at the end of PRRT were 78.5% vs 72.9% in G0 (normal), 18.8% vs 21.9% in G1, 2.4% vs 4.8% in G2, and 0.3% vs 0.2% in G3. TER changed from 207.7 ± 56.6 to 186.3 ± 53.8 ml/

min ($p<0.05$); 45.5% of patients had a clinically non-significant fall in renal function ($>10\%$), whereas 32% showed an improvement of renal parameters after treatment. GFR changed from 83.9 ± 24.3 to 76.4 ± 25.7 ml/min/1.73 m² ($p<0.05$), including a not relevant decline of $>10\%$ in 46.2%, whereas 33.0% showed an improvement. **Conclusion:** This retrospective analysis with prospective documentation in a large cohort of 1361 NEN patients, receiving 4048 cycles of PRRT treated at a single institution over 20 years (with a median follow-up time of 91.8 months) did not reveal any evidence of significant long-term nephrotoxicity after PRRT.

OP-571

Long-Term Follow-Up of Advanced Paraganglioma Patients Treated With ¹⁷⁷Lu-Dotatate or ⁹⁰Y-Dotatoc PRRT in Phase-II Perspective Protocols: Activity And Toxicity Reports

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Aim: besides surgery, treatment of advanced paraganglioma (mPGL) patients has little evidence of activity. As part of the neuroendocrine tumors family, mPGL can intrinsically express somatostatin receptor and therefore may benefit from peptide receptor radionuclide therapy (PRRT). **Methods:** since March 2018, we enrolled 33 consecutive advanced mPGL patients with SSTR2 positive Octreoscan or ⁶⁸Ga PET. They started treatment with ¹⁷⁷Lu-dotatate or ⁹⁰Y-dotatoc PRRT according to the available phase-II protocols. Therapeutic cumulative dosages, were divided into 4 to 5 cycles and ranged between 18.5 and 27.8 GBq for Lutetium177, and 7.4 and 9.3 GBq for Yttrium 90 in reason of the presence of kidney or bone marrow risk factors. CTCAE and RECIST criteria were used to evaluate toxicity and activity data. **Results:** All 33 patients were evaluable, of whom 18 were female, with a mean age of 52 years. Of these, 28 had been previously operated (11 for relapse), 2 had undergone local embolization and 3 had locally advanced disease. Twenty-two patients were treated with ¹⁷⁷Lu-dotatate with a mean activity of 22.2 GBq, and 11 with ⁹⁰Y-dotatoc with a mean activity of 8.5 GBq. Neither treatment reported any $>G1$ toxicity, with a mean of 10% $G1$ haematological toxicity. ¹⁷⁷Lu-dotatate and ⁹⁰Y-dotatoc had both 18% disease progression, 9% partial response, 73% stable disease, with 82% disease control rate. Median progression-free survival was 139.2 months (96.2-145.3) with ¹⁷⁷Lu-dotatate, and 84.1 months (53.1-92.1) with ⁹⁰Y-dotatoc, with an unexpected statistically significant difference ($p=0.0006$) in favor of ¹⁷⁷Lu-dotatate. Overall survival was not reached in either case. **Conclusions:** on the basis of our phase-II studies, PRRT has proven to be well tolerated and active in advanced mPGL SSTR2 positive patients. Despite the same disease control rate, ¹⁷⁷Lu-dotatate has a clear superiority over ⁹⁰Y-dotatoc in terms of progression-free survival. Although these data must be confirmed in larger series, they strongly support the utility of ¹⁷⁷Lu-dotatoc PRRT in an orphan pathology.

OP-572

Renal and Haematological Toxicity in patients undergoing Lu-¹⁷⁷-DOTATATE Capecitabine therapy for NeuroEndocrine Tumors

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Introduction: Neuroendocrine tumors (NETs) have neuro-endocrinal origin and most of them express the somatostatin receptors 2 and 5. Positron emission tomography (PET) imaging using ⁶⁸Ga-somatostatin analogues is done to assess the spread of disease, prognostication and indicating the patient's suitability for Peptide Receptor Radionuclide Therapy (PRRT). PRRT is used in patients with metastatic/inoperable disease using ¹⁷⁷Lu-labelled somatostatin analogues. Capecitabine is a pro drug of 5 fluoro-uracil (5FU) which is radio-sensitising agent. Radiosensitization by 5FU is effected by inhibiting the thymidylate synthetase. Thymidine phosphorylase converts capecitabine and makes the cell sensitive. The kidneys are the critical organ in ¹⁷⁷Lu-DOTATATE-Capecitabine therapy because the uptake is mediated by the endocytic receptor megalin in the PCT of the nephron followed by haematological toxicity. The aim of this study is to assess the renal and haematological toxicity in patients undergoing PRRT with ¹⁷⁷Lu-DOTATATE along with Capecitabine. **Methods:** 61 patients underwent NETs therapy with ¹⁷⁷Lu-DOTATATE after fulfilling the eligibility criteria. Out of the 61 patients 18 patients underwent 1 cycle of therapy and 7 patients underwent 2 cycles, 9 patients were given 3 cycles, 21 patients were given 4 cycles, 5 patients were given 5 cycles and 1 patient underwent 7 cycles of PRRT respectively. The mean administered activity per cycle was 189 ± 29 mCi. The patients were administered 500mg of Capecitabine twice a day for 14 days during each cycle. Amino acid infusion was done along with ¹⁷⁷Lu-Dotatate for nephro-protection. A post therapy scan was performed 24 hr post administration of therapy dose. The patients were followed-up with determination of renal function including GFR evaluation, liver function and complete haemogram on 3rd, 6th and 9th week after each cycle of Lu-177-Dotatate therapy. **Results:** Evaluation of renal function at 3, 6 and 9th week intervals did not show significant reduction in renal parameters. Also the blood profiles at these time intervals did not show significant reduction in cell counts and haemoglobin content. In few patients, a significant increase in the serum creatinine level and mild drop in the platelet count was observed during the therapy. **Conclusion:** PRRT with ¹⁷⁷Lu-DOTATATE combined with Capecitabine in NET's with amino acid infusion is an effective and safe treatment with transient toxicity in few of patients of the study group. Radiation induces thymidine which causes the inhibition of phosphorylase enzyme making the cell radiosensitive and synergistic effects of both radiation (¹⁷⁷Lu-Dotatate) and radio-sensitizers (capecitabine) aid in better treatment of NET'S

OP-573

Neoadjuvant PRRT with ¹⁷⁷Lu-dotatate in non-functioning G1/2 p-NET patients, not candidate for primary surgery: preliminary toxicity and activity data from a phase-II low-dosage protocol.

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Background: in the treatment of nonfunctioning pancreatic neuroendocrine tumors (p-NET) curative surgery is the main object and surgical resection is indicated also for advanced disease. Nevertheless, since the primary tumor is not always resectable, neoadjuvant cytotoxic therapies are employed to shrink locally advanced p-NET. 177Lu-dotatate PRRT (Lu-PRRT) is under registration for treatment of GEP-NETs, and has shown good activity and low toxicity in many phase-II trials with different dosages and schedules. In our study we evaluate toxicity and efficacy profiles of low dosages of 177Lu-PRRT as a neoadjuvant therapy for non-resectable p-NET. **Methods:** from January 2015 to January 2018 we enrolled consecutive inoperable non-functioning advanced G1/2 p-NET patients, to receive Lu-PRRT in a neoadjuvant phase-II trial. All patients had histologically proven p-NET and a positive baseline functional imaging with either Octreoscan or 68Ga-DOTA-peptide PET. Patients were treated with personalized Lu-PRRT dosages ranging between 18.5 and 27.5 GBq in 4 to 5 cycles, depending on the presence of risk factors for kidney and bone marrow. Response to treatment was assessed according to CTCAE and RECIST 1.1 for toxicity and activity data. Post-treatment surgical indication was also recorded. **Results:** We enrolled 23 consecutive patients, of whom 9 were female, with a mean age of 52 years. Mean administered activity was 22.1 GBq in 4.4 cycles. Eighteen patients completed the phase-II protocol with 1 G3 and 2 G2 platelets toxicities, all recovered within six months. We had 1 disease progression, 2 complete responses, 5 partial responses and 10 stable diseases, with 94.5% disease control rate. After the end of the treatment, surgery was indicated for 12 (66.6%) of the 18 patients. Eight patients have undergone surgery so far. **Conclusions:** preliminary data from our neoadjuvant phase-II trial with a low dosage of Lu-PRRT suggest the possibility to treat safely and with good outcomes inoperable patients with non-functioning advanced G1/2 p-NET. This therapeutic option, which is also indicated for patients with risk factors, still awaits the completion of the protocol and confirmation in larger series of patients.

1410 Tuesday, October 16, 2018, 14:30 - 16:00, Hall 28

Paediatrics: Paediatrics

OP-574

Role of Ga-68 labelled DOTANOC PET/CT in paediatric patients presenting with opsoclonus-myoclonus-ataxia syndrome

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Objective: Opsoclonus-myoclonus-ataxia syndrome also known as "Kinsbourne Syndrome" or "Dancing Eye Syndrome" is

a rare but most common paraneoplastic entity associated with paediatric neuroblastic tumors. In this retrospective study we aimed to evaluate the role of Ga-68 DOTANOC PET/CT imaging in early detection of neuroblastic tumors in paediatric patients presenting with this syndrome. **Materials and methods:** We analysed the Ga-68 DOTANOC PET/CT findings of thirty-one pediatric patients (males-5, females-26) aged 3 months to 8 years, who had clinical features suggestive of opsoclonus-myoclonus-ataxia syndrome from January 2012 to January 2018 at our Institute. All the patients underwent whole body PET/CT scan, 60 minutes after intravenous injection of Ga-68 DOTANOC (100 micro curie/kg body weight). The scans were done under sedation with Midazolam in patients less than four years of age and in non-co-operative paediatric patients. All the scans were evaluated by two expert nuclear medicine physicians and any abnormal tracer uptake with corresponding lesion on CT was interpreted as positive. The final reports were given with mutual consensus. To check the diagnostic performance of the procedure, histopathology reports were reviewed. For confirmation of negative results, clinical or imaging follow-up was done. **Results:** Of the 31 patients, somatostatin receptor expressing lesions were noticed in sixteen patients. Of these sixteen patients, fifteen patients had neuroblastic tumors on histopathological examination (neuroblastoma -12, ganglioneuroblastoma -2 patients and ganglioneuroma -1), while remaining one patient had reactive adrenal hyperplasia. Among the 12 patients with neuroblastoma, lesions were abdominal paravertebral (n=7), mediastinal paravertebral (n=3) and suprarenal (n=2) locations. No structural disease was detected in the remaining 15 patients on follow-up. The average SUVmax of the PET positive lesions were 10.3 (range 2.8 to 34.5). DOTANOC PET/CT results revealed 15 true positive, one false positive, 15 true negative and no false negative. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 100.00%, 93.75 %, 93.75%, 100.00 %, 96.77% respectively with a positive likelihood ratio of 16. **Conclusion:** Our findings revealed that opsoclonus - myoclonus - ataxia syndrome in paediatric patients has association with neuroblastic tumors and Ga-68 DOTANOC PET/CT had successfully identified the tumor in this subset of patients and had shown a high diagnostic performance.

OP-575

18FDG PET/CT for evaluating early response to neoadjuvant-chemotherapy in pediatric patients with sarcoma. Results of a prospective single-center trial

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Aim: the primary aim of this study was to evaluate the relationship between FDG standardized uptake values (SUV) at baseline and early during neoadjuvant-chemotherapy with overall (OS) and disease-free survival (DFS), in pediatric patients with

bone or soft tissue sarcoma. The secondary aim was to evaluate if the early response to therapy assessed by 18F-FDG-PET/CT can predict the histological response defined by the percent tumor necrosis. **Materials and Methods:** This is a prospective, single-center trial approved by the local ethics committee (UC-LA-IRB#10-000246). Patients have been enrolled from June 2010 to November 2016 according to the following inclusion criteria: a) biopsy-proven bone or soft tissue sarcoma; b) 18F-FDG-PET/CT at baseline within four weeks before the start of neoadjuvant-chemotherapy (PET1); c) 18F-FDG-PET/CT six weeks after the start of neoadjuvant-chemotherapy (PET2); d) radical therapy after neoadjuvant-chemotherapy; e) estimation of percentage tumor necrosis after neoadjuvant-chemotherapy; f) age < 18 years-old. Primary tumor SUVmax, SUVmean, SUVpeak were calculated for PET1 and PET2. SUV-ratios to the liver (SUVmax and SUVmean) were also calculated. The metabolic response was calculated for each SUV parameters as follow: $[(SUV1-SUV2)/SUV1] \times 100$. Necrosis $\geq 95\%$ in excised tumor tissue was considered a complete histopathological response to neoadjuvant-chemotherapy. **Results:** 34 patients were enrolled: 10 females; 24 males; median age = 15.1 years. 50% (17/34) of patients had Osteosarcoma, 38.2% (13/34) Ewing Sarcoma, 5.9% (2/34) Liver Embryonal Sarcoma and 5.9% (2/34) Synovial Sarcoma. Mean follow-up was 38.8 months (range 16.3–84.1). 23% (8/34) of patients died from cancer-related causes while 23.5% (8/34) were alive with disease and 53% (18/34) had no evidence of residual/recurrent disease. 32% (11/34) of patients were considered histopathological responders. Cox proportional-hazards regression demonstrated an association between PET2 SUV-parameters and DFS (PET2-SUVmax $p=0.0113$; PET2-SUVpeak $p=0.0111$; PET2-SUVmax/SUVmean-liver $p=0.03$; PET2-SUVpeak/SUVmean-liver $p=0.032$; PET2-SUVmax/SUVmax-liver $p=0.04$; PET2-SUVpeak/SUVmax-liver $p=0.035$). No significant association was observed between PET1-SUV parameters and changes in tumor SUV parameters with OS and DFS. Logistic regression demonstrated no potential association between histological response to therapy (necrosis $\geq 95\%$) and PET1-SUV parameters, PET2-SUV parameters and metabolic response. However, patients with PET2-SUVmax ≥ 2.5 were less likely to be responders (response rate = 20.8%), while patients with PET2-SUVmax < 2.5 were more likely to be responders (response rate = 60%). **Conclusion:** according to our data 18F-FDG-PET/CT performed six weeks after the start of neoadjuvant-chemotherapy is correlated with patients' prognosis, since low FDG uptake in the primary lesion in PET2 is associated with better DFS.

OP-576

Validation of Standardized Interpretation Criteria for Early Response Evaluation with ^{18}F -FDG-PET/CT in Pediatric Lymphoma- A Report on an IAEA Multicenter Prospective Study

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Purpose: To evaluate the prognostic impact of Lugano criteria in the evaluation of pediatric ^{18}F -FDG PET/CT examinations in children with lymphoma; Hodgkin lymphoma (HL) and Non-Hodgkin lymphoma (NHL) in a worldwide multicenter trial. **Subjects and Methods:** Between 2013 and 2017, eleven worldwide centers prospectively performed ^{18}F -FDG-PET/CT studies for staging and interim response evaluation in pediatric lymphoma patients. Clinical and PET/CT findings, events, and mortality data were collected. Expert panel central review of baseline and interim ^{18}F -FDG PET/CT examinations were evaluated for multiple visual and quantitative variables including change in SUVmax as well as Lugano classification (LC). LC scores of 1–3 were considered as LC negative (LC-); likewise, LC 4–5 = LC+. For events outcome, the independent predictors were selected based on a Cox proportional model that included LC score, change in SUV, and clinical covariate of age, female gender, HL, clinical stage, lymphoma in spleen, extranodal lesions, bulk disease, and SUVmax. **Results:** Whole-body ^{18}F -FDG PET/CT acquisitions were performed in 260 patients (M:189; F:71), mean age = 10 ± 4 years, HL = 193 (74.2%); NHL = 67 (25.8%) with Stage I–IV represented. There were 201 patients with LC- interim studies. LC+ studies were significantly and independently associated with increased overall mortality (N=9) (HR=8.82; CI = 2.20, 35.40; $p=0.002$) and with more events (N=36) (HR=4.06; CI = 2.00, 8.25; $p<0.001$). However, LC+ studies were associated with more events in children with HL (HR=7.58; CI = 3.03, 18.62; $p<0.001$) than in NHL (HR=1.49; CI = 2.00, 8.25; $p=0.50$). **Conclusion:** Lugano criteria positive ^{18}F -FDG PET/CT scan at interim evaluation is an independent predictor of decreased overall survival in pediatric lymphoma patients. LC+ studies are able to independently predict decreased event free survival in patients with HL but not patients with NHL.

OP-577

True Whole-Body Versus Standard ^{18}F -FDG PET/CT Acquisition For Staging Pediatric Lymphoma

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Purpose: To estimate the incidence of clinically significant lesions in the lower extremities in pediatric patients with lymphoma on PET/CT studies conducted by a worldwide multicenter study. **Subject & Methods:** Between 2013 and 2017, eleven worldwide centers prospectively performed true vertex to toes whole-body PET/CT studies for staging and at interim treatment evaluation of response in pediatric lymphoma patients. Abnormalities identified in the lower limbs were analyzed for true whole-body involvement and the clinical impact of this information was evaluated. **Results:** True whole-body FDG PET/CT acquisitions were performed in 260 patients (189 males), mean age=10±4 years, 193 Hodgkin lymphoma; 67 Non-Hodgkin lymphoma. At staging PET/CT study, lower limb lesions were detected in soft tissue, bone marrow, skin in 10 (3.8%) patients. All patients were stage IV regardless of lower limb lesions. None of the patients presented with disease involvement only in the lower limbs. On interim response PET/CT study, no FDG-avid disease was identified outside of limited whole-body images (eyes to thighs) in all patients who did not present with lower limb disease. **Conclusion:** If no lower limb lesion is detected on staging scan, limited whole-body PET/CT for evaluation of response is appropriate in pediatric lymphoma patients, decreasing scanning time and radiation exposure.

OP-578

Added Value Of ¹⁸F-FDG PET/CT On Therapeutic Management Of Patients With Neuroblastoma

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Objective: To assess the clinical impact of ¹⁸F-FDG PET/CT on therapeutic management of patients with Neuroblastoma. **Methods:** Twenty-seven ¹⁸F-FDG PET/CT studies in 21 patients with Neuroblastoma (mean age: 5-year-old; range 1–14-year-old) were performed in 2007–2015. All patients were already treated and underwent a ¹²³I-MIBG SPECT/CT study within 6 months of the PET/CT. The main reason for requesting the ¹⁸F-FDG PET/CT was due to inconsistent findings in clinical or biochemical data that prompted reasonable doubts concerning the clinical and therapeutic management of these patients. Findings of ¹⁸F-FDG PET/CT and ¹²³I-MIBG SPECT/CT were retrospectively compared, and the clinical impact of PET/CT results on clinical management of these patients was also analysed. **Results:** A diagnostic concordance of 77.8% was reached between ¹⁸F-FDG PET/CT and ¹²³I-MIBG SPECT/CT studies (3 studies were both negative and 18 studies were both positive for the same regions). There

were 6 non-concordant studies (22.2%); they all were ¹²³I-MIBG SPECT/CT positive and ¹⁸F-FDG PET/CT negative. Non-concordant cases corresponded with bone morphological lesions with ¹²³I-MIBG persistent uptake and non-significant glucose metabolic activity. Therapeutic management: ¹⁸F-FDG PET/CT results resulted in changes in therapeutic management in 5 out of the 6 non-concordant cases, in whom clinical surveillance was ensued, with no additional treatment administered and good clinical outcome was observed. **Conclusions:** In patients with high-risk neuroblastoma under chemotherapy-radiotherapy, ¹⁸F-FDG PET/CT provided valuable additional metabolic information with respect to ¹²³I-MIBG SPECT/CT, which resulted in a clinical impact on patient therapeutic management.

OP-579

Prediction of unfavorable histopathology in neuroblastoma patients using semi quantitative and quantitative methods of ¹²³I-MIBG uptake

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Introduction: ¹²³I-metaiodobenzylguanidine (¹²³I-MIBG) scintigraphy is widely used for the detection and staging of neuroblastoma. Risk-adapted treatment in patients with neuroblastoma (NB) is based on many clinical and genetic factors including histopathology. The aim of this study is to predict unfavorable histopathology in neuroblastoma patients using semiquantitative (tumor to liver count rate ratio - TLCRR) and quantitative (SUV_{max}) methods of ¹²³I-MIBG uptakes. **Materials and Methods:** 40 patients (23 boys and 17 girls; median age 18 months) were included in this retrospective study with newly diagnosed neuroblastic tumors. ¹²³I-MIBG-scintigraphy including whole body conventional images and SPECT/CT of tumor and liver were performed for all patients before any type of treatment. TLCRR and SUV_{max} were calculated and analyzed by two independent physicians. **Results:** In all patients corresponding histopathological findings were reviewed (22 neuroblastoma, 10 ganglioneuroblastoma and 8 ganglioneuroma). The TLCRR and SUV_{max} were significantly higher in the neuroblastoma group (mean TLCRR and SUV_{max} were 7.2 and 8.4 respectively) than in the ganglioneuroblastoma (mean TLCRR and SUV_{max} were 1.1 and 1.2 respectively) and ganglioneuroma group (mean TLCRR and SUV_{max} were 0.89 and 0.92 respectively). The TLCRR range for neuroblastoma varies from 2.1 to 14.21, for ganglioneuroblastoma from 0.45 to 3.2 and for ganglioneuroma from 0.62 to 1.34. SUV_{max} range for neuroblastoma varies from 2.9 to 22.68, for ganglioneuroblastoma from 0.44 to 2.5 and for ganglioneuroma from 0.5 to 1.85. **Conclusion:** According to our results TLCRR and SUV_{max} can predict unfavorable histopathology in patients with neuroblastic tumors by measuring ¹²³I-MIBG uptake. To differentiate neuroblastoma from ganglioneuroblastoma and ganglioneuroma the optimal cut-off for TLCRR and SUV_{max} can be used 3.3 and 2.9 respectively. TLCRR values between 2.1 and 3.2

are unspecific to differentiate neuroblastoma from ganglioneuroblastoma and ganglioneuroma. Both methods are unable to distinguish ganglioneuroblastoma and ganglioneuroma from each other. However, the quantitative assessment (SUVmax) of ¹²³I-MIBG uptake is more precise, easier to use. To obtain reliable data it is necessary to continue the study with further recruitment and analysis.

OP-580

Bone scintigraphy with SPECT CT in paediatric patients with back pain: The experience of a paediatric tertiary referral centre

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Introduction: A retrospective review on the added clinical value of bone scan with SPECT/CT in children and adolescents with back pain. **Subjects and Methods:** 107 consecutive paediatric patients (37 males, 70 females, age range 5-17, median age 15), referred to the spinal surgery clinic of a tertiary paediatric teaching hospital between November 2009 and February 2017, were included. All patients had spinal x-ray, MRI (except 9 patients, who had CT) and bone scan with planar whole body images (and spot views of the area of pain) and SPECT/CT, centred on the area of pain. CT settings were adjusted to minimise the radiation burden (50 mAs, 80kVp under 8 years; 24 mAs, 110 kVp over 8 years). A Siemens Symbia T2 SPECT/CT gamma camera was used. All bone scintigraphies were reviewed by two consultant nuclear medicine specialists. Reports of x-rays, MRI (and CT) scans were available from the Radiology Information System. Details on patients' presentation and follow up were available from the clinical documents database. The decision on whether SPECT/CT added clinical value was made in a combined review session with the consultant spinal surgeon. **Results:** SPECT CT reported relevant positive findings in 53% of cases (57 of 107) and relevant negative findings in a further 16% (17/107). In those cases where SPECT CT reported positive findings, a likely pain generator corresponding to the clinical history was identified in 86% of cases (49 of 57). Of those with positive findings, SPECT CT added clinical value, important for patients' management, in 36 of 57 (63%) cases. SPECT CT identified focal mechanical stress from facet or sacroiliac joints in 32 of 57 cases (56%). It showed that the MRI abnormalities (mild disc herniation, Shmorl's nodules, hydromelia, Tarlov cyst) were not the cause of pain in 4 cases, and identified loose metalwork in 9 patients, not previously diagnosed on MRI or plain radiograph. In 8 cases of spondylolysis SPECT/CT showed a cold pars defect, thus prompting pars fusion with bone grafting. The mean effective dose equivalent from the limited CT associated to the SPECT was 0.37 mSv +/-0.22 mSv (0.15 - 0.98 mSv). **Conclusion:** These results suggest that a prospective evaluation of the role of SPECT/CT in paediatric patients with orthopaedic back pain is justified in a selected patients' population. The CT component of the SPECT CT study, whilst producing bone images of diagnostic quality, gave a particularly low radiation dose.

OP-581

Colonic transit evaluation in pediatric patients with chronic constipation using radiopharmaceutical administration directly into the bowel via an ostomy

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Introduction: The purpose of this study was to evaluate colonic transit in pediatric patients with chronic constipation with a novel technique using direct administration of radiopharmaceutical into the bowel via cecostomy or appendicostomy. **Methods:** We retrospectively reviewed the colonic transit studies in 22 patients (12 males and 10 females) with an age range between 9 and 22 years (mean 15 years). All patients had history of chronic constipation requiring a cecostomy or appendicostomy for bowel irrigation. All patients underwent measurement of colonic transit time performed following administration of 100 microcuries of Ga-67 citrate in a 2cc liquid form followed by 8cc of saline flush. The tracer was administered directly into the cecum via either the cecostomy or appendicostomy. Static images of the abdomen and pelvis were obtained in the anterior and posterior projections at baseline, 24, 48, and 72 hours post administration. The patients were instructed to avoid saline bowel irrigation during the imaging period. The colonic geometric center (weighted average of residual non-evacuated radioactivity over four regions) was calculated for each time point using regions of interest drawn in the ascending, transverse, descending, and rectosigmoid colon. Anatomic regions were estimated based on correlative abdominal radiograph obtained at baseline. **Results:** All studies and quantitative analyses were easily performed by a technologist, as activity was clearly identified in the colon. No patient reported discomfort. There were a total of 8/22 patients having no evacuation (100% of the activity still remaining in the bowel at 72 hours), 11/22 patients had evacuation >40% at 72 hours; and 5/22 had evacuation >90% at 72 hours. Evaluation of the geometric center at 72 hours showed that 7/22 patients had most retention in the right side of the colon while 15/22 patients had the majority of activity in the left side of the colon. **Conclusion:** This technique provides an easily performed method for evaluation of the colonic transit time in patients with chronic constipation who have a cecostomy or appendicostomy. Since this technique does not require oral administration, it can be performed in all patients, including young children who may have difficulty swallowing pills. This technique presents a significant theoretical advantage over oral administration because direct administration into the cecum yields high image quality and avoids the problems of variable gastric emptying and small bowel

1501 Tuesday, October 16, 2018, 16:30 - 18:00, Plenary Hall
CME 12 - Oncology: PET Guided Biopsy

OP-582

PET Guided Biopsy - Soft Tissues and Organs

J. Cerci; *Quanta - Diagnóstico e Terapia, Rua Almirante Tamandaré, Couritiba, BRAZIL.*

OP-583

PET Guided Biopsy - Lymphoma and Bone

C. Nanni; *Metropolitan Nuclear Medicine, AOU S.Orsola Malpighi, Bologna, ITALY.*

OP-584

New Perspectives by Combining Advanced Tools and Navigation with Radio-Guided Surgery

F. van Leeuwen; *Leiden University Medical Center, LUMC, Leiden, NETHERLANDS.*

1502 **Tuesday, October 16, 2018, 16:30 - 18:00, Hall 2**

Joint Symposium 23 - EANM/EARL: New Developments of EANM Oncology PET/CT Guidelines and Update of the EARL Accreditation Standards

OP-585

Current Status and Achievements of EARL Accreditation

A. Kaalep; *North Estonia Medical Center Foundation Hospital, Department of Medical Technology, Tallinn, ESTONIA.*

OP-586

New EARL PET/CT Performance Standards for Oncological PET/CT Studies

R. Boellaard; *VU University Medical Centre, Radiology and Nuclear Medicine, Amsterdam, NETHERLANDS.*

OP-587

Clinical Impact of New PET Reconstruction Technologies on Quantitative Oncological and Haematological PET/CT Studies

C. Kobe; *University Hospital of Cologne, Department for Nuclear Medicine, Cologne, GERMANY.*

1503 **Tuesday, October 16, 2018, 16:30 - 18:00, Hall 3**

Joint Symposium 24 - Thyroid / ETA-CRN: Molecular Mechanism of Iodine Resistance and Their Clinical Implications

OP-588

Molecular Basis of RAI-Resistance

D. Führer-Sakel; *University Hospital Essen, Department of Endocrinology, Essen, GERMANY.*

OP-589

Defining Non-Radioiodine-Avid Thyroid Cancer

D. Deandreis; *University Hospital Turin, Department of Nuclear Medicine, Torino, ITALY.*

OP-590

Re-Differentiation Strategies

E. Seregni; *Istituto Nazionale Tumori, Department of Nuclear Medicine, Milan, ITALY.*

1504 **Tuesday, October 16, 2018, 16:30 - 18:00, Hall 5**

CTE 6 - Interactive: Technologists: Renal Imaging

OP-591

Renal Imaging in the Transplanted Patient

M. Janssen; *Radboudumc, Department of Radiology and Nuclear Medicine, Nijmegen, NETHERLANDS.*

OP-592

Renal Imaging in Paediatrics

A. I. Santos; *Hospital Garcia de Orta, E.P.E., Nuclear Medicine Department, Almada, PORTUGAL.*

OP-593

Detection of Renal Tumours by Using SPECT and Fluorescent Imaging

M. Hekman; *Radboudumc, Nijmegen, NETHERLANDS.*

1505 **Tuesday, October 16, 2018, 16:30 - 18:00, Hall X**

M2M: Novel Tracers in Oncology

OP-594

Preclinical evaluation of a mTOR specific PET ligand in a RAD001 sensitive/resistant breast cancer model system

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Introduction: Targeting the tyrosine kinases, EGFR and HER2, has dramatically improved patient outcomes in several tumor types such as in breast and colorectal cancer. Inevitably however, treatment loses its efficiency due to increasing tumor resistance to therapy. The PI3K/AKT/mTOR pathway is commonly deregulated in a variety of human cancers and appears to be involved in the development of HER2 therapeutic resistance. Altered biomarker levels indicating upregulation of mTOR activity have been correlated to increased efficacy of everolimus (RAD001) combination therapy in phase III clinical trials (BO-LERO-1/3). Molecular imaging of the mTOR pathway provides an excellent opportunity to guide personalized therapeutic options by identifying resistant patient populations. **Methods:** The difference in cell uptake of ¹⁸F-MPC-1-1 in RAD001 sensitive compared to resistant breast cancer cell lines was investigated using internalization assays. The specificity was evaluated in competition studies with a non-radioactive inhibitor. Cellular localization of a fluorescently labelled derivative, MPC-1-1-488, was explored using confocal microscopy. **In vivo** properties

were characterized using PET/MR images of murine xenografts of a panel of RAD001 sensitive and resistant breast cancer cell lines. **Results:** Internalization assays showed up to 2.5- and 1.7-fold increased cell uptake compared to the negative control in RAD001 sensitive HCC-1419 and BT-474 breast cancer cells, respectively. In competition assays, cell uptake could be blocked to 25% and 35% of the unblocked uptake, respectively. Confocal microscopy confirmed accumulation of MPC-1-1-488 in the cytoplasm and showed exclusion of the nucleus. The biodistribution in mice was dominated by large uptake in organs related to renal and hepatobiliary excretion. ^{18}F -MPC-1-1 showed accumulation in tumor tissue in BT-474 xenografts over time. Simultaneous clearance from muscle tissue resulted in a mean T/M ratio of 1.7 ± 0.2 at 90 minutes p.i. in RAD001 sensitive xenografts. Mice bearing RAD001 resistant xenografts showed a mean T/M ratio of 0.9 ± 0.2 at the same time point. The mean uptake in BT-474 tumours at 90 minutes p.i. was $2.8\% \pm 0.3\%$ ID/ccm. **Conclusion:** ^{18}F -MPC-1-1 showed potential as a PET ligand capable of discriminating between RAD001 sensitive and resistant breast cancer cell lines. Its cellular localization in the cytoplasm was confirmed and uptake was shown to be specific in competition assays. *In vivo* studies reflected the *in vitro* results, showing significant differences between RAD001 sensitive and resistant xenograft models. Further studies investigating the *in vivo* uptake threshold of ^{18}F -MPC-1-1 which correlates with positive response to mTOR inhibitor therapy are warranted.

OP-595

PET Imaging of Parp Expression using [^{18}F]olaparib

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Imaging of poly (ADP-ribose) polymerase (PARP) using a radiolabelled inhibitor has been proposed for cancer patient selection, prediction of outcome, dose optimisation, for genotoxic therapy evaluation, and for imaging target engagement of novel PARP-targeting agents. We developed a radiolabelled structural equivalent of the FDA-approved PARP inhibitor olaparib, substituting fluoride for ^{18}F to allow PET imaging in preclinical tumour models. A small panel of pancreatic ductal adenocarcinoma (PDAC) cell lines including Panc-1, MiaPaCa-2 and Capan-1 was used in cell uptake experiments with [^{18}F]olaparib. PARP expression levels were determined using Western blot and confirmed by immunofluorescence microscopy. Specificity of [^{18}F]olaparib cell uptake was determined by blocking experiments using an excess of cold, unlabelled olaparib, or other PARP inhibitors (rucaparib, talazoparib). Dynamic PET/CT images were acquired for 1 h following an intravenous bolus injection of (3 MBq) [^{18}F]olaparib and ex-vivo biodistribution studies. Specificity of tumour uptake was evaluated by co-administration of an excess of unlabelled olaparib. Experiment were also performed after external beam gamma-irradiation of the cells or the tumour (10 Gy). *In vitro*, [^{18}F]olaparib was taken up differently among PDAC

cell lines: Panc-1 > MiaPaCa-2 > Capan-1. PARP1 expression levels determined by Western blot analysis correlated with cell uptake of [^{18}F]olaparib. Cell-associated uptake of [^{18}F]olaparib in all three cell lines could be blocked by more than 99% by addition of an excess of cold, unlabelled PARP inhibitor. [^{18}F]olaparib uptake in all cells was increased 48 h after receiving gamma-irradiation. *In vivo*, dynamic PET imaging of wild type naïve mice injected with [^{18}F]olaparib revealed a weighted blood half-life of 19.3 min. Tumour uptake of [^{18}F]olaparib in both Panc-1 or Capan-1 mouse xenografts was consistent with PARP1 expression determined by immunohistochemistry, *in vitro* uptake and immunoblotting analysis. Ex-vivo biodistribution analysis showed uptake of $3.16 \pm 0.36\%$ ID/g of [^{18}F]olaparib in Panc-1 tumours. Two hours after irradiation of Panc-1 tumour (10 Gy), uptake of [^{18}F]olaparib increased by 70% ($P=0.025$). Western blot analysis demonstrated that PARP1 expression in Panc-1 tumour increased in the irradiated group. Tumour uptake was significantly decreased after co-administration of an excess of cold, unlabelled olaparib ($1.20 \pm 0.17\%$ ID/g; $P=0.0016$), whereas tumour uptake of [^{18}F]olaparib in Capan-1 xenografts was significantly lower ($2.59 \pm 0.32\%$ ID/g), but also specific (blocked to $1.00 \pm 0.17\%$ ID/g; $P = 0.015$). Taken together, we demonstrated that [^{18}F]olaparib can be used for quantifying olaparib tumour accumulation, *in vitro* and *in vivo*.

OP-596

Development of [^{18}F]FAMTO: a novel fluorine-18 labelled positron emission tomography (PET) radiotracer for imaging CYP11B1 and CYP11B2 enzymes in adrenal glands

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Introduction: Primary aldosteronism accounts for 6-15% of hypertension cases, the single biggest contributor to global morbidity and mortality. Whilst ~50% of these patients have unilateral aldosterone-producing adenomas, only a minority have curative surgery as the current diagnosis of unilateral disease is poor. Carbon-11 radiolabelled metomidate ([^{11}C]MTO) is a positron emission tomography (PET) radiotracer able to selectively identify CYP11B1/2 expressing adrenocortical lesions of the adrenal gland. However, the use of [^{11}C]MTO is limited to PET centres equipped with on-site cyclotrons due to its short half-life of 20.4 minutes. Radiolabelling a fluorometomidate derivative with fluorine-18 (^{18}F radioactive half life 109.8 min) in the aromatic position ([^{18}F]FAMTO) has the potential to overcome this disadvantage and allow it to be transported to non-cyclotron-based imaging centres. **Methods:** [^{18}F]Fluoride in [^{18}O]H₂O was trapped on a Sep-Pak QMA cartridge and released with a solution of kryptofix 222/K₂CO₃ in acetonitrile/H₂O. After drying solvents, boronic ester precursor and tetrakis(pyridine)copper(II) triflate in DMF was added. Radiofluorination was conducted at 118 °C for 20 min. The crude mixture was purified by semi-preparative HPLC. Crude [^{18}F]FAMTO was subsequently diluted with PBS, the mixture loaded onto a Sep-Pak tC18 cartridge and eluted with ethanol. The *in vitro* binding of purified [^{18}F]FAM-

TO was evaluated by autoradiography using pig adrenal tissue. Stability studies of [^{18}F]FAMTO in human blood and plasma were performed. The preclinical PET imaging, *ex vivo* biodistribution and metabolite analysis of [^{18}F]FAMTO was performed in Sprague-Dawley rats. **Results:** [^{18}F]FAMTO was obtained in $32 \pm 2\%$ ($n=18$, decay corrected isolated radiochemical yield), with $>98\%$ radiochemical purity and molar activity of 105 ± 39 GBq/ μmol . *In vitro* autoradiography studies demonstrated specific binding of [^{18}F]FAMTO to pig adrenal glands. No degradation of [^{18}F]FAMTO was observed after incubation for 20 min with human blood. *Ex vivo* biodistribution data and PET image analysis underline high selective [^{18}F]FAMTO uptake in rat adrenal glands (3.84% ID/g at 30 min). Metabolite analysis showed 20% unchanged [^{18}F]FAMTO in the blood at 10 minutes post administration and rapid urinary excretion. **Conclusions:** [^{18}F]FAMTO, a new ^{18}F -labelled analogue of metomidate, was successfully synthesized with good yield. *In vitro* and *in vivo* experiments have shown that [^{18}F]FAMTO accumulates in adrenal glands, with good adrenal to liver ratios in rats and fast metabolism. The simplicity of radiolabeling and encouraging results from preclinical studies justify a further evaluation of [^{18}F]FAMTO in humans as diagnosis tool to enable curative hypertension strategies for this patient demographic.

OP-597

Early Detection of Pancreatic Cancer in KPC Mice by Imaging DNA Damage Signalling

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Aim: Despite its widespread use, the PET radiotracer ^{18}F -FDG has been shown in clinical settings to be ineffective for improving early diagnosis of pancreatic ductal adenocarcinoma (PDAC).¹ An alternative strategy for early detection of pancreatic cancer involves targeting pancreatic intraepithelial neoplasia (PanIN) lesions which are the non-invasive precursors of PDAC. As the DNA damage response is known to be activated during the progressive development of PanINs², we sought to investigate whether the SPECT imaging agent, ^{111}In -anti- γH2AX -TAT³, would allow visualisation of the DNA damage repair marker γH2AX and thus facilitate early detection of PDAC in a genetically engineered mouse model. **Methods and Materials:** Genetically engineered KPC mice ($\text{K-ras}^{\text{LSL.G12D/+}}$; $\text{p53}^{\text{R172H/+}}$; PdxCre) were regularly monitored by ^{18}F -FDG-PET as part of a longitudinal imaging study. At various ages, mice were co-imaged with both ^{18}F -FDG and ^{111}In -anti- γH2AX -TAT. *Ex vivo* analysis of harvested tissues and organs was also performed. The PanIN/PDAC status of these mice was confirmed by haematoxylin and eosin (H&E) staining of the pancreata which were co-registered with autoradiography and immunofluorescence microscopy images of the relevant tissue sections to examine how uptake of ^{111}In -anti- γH2AX -TAT was influenced by the upregulation of γH2AX within PanIN-3 lesions. **Results:** Uptake of ^{111}In -anti- γH2AX -TAT within the pancreas was positively correlated with the proportion of PanIN-3 lesions determined from histology. Such correlation was not observed with the non-specific control agent,

^{111}In -IgG-TAT. Co-registration of H&E, autoradiography and immunofluorescence images revealed that ^{111}In -anti- γH2AX -TAT localises in regions of high grade PanIN lesions, which are the direct precursors for fully invasive PDAC, while radioactive signal was absent in regions of PDAC. This is consistent with the timeline of expression of γH2AX in PDAC progression, and literature data on other cancers.⁴ **Conclusions:** ^{111}In -anti- γH2AX -TAT allows non-invasive detection of γH2AX upregulation in pre-invasive PanIN-3 lesions and could potentially be used to aid in the early detection and staging of pancreatic cancer. **References:** 1. Strobel, O. et al., Pancreatic Cancer: FDG-PET is not useful in early pancreatic cancer diagnosis. *Nat. Rev. Gastroenterol Hepatol.*, 2013, 10, 203-205. 2. Koostra J.-B. et al., Widespread Activation of the DNA Damage Response in Human Pancreatic Intraepithelial Neoplasia. *Mod. Pathol.*, 2009, 22, 1439-1445. 3. Knight, J. C. et al., Imaging DNA Damage by PET and SPECT. *Eur. J. Nucl. Med. Mol. Imaging*, 2017, 44(6), 1065-1078. 4. Bartkova J, Hořejší Z, Koed K, Krämer A, Tort F, Zieger K, et al. DNA damage response as a candidate anti-cancer barrier in early human tumorigenesis. *Nature*. 2005;434(7035):864-70.

OP-598

Development Of Stroma-targeted Theranostics Based On Inhibitors Of Fibroblast Activating Protein

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Aim: Cancer associated fibroblasts (CAFs) are an important subpopulation of stromal cells and present in more than 90% of epithelial carcinomas such as pancreatic, colon and breast cancer. Due to their involvement in remodeling of the extracellular matrix, angiogenesis, immunosuppression and resistance to chemotherapeutics, an increased occurrence of CAFs correlates with a poor prognosis. One feature of CAFs is the overexpression of fibroblast activating protein (FAP), a protease which is almost undetectable in healthy tissues. In recent studies, we were able to demonstrate the efficiency of radiolabeled FAP inhibitors for positron emission tomography (PET) and successfully introduced the theranostic agent FAPI-04. Since the retention time in tumors only allows therapy with short lived nuclides, the aim of this work is the further development of theranostic probes by fine tuning the pharmacokinetic properties. **Materials and Methods:** Based on variations of the linker between the bifunctional chelator and the inhibitor moiety, a subset of 10 novel tracers was investigated. FAP modified HT1080 (human fibrosarcoma) cells were used to determine EC_{50} -values as well as internalization and efflux rates. The same cell line was also used for subcutaneous xenografts in BALB/c nu/nu mice for *in vivo* imaging by PET and biodistribution studies. To ensure target specificity, HEK cells carrying the closely related serine protease dipeptidyl peptidase 4 (DPP4) were used as a negative control *in vitro*. **Results:** All novel derivatives showed high selectivity towards FAP over DPP4. Regarding the deviations, the EC_{50} -values of all compounds were approximately in the range of 10-20 nM. Therefore the selection of a promising candidate was based on the tumor accumulation and rapid background clearance in small animal PET imaging as well as the *in vitro* efflux kinetics. In

terms of these requirements two candidates with an increased lipophilicity of the linker moiety were further characterized in biodistribution studies. Compared to FAPI-04, the current lead compound for use in humans, these studies showed a substantially delayed elimination from tumor tissue for FAPI-21 while upholding an excellent tumor/background ratio. **Conclusion:** By variation of the linker moiety we were able to obtain a tracer with an extended tumor retention time. Still, further development is required to enable the use of longer lived nuclides e.g. ^{177}Lu or ^{225}Ac to complement the therapeutic toolkit. Additional experiments are ongoing to demonstrate the versatility of this approach.

OP-599

PET Tracking of ^{89}Zr -labeled Gamma-delta T-cells in a Xenograft Model of Breast Cancer: Combination with Liposomal Alendronate Increases Tumour Accumulation
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Introduction: The development of cellular immunotherapies against cancer would greatly benefit from *in vivo* cell tracking solutions. Vγ9Vδ2-T cells are a highly cytotoxic subset of immune cells and have been used successfully in several clinical trials in cancer immunotherapy. Using the recently developed PET tracer [^{89}Zr]Zr(oxinate)₄ ($t_{1/2} = 78.4$ h, $\beta^+ = 22.3\%$), human Vγ9Vδ2-T cells were tracked in a xenograft breast cancer model, using PEGylated liposomal alendronate (PLA) to attract Vγ9Vδ2-T cells towards tumour tissue. **Methods:** Human Vγ9Vδ2-T cells were isolated from peripheral blood and expanded *in vitro* using zoledronate and IL-2. MBA-MB-231.hNIS-GFP breast cancer cells were injected subcutaneously in the mammary fat pad of female SCID/beige mice. In one group ($n=9$), tumours were sensitised by intravenous administration of PLA (5 mg/kg alendronate) 4 days prior to Vγ9Vδ2-T cell injection. Control groups received placebo liposomes ($n=4$), non-liposomal alendronate ($n=3$) or Vγ9Vδ2-T cells alone ($n=5$). A final group ($n=3$) was administered radiolabelled cells killed by freeze-thawing. [^{89}Zr]Zr(oxinate)₄ was synthesised by reacting 8-hydroxyquinoline with [^{89}Zr]Zr(oxalate)₄. On day 0, γδ-T cells were radiolabelled with [^{89}Zr]Zr(oxinate)₄ (30/300 mBq/cell) for 20 min and injected in the tail vein (11×10^6 cells/animal). Animals were imaged by PET/CT on days 0, 2 and 7 and by SPECT/CT (^{99m}Tc) on days 0 and 2. Biodistribution and histology studies were performed on day 7. The cancer-cell-killing ability of radiolabelled γδ-T cells was evaluated *in vitro*. **Results:** Vγ9Vδ2-T cells were radiolabelled with $46.6 \pm 6.7\%$ efficiency and showed the expected biodistribution/pharmacokinetics for directly-labelled T-cells. Radiolabelling Vγ9Vδ2-T cells with ^{89}Zr did not affect their ability to kill MBA-MB-231.hNIS-GFP cells *in vitro*. Vγ9Vδ2-T *in vitro* proliferation was only affected by amounts of $^{89}\text{Zr} \geq 50$ mBq/cell. Accumulation of Vγ9Vδ2-T cells in tumours was demonstrated by PET/CT and confirmed by histology. Tumour uptake was higher in the PLA-treated group than in control groups

(Vγ9Vδ2-T +PLA: $2.1 \pm 0.8\%$ ID/g versus Vγ9Vδ2-T without PLA: $1.2 \pm 0.3\%$ ID/g, $n=9-12$, $p=0.0018$). Histology showed presence of Vγ9Vδ2-T cells around and within tumour tissue. Radiolabelling of liposomes with ^{111}In demonstrated accumulation of PLA in the tumour after 24–72 h. **Conclusion:** We demonstrated that [^{89}Zr]Zr(oxinate)₄ allows efficient delivery of ^{89}Zr to γδ-T cells and sufficient retention for *in vivo* tracking by PET over 7 days. *In vitro* studies showed no adverse effect of radiolabelling on γδ-T cell functionality. Accumulation of γδ-T cells in tumour tissue was enhanced by pretreatment with aminobisphosphonate-loaded liposomes.

OP-600

Radiolabelled *Bacillus anthracis* toxin-based probes for molecular imaging of MMP activity in tumour models
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Introduction: Increased activity of matrix metalloproteinases (MMP) 2, 9 and 14 is associated with poor prognosis and metastasis in different solid tumour types. To exploit this feature, the protective antigen-binding domain (PAWT) of the binary anthrax lethal toxin (LT) was modified to form a pore in cell membranes only when cleaved by MMPs (PAL1) instead of the furin enzyme. The anthrax lethal factor (LF) is then able to translocate through these pores into the cytosol of tumour cells. The current work describes the use of this system to measure MMP activity non-invasively in preclinical tumour models by SPECT. **Methods:** The activation of PAL1 was evaluated by cytotoxicity assays in a range of cancer cell lines, with or without a broad spectrum MMP inhibitor (GM6001). MMP2 and 9 activity from the different cancer cell lines was assessed by gelatin zymography. Expression levels of MMP14, and LT native receptors (TEM8 and CMG2) were evaluated by western blot analysis. Cell abundance of TEM8 and CMG2 onto the cell surface was determined by saturation binding assays using PAWT radiolabelled with indium 111 [^{111}In], [^{111}In]PAWT. After radiolabelling LF^{E687A} (LF with a defective catalytic domain) cell uptake experiments were performed in the presence or not of PAL1. Preliminary evaluation of the *in vivo* biodistribution of [^{111}In]PAL1, [^{111}In]PAWT or [^{111}In]LF^{E687A} was performed by SPECT/CT in naive mice and MMP14-expressing CAPAN1 tumour-bearing mice. **Results:** Cell-based cytotoxicity assays showed different sensitivities to PAL1₈₃/FP59 treatment, CAPAN1>HT1080>MDAMB231>KPC-B8484>>MCF7, which correlated with expression of MMP14 and of LT receptors, mainly CMG2. Activation of PAL1₈₃ was effectively blocked by GM6001, further suggesting MMP selectivity. The ability of PAL1₈₃ to deliver [^{111}In]LF^{E687A} or fluorescently labelled LF^{E687A} into CAPAN1 cells was demonstrated by cellular uptake assays and confocal microscopy respectively. The blood half-life obtained from dynamic SPECT data was 10 min for [^{111}In]PAWT and 82 minutes for [^{111}In]PAL1, while [^{111}In]LF^{E687A} exhibited a blood residence time of 52 min. **Ex vivo** gamma-count-

ing showed moderate accumulation of [^{111}In]PAL1 in CAPAN1 tumour xenografts ($4.64 \pm 0.52\%$ ID/g) at 4 hours post-injection of the tracer. Whereas [^{111}In]PAWT presented a lower tumour uptake ($2.40 \pm 0.52\%$ ID/g). **Conclusion:** Taken together, our results indicate that radiolabelled forms of mutated anthrax lethal toxin hold promise for non-invasive imaging of MMP activity in cancer patients.

OP-601

Two novel ^{68}Ga -Labeled Ligands of Carbonic Anhydrase IX to Noninvasively Image Hypoxic Tumors

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Aim: Carbonic anhydrase IX (CAIX) is an established marker for tumor hypoxia and certain malignancies. Several sulfonamides, such as acetazolamide (AAZ) and benzenesulfonamide, exhibit high binding affinity against CAIX and therefore they have been radiolabeled to noninvasively image CAIX expression in tumors. However, target specificity and pharmaceutical profiles of these sulfonamide-based probes still have to be optimized. We recently reported a rapid and regioselective 2-cyanobenzothiazole (CBT)/1,2-aminothiol ligation approach to prepare radiolabeled bio-vectors for PET imaging. Herein, we described the design, synthesis and ^{68}Ga -labeling of two AAZ-conjugated molecules bearing different linkers (PEG vs. charged amino acids) to investigate the effect of molecular composition, solubility and overall charge on biodistribution. **Materials and Methods:** The chelator NOTA-pyCBT was prepared in 3 steps starting from 2-cyano-6-hydroxybenzothiazole (6-OH-CBT) and the corresponding macrocyclic intermediate. Two CAIX ligands (Cys-PEG-AAZ and Cys-DRD-AAZ) containing an AAZ moiety, a spacer and a *N*-terminal cysteine residue were prepared by solid-phase synthesis. NOTA-pyCBT was labeled with $^{68}\text{GaCl}_3$ in NaOAc buffer (0.1 M, pH 5.5) at 90 °C for 15 min. The CBT/1,2-aminothiol cycloaddition was carried out by mixing [^{68}Ga]Ga-NOTA-pyCBT and Cys-PEG-AAZ (or Cys-DRD-AAZ) in an aqueous solution (0.1 M NaOAc, pH 7.0) at room temperature for 30 min. To confirm the identity of the conjugated products, direct ^{68}Ga -labeling of NOTA-Luc-PEG-AAZ and NOTA-Luc-DRD-AAZ were performed. All the radiolabeling reactions were monitored by RP-C18 HPLC. **Results:** NOTA-pyCBT was obtained with an overall yield of 52% from 6-OH-CBT. ^{68}Ga -labeling of NOTA-pyCBT was successfully achieved under slightly acidic conditions (NaOAc buffer, 0.1 M, pH 5.5, 90 °C) to give [^{68}Ga]Ga-NOTA-pyCBT with radiochemical yields over 95%. Treatment of Cys-PEG-AAZ and Cys-DRD-AAZ with [^{68}Ga]Ga-NOTA-pyCBT provided [^{68}Ga]Ga-NOTA-Luc-PEG-AAZ and [^{68}Ga]Ga-NOTA-Luc-DRD-AAZ with 96 and 95% yields, respectively. Identity of the ^{68}Ga -labeled final products was confirmed by direct labeling of NOTA-Luc-PEG-AAZ and NOTA-Luc-DRD-AAZ with $^{68}\text{GaCl}_3$. Finally, the radiolabeled products were found to be stable in PBS and EDTA solution for 2 h. **Conclusion:** Our CBT/Cys bioorthogonal approach has been conveniently and efficiently applied to the site-specific ^{68}Ga -labeling of two novel CAIX ligands. *In vitro* receptor binding affinity assay, cell internalization assay, *in vivo* biodistribution and μPET studies are underway to explore the effects of the molecular composition on the physicochemical properties of our CAIX radioligands.

1506

Tuesday, October 16, 2018, 16:30 - 18:00, Hall Y

Do.MoRe: Treatment Planning for Y-90 Radioembolisation Therapy

OP-602

Development of a routine method for dissolution of resin microspheres for ^{90}Y measurement

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Aim: A method currently used for the treatment of inoperable liver tumours is known as Selective Internal Radiation Therapy using ^{90}Y resin microspheres (known as SIR Spheres). Radionuclide calibrators are used in hospitals to measure the ^{90}Y activity before administering to the patient. Previous studies showed the difficulties of measuring ^{90}Y liquid solution using a radionuclide calibrator (Fenwick *et al.* 2014), with only 40% of the participants reporting values within $\pm 5\%$ of the certified value. Another study (Ferreira *et al.* 2016) showed the difficulties of measuring ^{90}Y resin microspheres using a radionuclide calibrator, and highlighted the differences in the radionuclide calibrator response when measuring aqueous and sphere forms. The radionuclide calibrator response for ^{90}Y liquid is well known, however, the response will be different for ^{90}Y resin microspheres. Therefore, there is a requirement to develop a procedure that can effectively transfer yttrium from the resin phase to the aqueous phase. **Materials and Methods:** The method consists of adding 5g of concentrated nitric acid (HNO_3) to the vial with a well-known amount of stable yttrium resin microspheres, shaken and left to rest. At regular time intervals, a subsample was taken and diluted to 10 mL in 2% HNO_3 and measured by inductively coupled plasma mass spectrometry (ICP-MS). Subsamples were also taken before adding the acid, enabling the distribution of stable yttrium between the aqueous and sphere phases to be calculated. Once the method was refined, active samples were prepared and measured using a high-pressure re-entrant secondary standard ionisation chamber and liquid scintillation counting (LSC). The same process of adding the HNO_3 was used for the active sources. **Results and conclusions:** The average yttrium recovery into the aqueous phase when using HNO_3 was $69.6 \pm 1.9\%$ for the measurements using stable yttrium and $84.4 \pm 2.2\%$ when using ^{90}Y . This work showed that the relative uptake within each experiment has been consistent and reproducible. It has been shown that the method is not time dependant after a period of one hour and solution is homogeneous throughout. The effect of different people attempting the method has also been noted. Additional work needs to be performed to reduce the uncertainties and to understand the differences between stable and ^{90}Y , however, this seems to be a possible method to cross calibrate aqueous ^{90}Y and ^{90}Y bound to microspheres. **References:** Fenwick, A.J. *et al.*, Appl. Radiat. Isot. 87, 10-13 (2014) Ferreira, K.M. *et al.* Appl. Radiat. Isot. 109, 226-230 (2016)

OP-603

⁹⁰Y Scout Dose Imaging In Hepatic Radioembolization

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Purpose: Prior to ⁹⁰Y radioembolization, a scout dose of ^{99m}Tc-macroaggregated albumin (^{99m}Tc-MAA) is administered to estimate the amount of activity shunting to the lungs. A high lung shunt fraction (LSF) may impose a lower treatment dose or even impede treatment. Accurate LSF measurement is therefore important, but is hampered by the deviant MAA particles. Ideally, ⁹⁰Y microspheres would also be used for scout imaging, but this would require this scout activity to be lower than an estimated safety threshold of about 100 MBq. However, ⁹⁰Y is very challenging to image, especially at extremely low activities. The aim of this study is to evaluate low ⁹⁰Y scout activity LSF estimation by PET/CT, Bremsstrahlung SPECT/CT and planar imaging by using an anthropomorphic phantom. **Materials and methods:** The lungs and liver of a thorax phantom (RS-800, Radiology Support Devices) were filled with ⁹⁰Y chloride to mimic an LSF of 15%. Several PET/CT (Siemens Biograph mCT), Bremsstrahlung SPECT/CT (Siemens Symbia T16) and planar images (Siemens Symbia T16) were acquired at a range of ⁹⁰Y activities (1586 to 25 MBq). PET images were reconstructed using a clinical protocol (attenuation correction, TOF, scatter and random correction, OP-OSEM) and included a background correction. SPECT images were reconstructed using both a clinical protocol (attenuation correction, OSEM) and a Monte Carlo (MC) based reconstruction method (MC based detector modelling and scatter correction, attenuation correction, OSEM) which included a background correction. For planar images the geometric mean was calculated and a background correction was included. The LSF was calculated by assessing the reconstructed activity in the lungs and liver delineated on the CT images. **Results:** PET reconstructions accurately estimated the LSF (error <1.0 percent point (pp)) when total activity was high (>350 MBq), but greatly overestimated the LSF (up to 25pp) when activity was low (<100 MBq). Bremsstrahlung SPECT clinical reconstructions overestimated the LSF (up to 13pp) when activity was both high and low. Similarly, planar images overestimated the LSF (up to 23pp). MC-based SPECT reconstructions accurately estimated the LSF with an error of less than 1.3pp for scout activities as low as 70 MBq. **Conclusion:** Bremsstrahlung SPECT/CT can accurately estimate the LSF for a theoretically safe ⁹⁰Y scout activity as low as 70 MBq, when reconstructed with an MC-based model.

OP-604

Comparison Between Planar and SPECT/CT Lung Shunt Fractions for Pre-Therapy SIRT Patients

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Purpose: Pre-therapy ^{99m}Tc-MAA is a common precursor for patients intended for selective internal radiation therapy (SIRT)

with the aim of assessing shunting of activity from the liver to the lungs. Administered activities are in part calculated using lung shunt fraction (LSF) whereby current standard of practice utilises whole body planar scintigraphy. SIRT patients routinely have SPECT/CT for the purpose of clinical assessment and this study aims to quantify the difference between planar LSF and SPECT/CT LSF. **Methods:** One hundred patients from November 2014 to January 2018 were retrospectively analysed to calculate planar and SPECT/CT LSF. LSF is calculated as the lung activity as a percentage of total liver and lung activity. SPECT/CT data was reconstructed using *HERMES Hybrid Recon* (HERMES Medical Solutions AB) with attenuation, resolution recovery, and Monte Carlo scatter corrections applied. Two-dimensional outlines of the liver and lungs were drawn on the planar images using *HERMES Hybrid Viewer* and the area and total counts recorded. Planar LSF was calculated using the background-corrected geometric mean of anterior and posterior images. Three-dimensional outlines of the liver, lungs and background were acquired using *HERMES Hybrid3D* and the volume and total counts recorded and used to calculate a SPECT/CT LSF. For patients where no full CT of the lungs was available the visualised lungs were outlined and an estimate of the total lung volume was made, dependant on gender, and the total lung counts scaled to reflect this. **Results:** Results indicated a definitive correlation between LSF calculations using planar scintigraphy and SPECT/CT. Regression analysis was performed resulting in a correlation coefficient of $R=0.932$ (95% confidence interval, $CI = 0.900 - 0.954$, $p<0.001$) with a corresponding equation of $SPECT/CT/LSF = 0.467[95\%CI\ 0.431-0.504] \times PlanarLSF + 0.006[95\%CI\ 0.001-0.010]$. **Conclusion:** LSF is higher when utilising planar compared to SPECT/CT. Further investigation is required with full lung CT images with the aim of expanding into full lung dosimetry.

OP-605

Comparison of Pre- and Post-Therapeutic Dosimetry in Microsphere Treatment

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Aim: In this study, tumor doses, healthy injected liver doses (HILD) and healthy whole liver doses (HWLD) from pre-treatment Tc-99m MAA SPECT/CT and post-treatment Y-90 PET/CT studies were compared in patient with primary or metastatic liver disease. **Materials and Methods:** The study was retrospectively conducted with 23 pts (9F/14M) with primary or metastatic liver tumors. Approximately 185 MBq Tc-99m MAA was injected from various sub-branches of the hepatic artery. VOIs were drawn on iteratively reconstructed SPECT/CT images to obtain tumor and healthy injected liver volumes and counts. Tumor, HILD and HWLD were estimated using MIRD and multi-compartmental partition methods. Post-treatment Y-90 PET/CT scans were performed with 15 min/bed. SPECT/CT and PET/CT images were registered. Counts on PET/CT were obtained from VOIs used in SPECT/CT images. With these counts, tumor dose, HILD and HWLD were estimated from PET/CT scans. Relationship between pre- and post-treatment doses were investigated with Pearson's correlation coefficient test. **Re-**

sults: In Tc-99m MAA SPECT/CT dosimetry, average tumor, HILD and HWLD were calculated as 181.5 ± 50.3 ; 77.5 ± 19.0 ; 33.1 ± 11.0 Gy, respectively. Corresponding average dose values in PET/CT dosimetry were 154.8 ± 51.7 ; 84.9 ± 23.6 ; 35.9 ± 11.3 Gy, respectively. Average tumor dose was approximately 15% lower in PET/CT dosimetry, while average HILD and HWLD were approximately 9% lower in SPECT/CT dosimetry. Pearson's correlation coefficients were 0.714, 0.858, 0.924, respectively and $p < 0.001$ for all doses. **Conclusion:** Average dose ratios suggest that the differences mainly caused by the registration errors. As tumor regions have small volumes, dose differences between two modalities were higher than other dose quantities. On the other hand, statistically significant correlations were obtained between both dosimetry depends on different imaging methods. This finding concludes that post-therapeutic dosimetry depends on Y-90 PET/CT imaging in can be safely used for assessing treatment delivery accuracy.

OP-606

A novel lung dose calculation methodology with precision analysis for Y90-radioembolization using diagnostic chest-CT and Tc99m-MAA SPECT/CT

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Purpose: Current treatment planning for Y90-radioembolization estimates lung mean dose (LMD) by measuring lung shunt fraction (LSF) from Tc99m-MAA planar imaging and assuming a 1000g lung mass. The errors in these estimations are unknown, and therefore the precision of LMD is unknown. We propose an improved LMD calculation which derives LSF from Tc99m-MAA SPECT/CT (spectCT) and the patient-specific lung mass from diagnostic chest-CT (diagCT). Furthermore, we quantified the errors in these lung mass and LSF calculations to estimate the precision of the reported LMD. **Materials and Methods:** Our proposed LMD (LMDnew) calculation consists of the following: 1) estimate liver counts from spectCT liver contour; 2) estimate total lung counts by multiplying density [cts/g] from spectCT left-lung contour with the total lung mass [g] from diagCT lung contours; 3) compute LMDnew using LSFnew derived from liver and lung counts and the total lung mass from diagCT. The precision of LMDnew was quantified by calculating the relative errors in the liver count, lung count, and lung mass measurements. Finally, we compared LMDnew, LSFnew, and lung mass estimates to standard model values (LMDstd, LSFstd, 1000g) in 52 consecutive patients with hepatocellular carcinoma that underwent Y90-glass-radioembolization. **Results:** LSFnew ranged from 0.003–0.108 (median 0.021), and lung masses ranged from 548–1182g (median 816g). LSFnew was always lower than LSFstd (difference median: -0.044, range: -0.009 to -0.120). An LSFnew uncertainty of 9.0% was derived from uncertainties of 2.0% and 8.8% in liver and lung counts, respectively, due to variability in contouring. Patient-specific lung mass was lower than 1000g in 91% of cases (difference median: -184g, range: -452g to +178g) and had an uncertainty of 6.4% from variability in lung contouring. LMDstd (median: 6.9Gy, range: 1.0 to 30.7Gy) was always greater than LMDnew (difference median: +255%, range:

+108% to +617%). LMDnew, calculated with the same injected activities, was lower than LMDstd by up to 23.0Gy (median 4.9Gy). Error propagation yielded precision of 11.1% in the LMDnew calculation. **Conclusion:** We derived a method to calculate lung mass and LSF using routinely-available diagnostic chest-CT and Tc99m-MAA SPECT/CT. More importantly, we systematically quantified the errors in our measurements to establish the precision of the estimated lung dose (~11%). The current clinical model overestimates LSF and LMD and could therefore unnecessarily limit the dose to target volume(s). The proposed methodology provides a more accurate LMD and an estimate of its precision, which will improve treatment and re-treatment planning for Y90-radioembolizations.

OP-607

Investigation of the quantification of ^{111}In as a theragnostic tracer for ^{90}Y -microspheres after Selective Internal Radiation Therapy

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Introduction: Post-therapy ^{90}Y imaging can be used for absorbed dose estimation following ^{90}Y -microsphere SIRT. ^{90}Y bremsstrahlung SPECT-CT has relatively poor resolution and quantitative accuracy. It is proposed that the quantitative accuracy of post-SIRT SPECT can be improved by the co-administration of microspheres labelled with a gamma-emitting tracer. The aim of this study was to investigate the quantitative accuracy of ^{111}In SPECT in the presence of an ^{90}Y background. $^{90}\text{Y}/^{111}\text{In}$ SPECT was compared with ^{90}Y SPECT-CT for quantitative accuracy. **Method:** A 3D printed liver phantom with two spherical inserts of 40mm and 20mm diameter was filled with 600MBq of ^{90}Y at a sphere-to-background ratio of 6:1. An ^{90}Y SPECT-CT scan was acquired with a 56–268keV energy window. The phantom was then filled with a $^{90}\text{Y}/^{111}\text{In}$ mixture at ratios 50:1, 10:1, and 5:1 with a sphere-to-background ratio of 6:1 and SPECT-CT scans were performed with 15% energy windows centred on 171keV and 245keV. All SPECT scans were acquired for 20s per projection, 72 projections, and reconstructed using OSEM 4 iterations, 6 subsets, with CT attenuation correction. VOIs were drawn around the phantom and spheres on the CT scans and 'normal liver voxels' were defined by subtraction of the sphere VOIs from the phantom VOI. Quantitative accuracy was evaluated for phantom background and spheres by comparing the measured image activity to that of the known phantom activity. GATE Monte Carlo simulation was used to estimate the proportion of counts within the ^{111}In energy window due to ^{90}Y and ^{111}In respectively. **Results:** The differences from reference activity values for normal liver quantification were 6%, 8% and 9% (at 5:1, 10:1, 50:1 ratios) for $^{90}\text{Y}/^{111}\text{In}$ SPECT compared to 11% for ^{90}Y SPECT. $^{90}\text{Y}/^{111}\text{In}$ SPECT demonstrated differences for the large sphere of -12%, -20% and -24% for ratios 5:1, 10:1 and 50:1 and -44%, -61% and -61% for the small sphere. Differences for ^{90}Y SPECT were -38% for the large sphere and -69% for the small sphere. GATE Monte Carlo simulation demonstrated that 35%

of counts originated from ^{90}Y emissions for a 50:1 ratio, 10% for 10:1 and 5% for 5:1. **Conclusion:** ^{111}In showed promise as a theragnostic tracer for co-administration with ^{90}Y microspheres. ^{90}Y bremsstrahlung SPECT demonstrated equivalent accuracy to $^{90}\text{Y}/^{111}\text{In}$ for normal liver quantification. $^{90}\text{Y}/^{111}\text{In}$ showed superior performance for lesion quantification. A maximum therapeutic to diagnostic tracer ratio of 5:1 is recommended for accurate lesion quantification.

OP-608

High Quality Imaging and Dosimetry of Yttrium-90 (^{90}Y) SIRT Using a Digital PET/CT

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Objectives: Yttrium-90 radioembolization (RE) is a treatment modality for hepatic malignancies. Personalized dosimetry aims for maximum treatment effect while keeping toxicity acceptably low. Dose calculation methods are based on empirical evidence with regard to efficacy and safety, but do not take radiation absorbed dose in tumor or normal liver tissue into account. We assessed the accuracy for distribution and dosimetry and compared absorbed dose in tumor and normal liver tissue in pre- and post-therapy imaging. Furthermore, image quality of ^{90}Y post RE scans using a SiPM-based PET/CT was compared to standard of care pre-therapy $^{99\text{m}}\text{Tc}$ MAA SPECT/CT. **Methods:** We analyzed $^{99\text{m}}\text{Tc}$ MAA SPECT/CT and ^{90}Y PET/CT images using SurePlan (MIM) software. Tumor volume and normal liver tissue were contoured on the pre-therapy diagnostic CT and then registered to $^{99\text{m}}\text{Tc}$ MAA SPECT/CT and ^{90}Y PET/CT respectively. Image quality was evaluated using the 5-point Likert scale. **Results:** Eleven patients were treated with a median administered activity of 2.73 GBq. Mean tumor dose in $^{99\text{m}}\text{Tc}$ MAA SPECT/CT was 81.8 Gy versus 83.82 Gy in ^{90}Y PET/CT. There was no significant difference between Tumor-SPECT/CT and Tumor- ^{90}Y PET/CT doses ($t = -.335$, $p = 0.740$). On average, Tumor-SPECT/CT scores were 2 Gy lower than tumor- ^{90}Y PET/CT doses (95% CI [-20, 15]). For normal liver tissue, a mean dose of 26.8 Gy was found in the $^{99\text{m}}\text{Tc}$ MAA SPECT/CT images and 18.6 Gy for ^{90}Y PET/CT ($t = 1.260$, $p = 0.236$). On average, normal liver tissue doses in $^{99\text{m}}\text{Tc}$ MAA SPECT/CT were 8 Gy higher than ^{90}Y PET/CT doses (95% CI [-6, 22]). For ^{90}Y PET/CT imaging, the best image quality was found at 20 min scan time (Likert-Scale 4.5 ± 0.5) vs. 15 min Likert-Scale 4 ± 0.6 and 10 min Likert-Scale 2 ± 0.6 . **Conclusion:** Our preliminary data show excellent image quality from digital ^{90}Y PET/CT at a reduced scan time of 20 minutes. MIM software computed no significant divergent tumor or normal liver tissue doses for $^{99\text{m}}\text{Tc}$ MAA SPECT/CT or ^{90}Y PET/CT. However, more patients have to be evaluated to confirm these findings. The faster imaging time may allow for inclusion of ^{90}Y PET/CT in routine clinical workflows.

OP-609

Variations in Dose to Critical Micro Structures in Y-90 Radioembolization Treatment of Liver Cancer

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Background: Patient-specific treatment planning in radioembolization (RE) therapy for liver cancer requires accurate estimation of normal tissue complication probabilities (NTCP). While NTCP models for external beam liver therapies have proved quite successful, NTCP models for RE therapies have yet to attain the accuracy required for safe dose escalation. It has been postulated that errors in RE NTCP estimation are driven by the non-uniformity in the absorbed dose in critical structures (central vein, parenchyma, portal vein etc.) within liver lobules. Lobule level microdosimetry using Y-90 PET or SPECT images for defining spatial activity distributions is not feasible. We have therefore proposed a model which couples imaging data with tabulated data from a two-component lobule-level dosimetry model. One component of the model involves determination of appropriate maps of microsphere clustering in the hepatic vascular system. The second component (the subject of this work) involves the development of tabulated data of relative doses to lobule microstructures for given microsphere cluster maps. **Methods:** Basic liver lobule microanatomy is modeled as an array of regular hexagons, with a cylindrical central vein, and a set of cylinders at each vertex, representing bile duct, hepatic artery and portal vein (the portal triad). To better model actual anatomy, the vertices of the lobules are displaced slightly, distorting the hexagons, and not every vertex is assumed to contain a portal triad. The general Monte Carlo program EGS5 was used to simulate dose deposition in the various structures, from which dose volume histograms were derived. Microspheres were placed in the individual hepatic arteries of the triads in varying numbers and locations to simulate clustering seen in tissue biopsies. **Results:** Variations in lobule average dose, central vein dose, and dose to portal triad structures are strong functions of microsphere cluster non-uniformity. Maximum doses in triads were 4-25 times doses to nearby lobules, and 7-30 greater than dose to nearby central veins. However, while central vein DVHs were somewhat similar to average lobule DVHs, the fraction of triad elements receiving at least 50% of the average lobule dose could be as low as 50%. This variation in triad element dose may suggest a lobule survival mechanism which might explain liver NTCP in non-uniform dose environments. **Conclusions:** A model of differential dose distributions to critical structures of the liver microanatomy has been developed. When coupled with a representative microsphere clustering model, this should lead to better prediction of NTCP for RE therapy.

1507

Tuesday, October 16, 2018, 16:30 - 18:00, Hall 1

Teaching Session 6 - Interactive Clinical Cases: Lung Cancer Interactive Session Testing your Knowledge with Live Cases

OP-610

Interactive session TNM with Case Discussions and Live Voting on the Staging of Cases - Where do we go Wrong?

T. Lynch; Belfast, UNITED KINGDOM.

OP-611**Interactive session TNM with Case Discussions and Live Voting on the Staging of Cases - Where do we go Wrong?**

N. Magee; Belfast City Hospital, Consultant Respiratory Physician, Belfast, UNITED KINGDOM.

OP-612**Interactive session TNM with Case Discussions and Live Voting on the Staging of Cases - Where do we go Wrong?**

K. McManus; Belfast Health and Social Care Trust, General Thoracic Surgeon, Belfast, UNITED KINGDOM.

1508

Tuesday, October 16, 2018, 16:30 - 18:00, Hall 4

Clinical Oncology - Rapid Fire Session: In the Air and Beyond**OP-613****Circulating Tumor Cells In Metastatic NSCLC Patients Candidate To Immunotherapy With Checkpoint Inhibitors**

A. Castello, **S. Monterisi**, **F. Grizzi**, **L. Toschi**, **S. Rossi**, **D. Qehajaj**, **G. Finocchiaro**, **G. Veronesi**, **E. Lopci**; Istituto di Ricerca e Cura a Carattere Scientifico (IRCCS), Milano, ITALY.

Background and Aim: Detection of circulating tumor cells (CTCs) in the bloodstream is emerging as a minimally invasive biomarker in patients with different malignancies. Our aim was to investigate CTCs counting in patients affected by metastatic non-small cell lung carcinoma (NSCLC) candidate to immunotherapy and correlate findings with clinical and metabolic parameters. **Materials and Methods:** Overall, 17 patients (11 male, 3 female) affected by metastatic NSCLC and referred to our Institution for immunotherapy with checkpoint inhibitors were prospectively enrolled. All patients underwent FDG PET before treatment and CTCs detection from whole blood drawn at baseline. The trial has been approved by the local IRB. For CTCs isolation, 10 ml of blood are collected in EDTA tubes and processed within 2 hours. Isolation by Size was carried out with the ISET method. Patients were considered positive for CTCs based on cytopathological analyses considering as malignant features: a) nuclear hyperchromatism, b) increased nuclear volume, c) irregular nuclear borders, and d) increased nucleic ratio/cytoplasm. CTCs were computed when at least 3 of the above criteria were fulfilled. As negative control, the blood drawn from 7 healthy donors was collected. The presence of CTCs was compared with age, gender, smoking status, histologic subtype, chemotherapy pre-immunotherapy, PDL-1 expression, Performance status, and semi-quantitative parameters on FDG PET, including SUVmax, SUV mean, metabolic tumor volume (MTV) and total lesion glycolysis (TLG). All statistical analyses were performed with GraphPad Prism (version 7). **Results:** CTCs were identified in 10 out of 17 patients (59%). At baseline, mean number of CTCs was 3 (range 1-7). Only one cell with malignant features was detected in the blood of a healthy volunteer out of 7 donors analyzed (16%). We found a significantly lower number of CTCs in patients who had previously undergone chemother-

apy ($p=0.031$), whereas no further correlations between CTCs and clinicopathologic characteristics were observed. According to semi-quantitative parameters on FDG PET, patients with an extended tumor burden, expressed by TLG and MTV, were associated with a higher number of CTCs ($p=0.011$ and $p=0.004$, respectively). Likewise, patients with a higher SUVmean value resulted having a higher CTCs count ($p=0.04$). **Conclusion:** In our cohort, the presence of CTCs seems to be associated with metabolic parameters on FDG PET and is influenced by previous chemotherapy. In the future, the combination of these two techniques might be useful in driving therapeutic strategies in this clinical setting.

OP-614**Total Metabolic Tumor Volume by 18F-FDG PET/CT As a Predictor of Outcome in Patients with Non-Small Cell Lung Cancer**

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Purpose: The aim of the present study was to test whether volumetric imaging parameters derived from 18F-FDG PET/CT may predict clinical outcome in patients with non-small cell lung cancer (NSCLC). **Subjects & Methods:** Seventy-three patients (50 men, 23 women; mean age $\pm$ SD, 66 y $\pm$ 12 y), with histologically proven NSCLC who had undergone 18F-FDG PET/CT scan before any therapy, were included in the study. Imaging parameters including SUVmax, SUVmean, total metabolic tumor volume (MTV_{TOT}) and whole body total lesion glycolysis (TLG_{WB}) were determined. MTV of each lesion was calculated using an automated contouring program setting a threshold for SUVmax at 2.5. TLG of each lesion was calculated by multiplying MTV for SUVmean. The values of all lesions were then summed to derive MTV_{TOT} and TLG_{WB}. The median follow-up period after 18F-FDG PET/CT scan was 12 months. Univariate and multivariate analysis of clinical and imaging variables were performed using Cox proportional hazards regression. Survival analysis was performed using Kaplan-Meier method and log-rank tests. **Results:** MTV_{TOT} and TLG_{WB} could be determined in 66 patients (20 in stage I, 5 in stage II, 13 in stage III and 28 in stage IV). A total of 270 lesions were analyzed including 66 primary tumors (mean diameter: 3.2 cm $\pm$ 2.1 cm), 101 metastatic lymph nodes, 5 contralateral lung nodules, 72 bone metastases, 7 hepatic lesions, 3 adrenal metastases and 16 lesions in other sites. Mean value of MTV_{TOT} was 79.63 ml $\pm$ 14.39 ml (SE) whereas mean value of TLG_{WB} was 445.69 g $\pm$ 75.86 g (SE). Univariate analysis showed that, among the variables tested, age ($p=0.0220$), stage ($p<0.0001$), surgery ($p<0.0001$), MTV_{TOT} ($p=0.0001$) and TLG_{WB} ($p=0.0009$) predicted overall survival in NSCLC patients, while primary tumor diameter ($p=0.0431$), stage ($p<0.0001$), surgery ($p<0.0001$), MTV_{TOT} ($p=0.0005$) and TLG_{WB} ($p=0.0005$) predicted progression free survival in NSCLC patients. At multivariate analysis age, stage and MTV_{TOT} were retained in the model for prediction of overall survival

($p < 0.0001$) and progression free survival ($p < 0.0001$). Similar results were obtained in a subgroup of 41 patients with advanced disease (stage III and IV). By Kaplan-Meier analysis and log-rank testing, overall survival was significantly better in patients showing a $MTV_{TOT} \leq 9.6$ ml as compared to those having $MTV_{TOT} > 9.6$ ml ($p < 0.0001$). **Conclusion:** PET-based volumetric imaging parameters are capable of predicting outcome in NSCLC patients.

OP-615

Functional lung volume mapping with perfusional ^{99m}Tc -MAA SPECT for radiotherapy planning in patients with locally advanced NSCLC

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Purpose: Combined chemo-radiotherapy represents the standard treatment for locally advanced Non-Small Cell Lung Cancer (NSCLC). Radiation-induced toxicity is a dose-limiting complication of radiotherapy. The incidence of radiation pneumonitis is dose and volume-dependent, and it is related to Mean Lung Dose (MLD). Aim of this study was to perform a tailored dosimetric evaluation for Intensity-Modulated Radiation Therapy (IMRT) planning based on functional lung volumes derived from fused SPECT/CT images and to compare functional and conventional dose-volume parameters. **Subjects and methods:** Patients with locally advanced NSCLC eligible to combined chemo-radiotherapy were prospectively enrolled. Planning CT scan was performed in RT treatment position. Lung perfusion scintigraphy was performed in the same position before RT and 3 and 6 months after RT completion. SPECT images were acquired after i.v. administration of 185 MBq of ^{99m}Tc -MAA, with step-and-shoot technique (128x128 matrix, 360° orbit, rotation angle 3°, 20s per view) and reconstructed with OSEM method. SPECT and CT images were co-registered using MIM-MAESTRO™ software with 3D-PET EDGE™ algorithm. Lung volumes were defined anatomically as Total Lung (TL) and functionally as Total Not Functional Lung (T-NFL) and Total Functional Lung (T-FL). Dose-Volume Histograms (DVH) were calculated using QUANTEC constraints (MLD < 20 Gy, lung volume receiving 20 Gy-V20 < 30%). For each patient, RT planning was elaborated with and without functional SPECT contribution. Patients underwent IMRT treatment with 50-60 Gy using the most appropriate plan based on the two estimated DVH. **Results:** 15 NSCLC patients were consecutively enrolled (mean age 69y, 7 stage IIIA, 8 stage IIIB). Mean MLD was 10.63 Gy ± 2.35 for TL volume and 9.24 Gy ± 3.04 for T-FL volume, with a difference of 1.39 Gy which was not significant at Student *t* test ($p = 0.016$, CI 95%). Mean V20 for TL volume was 723.06 cc ± 298.66 and 284.06 cc ± 155.16 for T-FL volume, with a statistically significant difference between the two groups (439 cc, $p < 0.001$, CI: 95%). At the time of analysis, 10 patients completed the 6-months follow-up, 3 completed the 3-months follow-up and 2 patients were receiving RT. Eval-

uation of late radiation-induced toxicity will be performed after completion of scheduled follow-up SPECT scans. **Conclusions:** Functional parameters derived by fused SPECT/CT images may be useful to minimize exposure of functional lung in IMRT planning, while maintaining target coverage and constraints for contralateral lung. SPECT-guided IMRT planning provided superior lung sparing of both anatomical and functional volumes as compared to the conventional anatomic planning, with the possibility to reduce radiation-induced toxicity and to perform an effective dose escalation.

OP-616

Comparison of ^{18}F -FDG and ^{68}Ga -DOTA-peptide PET/CT in pulmonary carcinoid and correlation with histological features

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Purpose/introduction: Pulmonary carcinoid tumors (PCs) are a rare group of lung neoplasms. The typical carcinoids showed higher uptake of ^{68}Ga -DOTA-peptide than ^{18}F -FDG on PET-CT but despite encouraging, few data are available reporting the detection rate (DR) of ^{68}Ga -DOTA-peptide and ^{18}F -FDG PET/CT in patients with PCs. In this study, we describe the diagnostic performances of both ^{68}Ga -DOTATOC and ^{18}F -FDG PET/CT scans in detecting PCs and their inter-relationship with histological features. **Subjects and Methods:** From 01/09 to 08/17, we have selected and recovered the clinical data, ^{18}F -FDG and ^{68}Ga -DOTATOC PET-findings, surgical and pathological information of 62 PCs occurring in 57 patients. T- and chi-square tests were adopted to compare continuous and categorical variables. **Results:** Mean age and female/male ratio were 68.2 ± 12.3 and 3:1, respectively. Typical carcinoids (TCs) were observed in 55 lesions while Atypical Carcinoids (ACs) in 7. All patients underwent at least one PET/CT scan: ^{68}Ga -DOTATOC in 26 patients, ^{18}F -FDG in 52 patients and both techniques in 20 patients. When adopted SUVmax = 2.5 as threshold, overall detection rates (DR) of ^{68}Ga -DOTATOC PET/CT and ^{18}F -FDG PET/CT were 88.4% and 53.8%, respectively. The DRs increased to 100% and 80.8%, respectively when adopted SUVmax = 1.5 as cutoff. Mean SUVmax of ^{68}Ga -DOTATOC PET/CT and ^{18}F -FDG PET/CT was 15.5 and 3.2, respectively. The DRs of both technique remarkably vary according with histology, with a higher DR of ^{68}Ga -DOTATOC PET in TCs than in ACs (91.7% vs 50.0%, $p = 0.076$ when adopted SUVmax = 2.5 as threshold and 100% vs 50% when adopted SUVmax = 1.5 as threshold) and a higher DR ^{18}F -FDG PET/CT in ACs than in TCs (71% vs 51% when adopted SUVmax = 2.5 as threshold). Considering the relationship between the number of mitoses and the presence of necrosis with both PET-findings, we found as a low number of mitosis (<2/10HPF) significantly correlates with ^{68}Ga -DOTATOC PET-positivity ($p = 0.004$); a trend of association ($p = 0.076$) was also observed between the presence of

necrosis and ^{68}Ga -DOTATOC PET-negativity. **Discussion/conclusion:** ^{68}Ga -DOTATOC PET/CT has a better diagnostic performance compared with ^{18}F -FDG PET/CT in detecting pulmonary carcinoids; the detection rates of both techniques remarkably vary according to histology with ^{68}Ga -DOTATOC PET performing at its best in typical carcinoids and ^{18}F -FDG PET in atypical carcinoids. Low number of mitosis results seems to be associated with ^{68}Ga -DOTATOC PET-positivity. It was also observed that ^{68}Ga -DOTATOC PET-negativity seems to be associated with the presence of necrosis.

OP-617

Evaluation of a fast protocol for staging patients with bronchial cancer using PET/MRI

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Purpose: To evaluate the applicability of a fast MR-protocol for whole-body staging of bronchial carcinoma patients using an integrated PET/MR system. **Material and Methods:** In this prospective study, 52 patients (16 female, 36 male, mean age 63.9 ± 8.7 years) underwent clinically indicated PET/CT and subsequent PET/MRI using ^{18}F -FDG as tracer. For PET/MRI imaging, a fast whole-body MR-protocol was implemented. MRI and PET/MRI datasets were analyzed to identify malignant manifestations. The accuracy for the identification of malignant manifestations was calculated and the tumor stage for each examination was determined using the actual TNM classification from UICC 8 (union international contre le cancer). In addition, radiation doses derived from administered tracer activities and CT protocol parameters were estimated and the mean scan duration of PET/CT and PET/MRI imaging was determined. In 26 patients, all available histopathological samples as well as results of prior examinations and follow-up imaging were used for the determination of the reference standard. In the other cases, the results of PET/CT imaging used for reference standard. **Results:** Active malignant lesions were present in 47/52 examinations. Both MRI and PET/MRI have a 100% accuracy to correctly identify the extent of the primary (T-stage). In comparison to nodal staging in PET/CT, PET/MRI revealed higher values of diagnostic accuracy than MRI alone (93.5% for PET/MRI, 83.9% for MRI, $p < 0.05$). However, the results between PET/MRI and MRI did not differ significantly. In identification of metastases, PET/MRI showed higher diagnostic accuracy than MRI alone (90.3% for PET/MRI vs. 77.4% for MRI, $p < 0.05$). In TNM classification, PET/MRI enabled higher values of correct stage than MRI (86.9% for PET/MRI vs. 64.5% for MRI, $p < 0.05$). The values of correct stage did not differ significantly between PET/CT and PET/MRI (93.5% for PET/CT vs. 86.9% for PET/MRI). Average scan duration of whole-body PET/CT and PET/MRI examinations were 17.5 ± 2.3 min and 29.4 ± 3.9 min, respectively. Estimated mean effective-dose for whole-body PET/CT scans were 61.3% higher than for PET/MRI.

Conclusion: Using ^{18}F -FDG PET data in addition to whole-body MRI leads to a more accurate evaluation of patients with bronchial cancer. With regard to patient comfort related to scan duration and reduced radiation exposure, fast PET/MRI may serve as a powerful alternative to PET/CT for a diagnostic workup of bronchial cancer patients.

OP-618

Prognostic Value Of Restaging 18-FDG PET/CT Volumetric Parameters For Post-index Irradiation Recurrence Of Head And Neck Squamous Cell Carcinoma

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Background: Statistical image features of tumor metabolism from pretreatment ^{18}F -FDG-PET/CT scans were studied for their potential to predict clinical outcome of the recurrent squamous cell carcinoma of head and neck (HNSCC). **Materials and Methods:** Pretreatment PET/CT scans and after treatment PET/CT scans of 69 patients who underwent salvage treatment for recurrent HNSCC, were retrospectively evaluated. Metabolic response was assessed using PET response criteria for solid tumors (PERCIST). Multiple statistical image features related to the standard uptake value (SUV) were computed: metabolic tumor volume, maximum SUV, mean SUV, total lesion glycolysis (TLG). The correlation between the image features and local control and overall survival was calculated. **Results:** In this study we reported on the utility of PET/CT in survival prognostication for recurrent head and neck cancer. Our analysis indicates that whole body metabolic tumour volume WB MTV has potency in estimating the overall survival. High WB MTV (over 21,5 cc) corresponds with poor prognosis and low one-year survival rate (56,0% of patients will not survive over 12 months); on the other hand, one-year survival at WB MTV $< 21,5$ cc is estimated as 93,2%. This observation remained robust even after accounting for other known prognostic factors including salvage re-irradiation and recurrence location. **Conclusions:** With this study we established a pre-salvage volumetric cut-off point (whole body metabolic tumour volume WB MTV of 21,5 cc) that predicts one-year survival with high accuracy. A more extensive study is warranted to decide if this cut-off point is acceptable for subgroup of patients who will undergo a salvage re-irradiation.

OP-619

Exploratory analysis of using supervised machine learning in [^{18}F] FDG PET/CT images to predict treatment response in patients with metastatic and recurrent ENT tumors

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Aim: The prognosis of patients that suffer from metastatic and recurrent squamous cell carcinoma (SCC) of the head and neck region is generally poor. Treatment could be improved and perhaps standardized if more reliable markers for tumour progression and poor prognosis could be developed. The aim of this study was to evaluate whether in vivo radiomic and patient-based machine learning (ML) driven analysis of 2-deoxy-

2-(^{18}F)fluoro-D-glucose PET/CT (^{18}F FDG-PET/CT) is feasible to predict for treatment response and overall survival (OS) in patients with ENT tumours. **Materials and Methods:** In total 125 patients with the diagnosis of metastatic and recurrent SCC of the head and neck, who had a positive ^{18}F FDG-PET/CT scan between 12/2008 and 12/2015 were included in this analysis. Up to five malignant lesions were delineated on the PET images using semi-automatic VOIs, which were summed up to one total tumour volume, followed by feature extraction. Clinical data such as age, tumour grade, OS, course of treatment, response and HPV status were collected. Machine learning (ML) approaches utilizing automated feature selection and feature weight estimation [1] were applied to establish automated predictive models on radiomic PET/CT and patient features for survival and response prediction. Predictive models were validated in the Monte Carlo cross-validation scheme [1]. **Results:** Median OS was 20.0 months (range: 0–89 mo). 43 patients received chemoradiation, 19 chemotherapy, 23 resection, 16 radioimmunotherapy and the remaining 20 best supportive care; response rates were 36/43, 9/19, 17/23 and 17/20 for the four treatment groups respectively. A treatment-based subgroup analysis yielded the best predictive models with 0.84 sensitivity (SNS), 0.65 specificity (SPC) and 0.74 area under the curve (AUC) of predicting for response and 0.75 SNS, 0.83 SPC and 0.8 AUC of predicting tumour grade after chemoradiation. Prediction over the whole cohort revealed the following SNS, SPC and AUC: OS (0.77, 0.48, 0.63), Response (0.62, 0.64, 0.63) and Grade (0.65, 0.72, 0.69). **Conclusion:** Our results demonstrate that the combined analysis of radiomic and patient features via ML is a valuable option for predicting OS, response and tumour grade in ENT tumours. References 1: L. Papp et al, J Nucl Med, 2017, doi: 10.2967/jnumed.117.202267

OP-620

Comparison between ^{18}F -FDG-PET/CT and ^{18}F -FDG PET/MRI in the detection of locoregional recurrence 3 months after chemoradiotherapy in HNSCC patients. A retrospective clinical experience

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Purpose: PET/MRI imaging is increasingly used in staging and restaging head and neck malignancies, although PET/CT maintains an established role in clinical practice. The aim of this study is to compare the diagnostic performance of ^{18}F -FDG-PET/CT and ^{18}F -FDG-PET/MRI in the detection of loco-regional recurrence 3 months after the end of chemoradiotherapy in patients with head and neck squamous cell carcinoma (HNSCC). **Subjects and Methods:** In this retrospective study, 104 patients with histologically confirmed HNSCC were enrolled. 52 of them underwent a ^{18}F -FDG-PET/CT and 52 a combined-sequential ^{18}F -FDG-PET/MRI 3 months after chemoradiotherapy treatment. Image interpretation was based on visual and semi-quantitative

(SUVmax) analysis of increased focal ^{18}F -FDG uptake, compared with the surrounding background and contralateral physiologic uptake. All patients had clinical and instrumental follow-up for at least of 12 months (range 12–48 months). Histopathological sampling as well as cross-sectional and clinical follow-up were considered as a reference standard in recurrence diagnosis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy for both techniques were calculated. A comparison based on tumor location, stage and HPV status was also performed. **Results:** 15/52 (29%) patients that underwent PET/CT and 20/52 (38%) that underwent PET/MRI had a pathological ^{18}F -FDG uptake, suspicious for loco-regional recurrence. TP and FP rate for PET/CT and PET/MRI was 10 (67%)/5 (37%) and 18 (90%)/2 (10%) respectively. PET/CT was able to identify correctly 32/37 (86%) negative findings, with 5/37 (13%) FN results. PET/MRI diagnosed correctly 100% of negative scans (32/32) and no false negative results were recorded. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of ^{18}F -FDG-PET/MRI and ^{18}F -FDG-PET/CT were 100%/67%, 94%/86%, 90%/67%, 100%/86%, 96%/81% respectively. According to tumor location, oral cavity, nasopharynx and larynx were the regions where wrong PET interpretations were made. In oral cavity HNSCC, FP results occurred in both examinations (PET/MRI: 2, PET/CT: 3). On the other hand, PET/MRI interpreted correctly all findings in the nasopharynx and larynx region, compared to PET/CT (FN: 5, FP 2). According to stage, in PET/MRI scans FP results occurred in patient with stage $\geq$ IVa, in PET/CT examinations FP and FN findings were found in patients with stage $\geq$ III. HPV positive patients had a higher percentage of true negative scans confirmed in the follow-up (100% on PET/MRI and 84% on PET/CT) and therefore better outcome, compared to HPV negative patients. **Conclusions:** In patients with HNSCC, ^{18}F -FDG-PET/MRI yielded a better diagnostic capability, especially in terms of sensitivity and NPV, than ^{18}F -FDG-PET/CT in detecting recurrence 3 months chemoradiotherapy.

OP-621

Prognostic value of texture features based on pretreatment ^{18}F -FDG PET/CT in patients with oropharyngeal cancer

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Purpose: This study was designed to evaluate the utility of textural features for predicting prognosis in patients with oropharyngeal carcinoma. **Materials and Methods:** From April 2008 through December 2014, a total of 25 patients with oropharyngeal cancer who underwent pretreatment ^{18}F -FDG PET/CT were enrolled. Maximum standardized uptake value (SUVmax), mean standardized uptake value (SUVmean), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) of both primary tumor and metastatic cervical lymph nodes, and textural features of primary tumor were measured by two independent nuclear physicians. Receiver operating characteristic curve analysis was used to estimate the area under the curve for each parameter. The significance of these prognostic parameters was assessed by Cox proportional hazards regression analysis.

Results: With a median follow-up of 38.8 months, 3-year overall survival (OS), disease-free survival (DFS), distant metastasis free survival (DMFS), local failure free survival (LFS) and regional failure free survival (RFS) were 95.5%, 78.5%, 87.3%, 90.9% and 91.3%. Since most of the primary tumor of patients were distributed in early stage, multivariate analyses with adjustments for N stage showed that SUVmax and SUVmean of total lesion were independent adverse parameters for DMFS. SUVmax, SUVmean, MTV and TLG extracted from primary tumor were not effective in predicting prognosis. However, in the texture analysis, NGLD-NN was an independent predictor for DFS. Co-Ho, Co-IDM, NCo-Ho, TFCCo-En and TFCCo-CE were independent predictors for OS. Conclusion: Texture features of 18F-FDG PET/CT are independent predictive factors in OS and DFS in patients with oropharyngeal cancer. Further investigations are needed for confirmation.

OP-622

The usefulness of 11C-Methionine PET/CT (MET-PET) in patients with adenoid cystic carcinoma (ACC) before and after carbon ion radiotherapy. A two centre study

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To evaluate MET-PET capability for the prediction of carbon ion radiotherapy (CIRT) response, patients' outcome and survival rate in ACC. We retrospectively enrolled 85 patients (mean age 55 years, range 19-83, 40 men, 45 women) with histological diagnosis of ACC addressed at our institutions between May 2013 and May 2017. All the patients received CIRT at CNAO (Italian acronym for National center of Oncological Hadrontherapy) in Pavia, underwent a planning MRI, as well as a MET-PET before and after CIRT at the S. Orsola Hospital in Bologna and Humanitas Research Hospital in Milan. All images before and after treatment have been revised for the current analysis by two expert nuclear medicine physicians and radiologists. Visual and semi-quantitative analyses at PET findings (SUVmax, SUVmean, TBR, metabolic tumor volume, delta volume and delta SUV) were compared with best response (best-MRI) and the more recent MRI response (last-MRI) classified as CR, PR, SD, PD. According to metabolic treatment response, each MET-PET was classified as CMR, PMR, SMD, PMD and compared to best- and last-MRI classification. PET results were correlated with patient's outcome (relapse, progression, death) and patient characteristics (age, gender, tumour primary site, time from surgery, presence of solid component). Statistical analysis showed that in planning-PET the SUVmax/mean of primary tumour (TSUV) were higher in

SD-patients respect to CR-patients ($p < 0.01$), as reported by best-MRI. Similarly, the values of TSUVmax/mean and TBRmax/mean in MET-PET after CIRT were effective in distinguishing CR from PR, SD, PD ($p < 0.01$). By means of ROC analysis optimal cut-off points for TSUVmax < 2.8 (Sensitivity 68%, specificity 82%, AUC 0.720) and TBRmax < 1 were identified (Sensitivity 66%, specificity 84%, AUC 0.720). Considering last-MRI response, PET before-CIRT showed lower TSUVmax/mean values in CR patients compared with the other groups ($p < 0.01$). We did not find any significant correlation between PET findings and patients' characteristics. In the evaluation of therapy response, PET classification showed good agreement (K-test) with best-MRI (71.8%, $p: 0.0035$) and limited agreement with last-MRI classification (57.6%, $p: 0.025$). Survival curves showed that patients classified as responders by post-CIRT PET survived longer ($p: 0.052$) than those in SMD/PMD, in particular CMR-group ($p: 0.042$). In our study, MET-PET showed a good correlation with MRI in the assessment of treatment response. While MRI has a primary role in ACC management, MET-PET analysis performed before and after CIRT resulted effective in predicting both therapy response and survival.

OP-623

Prognostic value of semiquantitative parameters in post-treatment in 18F-FDG PET/CT in patients with SCLC

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Aim: To determine the prognostic value of post-treatment 18F-FDG PET/CT semiquantitative parameters in patients with Small-cell Lung cancer (SCLC). **Materials and Methods:** Forty-eight patients (40 males and 8 females; mean age 64.48 years, range 48-86) with histologically proven SCLC and post-treatment 18F-FDGPET/CT scan were retrospectively reviewed. 14/48 (29.2%) performed combined CHT-RT treatment while 34/48 (70.8%) had chemotherapy only. SUVmax and SUVmean of primary tumour (T), lymph-nodes (N) and metastasis (M) were collected; metabolic tumour volume (MTV) and total lesion glycolysis (TLG) were collected for each patient summing the values of each lesion. The clinical endpoints were overall survival (OS) and progression-free survival (PFS) and the last follow-up was in January 2018. The survival time was estimated using Kaplan-Meier method. We identify two groups for each PET parameter based on the lower or higher value compared to its median and we assessed the difference of OS and PFS between groups by log-rank tests. P values < 0.05 were considered statistically significant. **Results:** Fortyone/48 (85.4%) patients had positive 18F-FDG PET/CT for T and 7/48 (14.6%) were negative; 28/48 (58.3%) were positive for N and 20/48 (41.7%) were negative; 9/48 (18.8%) were positive for M and 39/48 (81.3%) were negative. At the end of the follow-up 39/48 (81.3%) were alive while 9/48 (18.8%) were dead. Median OS was 20 months (range 5-128), median PFS was 22 months (range 2-128). OS resulted significantly different for SUVmax of N parameter (median 3.3; log rank=5.391; $p=0.02$), MTV (median 68818; log rank=4.836; $p=0.028$) and TLG parameter (median 14654; log rank=5.305;

$p=0.02$). Mean OS in patients with SUVmax of N lower than the median was 116 months, 68 months if higher than the median; mean OS in group with MTV lower than the median was 106 months, 77 months if higher than the median; mean OS in group with TLG lower than the median was 106 months, 67 months if higher than the median. PFS resulted significantly different only for TLG parameter (log rank=8.16; $p=0.004$). Mean PFS in group with TLG lower than the median was 78 months, while in group with TLG higher than the median was 30 months. **Conclusion:** The semiquantitative parameters evaluation can add information about prognosis, in particular the N involvement analysis is a fundamental step also in the semiquantitative evaluation. Furthermore, the evaluation of tumour burden using the TLG parameter is a valid prognostic factor both in OS and PFS analysis.

1510 Tuesday, October 16, 2018, 16:30 - 18:00, Hall 28

Cardiovascular: Myocardial Imaging - New Developments with CZT-Cameras

OP-624

One-day Myocardial Perfusion SPECT: Considerably Less Activity For Rest Studies Needed Than Generally Recommended

J. D. van Dijk, J. A. van Dalen, S. Knollem, M. Mouden, J. Ottervanger, P. Jager; Isala hospital, Zwolle, NETHERLANDS.

Background: Guidelines propose rest-stress activity ratios (SRAR) of three or more for one-day stress-rest SPECT myocardial perfusion imaging (MPI) but evidence is limited. Our aim was to determine and validate the minimal RSAR resulting in negligible 'shine through' in the rest scan in one-day stress-first rest SPECT MPI. **Method:** Forty-seven patients referred for rest after stress CZT-SPECT (Discovery 570, GE Healthcare) MPI were prospectively included. Rest acquisitions were performed 3h after stress using 800MBq and 200MBq, respectively. In addition to the stress and rest acquisitions, the first 22 patients underwent an additional acquisition prior to the rest injection to determine the remaining stress activity possibly resulting in shine-through during rest imaging. Next, we simulated five RSARs varying from 1.0 to 3.5 in patients and a phantom and compared the images to those using RSAR of 4.0. Differences in summed difference score (SDS) >2 or changes in ischemic defect interpretation were considered to significantly influence diagnostic outcome. After deriving the minimal RSAR, it was validated in 25 additional patients by comparing it to using RSAR 4.0 as reference. **Results:** The mean stress activity still present in the field of view after 3h was 26%. SDS differences >2 were found in one (4%) patient using RSARs of 3.5, 2.5 and 2.0, in three (12%) patients using RSAR of 1.5 and in five patients (20%) using RSAR of 1.0. These results were consistent with the phantom study showing SDS differences >2 for RSARs ≤ 1.5 . Visual interpretation showed an increased number of deviating scans for RSAR of 1.0. Validating RSAR of 2.0 resulted in a different SDS in comparison to RSAR 4.0 in one patients (SDS of 30 vs. 11). Moreover, two scans were interpreted as ischemic instead of normal when using RSAR 2.0

but in two other scans the opposite was the case. **Conclusion:** The minimal RSAR needed to prevent relevant occurrence of shine-through effects and, hence, reliable diagnostic outcomes using a one-day stress-first MPI SPECT protocol is 2.0.

OP-625

Assessment of myocardial CZT-SPECT recording in a forward-leaning "bicker-like" position: head-to-head comparisons with the more conventional supine and semi-upright positions

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Purpose: The "D.SPECT" cardiac CZT-camera allows positioning the patients in supine or semi-upright positions but also, in a forward-leaning "bicker-like" position. This latter might lower diaphragmatic attenuation as well as the breathing-related cardiac motions, similarly to that previously documented for prone position but with an enhanced patients comfort. This study aimed at assessing MPI recorded at rest in this "bicker-like" position, with head-to-head comparisons with supine and semi-upright positions. **Methods:** A total of 80 patients, routinely referred to a single-day stress-rest ^{99m}Tc-Sestamibi protocol on the D.SPECT and positioned in the "bicker" position with the camera head at 35° from vertical, had an additional resting SPECT recording in a supine position (n=40) or in a semi-upright position with the back at 30° from vertical (n=40). Segments with attenuation artifacts were identified on a 17-segments division of the left ventricle as those showing: $< 70\%$ uptake on rest-SPECT, definitely normal contractility at gated-SPECT and no defects reversibility between stress and rest images. **Results:** On average, the longitudinal amplitude of the breathing-related cardiac motions, scored on panograms, was lower for bicker than supine positions (1.58 ± 0.84 vs. 2.45 ± 1.63 , $p < 0.001$), but equivalent between bicker and semi-upright positions (1.26 ± 0.56 vs. 1.28 ± 0.86). Mean heart-to-detector distance was lower for bicker than supine (18.3 ± 1.6 cm vs. 20.2 ± 2.5 cm, $p < 0.001$) or semi-upright positions (18.3 ± 2.3 cm vs. 20.1 ± 2.4 cm, $p < 0.001$). The mean number of segments with attenuation artifact was lower for bicker than supine (1.10 ± 1.01 vs. 1.90 ± 1.74 , $p = 0.01$) or semi-upright positions (0.75 ± 0.93 vs. 1.38 ± 1.60 , $p < 0.001$), whereas no significant difference was documented regarding the number of ischemic or infarction segments. **Conclusion:** Myocardial perfusion images, recorded with the D.SPECT camera, are likely to be enhanced when the patients are positioned in a forward-leaning "bicker-like" position rather than in a supine or semi-upright position, with especially a lower rate of image artifacts.

OP-626

The Accuracy Of The Dynamic Single Photon Emission Computed Tomography In The Prediction Of Significant Ischemia According To Invasive Fractional Flow Reserve

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Purpose: To define the accuracy of myocardial dynamic CZT SPECT parameters in patients with moderate coronary artery stenosis submitted to invasive coronary angiography (ICA) and FFR. **Methods:** 23 consecutive patients (61.2±6.8 years; 12 women) with suspected and known stable CAD were enrolled. Within 7 days all patients underwent non-invasive assessment of myocardial blood flow (MBF) and coronary flow reserve (CFR), obtained by a dynamic acquisition with CZT and Tc99m-MIBI, and invasive assessment of coronary anatomy with the estimation of FFR values in at least one main coronary artery showing an intermediate coronary lesion (40-90% stenosis). The values of stress (adenosine pharmacological test) and rest MBF were calculated semi-automatically by a net retention model. The values of CFR were calculated as MBF ratio (MBF stress / MBF rest). Additionally, flow difference (FD) as the stress MBF minus the rest MBF was calculated. FFR was calculated invasively during the steady-state (60-90 sec) adenosine induced hyperemia as a ratio of the mean distal intracoronary pressure to the mean arterial pressure. **Results:** 7(30%), 3(13%), and 2(9%) patients had >70% coronary lesions in 1, 2, or 3 vessels, respectively. Complete coronary occlusions were revealed in 2 vessels from 2 patients, while 35(38%) vessels did not show any relevant coronary luminal narrowing. FFR was assessed in 28 vessels showing intermediate coronary lesions. The average FFR value was 0.81±0.1. A moderate correlation between stenosis severity and FFR values was revealed ($r=0.45$; $p=0.01$). We found moderate correlations between stenosis severity and stress MBF ($r=-0.46$; $p=0.01$) as well as FD ($r=-0.37$; $p=0.04$). Significant correlations between FFR values and absolute myocardial perfusion parameters on CZT were revealed. Based on the ROC analysis, abnormal FFR values were best predicted by CZT-derived absolute stress MBF, MFR and FD with values of ≤ 0.54 ml/min/g, ≤ 1.48 and ≤ 0.18 ml/min/g, respectively showing the highest accuracy in predicting the presence of invasively determined myocardial inducible ischemia. Specifically, when regional MFR was below the cut-off value of ≤ 1.48 , FFR was pathological in the 90% of the cases. Conversely, in the case of normal MFR values, FFR was preserved in the 78% of the cases. **Conclusion:** There is a good relationship between regional stress MFR and invasive FFR. In selected patients it could be of help in order to assess the hemodynamic significance of coronary artery stenosis non-invasively and to better stratify the risk of CAD.

OP-627

Radionuclide left ventricular ejection fraction may be determined with a dramatic reduction in recording times with the very high sensitivity “DSPECT” CZT-camera.

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Purpose: This study aimed at determining whether a more than 3-fold reduction in recording time may be applied when left ventricular ejection fraction (EF) is determined with radionuclide angiographies (RNA) recorded with the very high sensitivity “DSPECT” CZT-camera, similarly to what was previously observed for myocardial perfusion imaging. **Methods:** Patients routinely referred to 2D-RNA for a cardiomyopathy ($n=23$) or the monitoring of a chemotherapy ($n=50$) had an additional 10-min DSPECT recording. The EF obtained with the DSPECT images reconstructed with 100% of projection durations (3D-RNA100) or only 30% (3D-RNA30) were compared to those from 2D-RNA. **Results:** Mean effective dose was 5.9 ± 0.2 mSv, and mean EF were equivalent between 3D-RNA100 ($60\pm 18\%$) and 3D-RNA30 ($61\pm 18\%$) and were both higher than those from 2D-RNA (58 ± 15 , both $p<0.01$). This EF overestimation was mostly documented for supra-normal values ($> 60\%$), explaining logarithmic relationships with 2D-RNA values for the EF from 3D-RNA100 ($y=40.\ln(x)-106$ ($R^2=0.88$)) and 3D-RNA30 ($y=40.\ln(x)-103$ ($R^2=0.85$)). **Conclusion:** A dramatic reduction in recording times and presumably also in injected activity (-i.e. with an expected mean effective dose < 2 mSv) may be applied without any significant change in the EF determined with the DSPECT camera, but with an inherent overestimation for supra-normal EF values.

OP-628

Improved assessment of 99mTc-DPD myocardial uptake in patients with amyloidosis using CZT SPECT with 3D semi-quantitative analysis.

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Introduction: The aim of this study was to compare different methods for semi-quantitative analysis of 99mTc-DPD myocardial uptake in patients with suspected cardiac amyloidosis. **Subjects & methods:** Data from 25 patients with proven or suspected cardiac amyloidosis who underwent both whole body scan using a conventional Anger camera and a CZT myocardial SPECT using a DSPECT (Spectrum Dynamics) 3 hours after injection of 99mTc-DPD were analyzed. All data were acquired as part of clinical routine at Caen or Toulouse university hospitals. A visual scoring of cardiac retention was performed on whole body scan according to Perugini 4-point grading system from 0 (no uptake) to 3 (strong cardiac uptake with mild/absent bone uptake). Retrospectively, a heart to background

(H/B) uptake ratio was calculated as mean counts in a ROI over the heart divided by background counts in an identical size ROI over the contralateral chest (wb-H/B). In addition, CZT SPECT images were quantified according to 3 different methods: planar H/B uptake ratio were calculated from anterior reprojection (ant-H/B) and left anterior oblique reposition (LAO-H/B), and 3D-H/B uptake ratio was calculated from transaxial slices as mean counts in a VOI encompassing the heart divided by mean background counts in a VOI placed in the contralateral lung (3D-H/B). Interventricular septal thickness was measured using echocardiography. **Results:** All H/Bs obtained from planar and reprojected data were similar (wb-H/B: 2.39 ± 0.83 , ant-H/B: 2.28 ± 0.89 , LAO-H/B: 2.43 ± 0.84 , all $P = \text{ns}$) and well correlated (all $r \geq 0.80$). However, 3D-H/B was significantly increased compared to planar H/Bs (3D-H/B: 4.56 ± 2.05 , all $P < 0.0001$ vs. wb-, ant- and LAO-H/B). Bland-Altman plots demonstrated that the difference between 3D- and planar H/Bs increased with the mean value of myocardial uptake. All H/B ratios were similarly correlated to septal thickness (wb-H/B: $r = 0.51$, ant-H/B: $r = 0.54$, LAO-H/B: $r = 0.47$, 3D-H/B: $r = 0.47$). Finally, a linear model analysis demonstrated that only the 3D-H/B allowed a significant discrimination between all Perugini grades ($p < 0.01$). **Conclusion:** In this preliminary study, a 3D semi-quantitative analysis of CZT SPECT optimized the assessment of ^{99m}Tc -DPD myocardial uptake in patients with cardiac amyloidosis.

OP-629

First-in-man Study in Myocardial Perfusion Imaging with the New CZT SPECT Camera (VERITON®)

B. Enilorac¹, D. Bouthiba^{1,2}, P. Tager¹, C. Nganoa¹, N. Roth³, A. Manrique^{1,2}, D. Agostini¹; ¹CHU de Caen, Department of Nuclear Medicine, Caen, FRANCE, ²EA4650, Normandy University, Caen, FRANCE, ³Spectrum Dynamics Medical, Caesarea, ISRAEL.

Introduction: Based upon the breakthrough of cardiac CZT cameras, there is now an interest to apply this same technology to other SPECT imaging targets. Recently, an organ specific CZT-SPECT scanner (VERITON® Spectrum Dynamics, Caesarea, Israel) that utilizes a focused body/organ and contouring detector technology has been introduced, interesting for cardiac-imaging. In this study, we compare rest myocardial perfusion SPECT imaging between a conventional gamma camera and the VERITON® camera. **Subjects and Methods:** With the approval of the ethical committee, on patients undergoing the routine clinical procedures as part of their clinically referred care, myocardial perfusion SPECT imaging have been acquired with a conventional gamma camera and the VERITON® camera, with no additional injection of radiopharmaceutical to patients. The cardiac SPECT data was acquired for 8min in body contouring mode using 12 CZT detectors and 240 to 300 projections per detector. The images were reconstructed using OSEM iterative algorithm with resolution recovery, cardiac model prior, 2.46mm voxel size, 4 iterations and 16 subsets. **Results:** To date, myocardial perfusion SPECT imaging have been acquired in 6 patients (age 69 ± 11) suspected of coronary artery disease and injected with 216 ± 52 MBq of ^{99m}Tc -sestamibi. Initial experience with the CZT-SPECT system has shown that it is possible

to acquire a myocardial perfusion SPECT image in approximately 8 minutes, half the time required by a conventional SPECT system (~16 minutes), and with a better resolution. Diagnosis of myocardial infarction was done in 2 patients out of 6, the remaining cardiac perfusion was normal in both modalities. **Conclusion:** CZT technology has the potential to provide high resolution SPECT images with potentially lower time acquisition and/or radiation dose to the patient than when using conventional gamma camera technology. Further investigation is necessary to demonstrate the benefits of applying this new CZT-CT64 technology to stress-rest SPECT cardiac-nuclear imaging.

1601 Wednesday, October 17, 2018, 08:00 - 09:30, Plenary Hall

CME 13 - Neuroimaging / Cardiovascular: Myocardial ^{123}I -mIBG Imaging in Neurology - Is it Ready for Prime Time?

OP-630

Introduction on the Essentials of Myocardial ^{123}I -mIBG Imaging

H. Verberne; Academic Medical Center, Department of Nuclear Medicine, Amsterdam, NETHERLANDS.

OP-631

Myocardial ^{123}I -mIBG Imaging for the Differential Diagnosis of Parkinsonian Syndrome: The Nuclear Neurologist's Perspective

G. Treglia; Nuclear Medicine and PET/CT Center, Oncology Institute of Southern Switzerland, Bellinzona, SWITZERLAND.

OP-632

Myocardial ^{123}I -mIBG Imaging in Dementia with Lewy bodies (DLB) and Prodromal DLB: The Neurologist's Perspective

P. Tiraboschi; Division of Neurology, Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milan, ITALY.

1602 Wednesday, October 17, 2018, 08:00 - 09:30, Hall 2

Joint Symposium 25 - Radiation Protection / Dosimetry / Thyroid / ICRP: Risk Estimates for Patients Undergoing Molecular Radionuclide Therapy

OP-633

Lifetime Attributable Risk as an Alternative to Effective Dose to Describe the Risk of Cancer for Patients

M. Andersson; Lund University, Department of Medical Radiation Physics, Lund, SWEDEN.

OP-634

Risk of Secondary Malignancies after RNTs

F. Verburg; University Hospital Marburg, Department of Nuclear Medicine, Marburg, GERMANY.

OP-635**Risk Models for Patients Undergoing Radiation Therapy, Taking into Account Pathology, Deterministic and Stochastic Radiation Effects**

W. Bolch; University of Florida, Advanced Laboratory for Radiation Dosimetry Studies (ALRADs), Gainesville, UNITED STATES OF AMERICA.

1603 **Wednesday, October 17, 2018, 08:00 - 09:30, Hall 3**

Joint Symposium 26 - Translational Molecular Imaging & Therapy / IFCARS: Computer Assisted Image and Radioguided Intervention in Surgery and Radiology

OP-636**Trends in Computer Assisted Intervention**

A. Melzer; University Leipzig, Innovation Center Computer Assisted Surgery, Leipzig, GERMANY.

OP-637**Robotic Imaging and Augmented Reality for Computer Assisted Interventions**

N. Navab; Technical University of Munich, Computer Aided Medical Procedures & Augmented Reality, Munich, GERMANY.

OP-638**Portable Gamma-Ray and NIR-Devices for Image Assisted Surgery Using Hybrid Tracers**

F. van Leeuwen; Leiden University Medical Center, LUMC, Leiden, NETHERLANDS.

OP-639**Pairing SPECT/CT to PET/CT as Roadmap for Radioguided Intervention - Match the Tracers, Find the Metastasis**

M. Schottelius; Technical University of Munich, Department of Pharmaceutical Radiochemistry, Munich, GERMANY.

OP-640**ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room - Portable and/or Fixed Equipment? Will Interventional Workflows be Affected?**

S. Vidal-Sicart; Hospital Clínic, Department of Nuclear Medicine, Barcelona, SPAIN.

OP-641**ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room - Portable and/or Fixed Equipment? Will Interventional Workflows be Affected?**

A. Melzer; University Leipzig, Innovation Center Computer Assisted Surgery, Leipzig, GERMANY.

OP-642**ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room - Portable and/or****Fixed Equipment? Will Interventional Workflows be Affected?**

N. Navab; Technical University of Munich, Computer Aided Medical Procedures & Augmented Reality, Munich, GERMANY.

OP-643**ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room - Portable and/or Fixed Equipment? Will Interventional Workflows be Affected?**

F. van Leeuwen; Leiden University Medical Center, LUMC, Leiden, NETHERLANDS.

OP-644**ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room - Portable and/or Fixed Equipment? Will Interventional Workflows be Affected?**

M. Schottelius; Technical University of Munich, Department of Pharmaceutical Radiochemistry, Munich, GERMANY.

OP-644a**ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room - Portable and/or Fixed Equipment? Will Interventional Workflows be Affected?**

H. U. Lemke; Technical University Berlin, Berlin, GERMANY.

OP-644b**ROUND TABLE: Incorporating Imaging and Machine Intelligence in the Operating Room - Portable and/or Fixed Equipment? Will Interventional Workflows be Affected?**

R. Valdés Olmos; Leiden University Medical Centre, Interventional Molecular Imaging Laboratory and Nuclear Medicine Section, Department of Radiology, Leiden, NETHERLANDS.

1605 **Wednesday, October 17, 2018, 08:00 - 09:00, Hall X**

M2M: Neuroinflammation & Brain Imaging

OP-645**Early and longitudinal microglial activation but not fibrillar amyloid accumulation predict cognitive outcome and synaptic density in PS2APP mice**

*M. Brendel*¹, *C. Focke*¹, *M. Deussing*¹, *B. Zott*², *T. Blume*¹, *Y. Shi*³, *L. Beyer*¹, *G. Kleinberger*⁴, *S. Lindner*¹, *F. Gildehaus*¹, *P. Bartenstein*^{1,3}, *K. Baumann*⁵, *C. Haass*^{3,4}, *J. Herms*^{3,4}, *H. Adelsberger*², *A. Rominger*^{6,3}; ¹Department of Nuclear Medicine, Ludwig-Maximilians-University of Munich, Muenchen, GERMANY, ²Technical University of Munich, Muenchen, GERMANY, ³DZNE - German Center for Neurodegenerative Diseases, Munich, Muenchen, GERMANY, ⁴SyNergy, University of Munich, Muenchen, GERMANY, ⁵Roche Pharma Research and Early Development, Neuroscience Discovery, Rocije, Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, SWITZERLAND, ⁶Department of Nuclear Medicine, University of Bern, Bern, SWITZERLAND.

Introduction: Microglial activation is one hallmark in the pathophysiology of neurodegenerative diseases. However, results are still inconclusive whether neuroinflammation has beneficial or detrimental effects on cognitive outcome. 18kDa translocator protein (TSPO) PET imaging now facilitates to monitor regional alterations of microglial activity *in vivo*. Therefore, we objected to correlate serial measures of TSPO and amyloid PET with the terminal cognitive assessment in the PS2APP amyloid mouse model. **Methods:** N=10 PS2APP (TG) mice and N=7 C57BL/6 (WT) mice were imaged from 8 to 13 months of age by TSPO PET (F-18-GE180) and amyloid PET (F-18-Florbetaben). Morris water maze (MWM) was performed at 13.5 months of age. Z-score differences were obtained voxel-wise for TG mice versus WT mice at each time-point. Z-score images of serial PET were summed to an area under the curve (AUC) map for each individual TG mouse. Baseline and AUC maps of TSPO activation and amyloidosis were correlated voxel-wise with findings of cognitive testing deriving from MWM. The entire forebrain and brain regions associated with spatial learning were likewise evaluated to investigate general effects. Immunohistochemical and biochemical experiments were performed at study termination. Synaptic density served as a validation marker for MWM. **Results:** TG mice indicated a distinct poorer performance in MWM when compared to WT at 13 months of age (distance: +436%, $p<0.01$ / escape latency: +244%, $p<0.001$). A better cognitive outcome was associated with higher TSPO activation at baseline in the forebrain ($R = 0.71$, $p<0.05$) and even stronger in brain areas involved in spatial learning ($R = 0.82$, $p<0.01$). Peak clusters of the amygdala and entorhinal cortices showed a very strong association between the baseline TSPO signal and terminal MWM performance ($R = 0.95$, $p<0.001$). Higher longitudinal TSPO activation by AUC maps tended to correlate with a better clinical outcome in the forebrain ($R = 0.45$, $p=n.s.$), and in brain areas involved in spatial learning ($R = 0.60$, $p=n.s.$). Peak clusters of longitudinal TSPO activation in hippocampal areas were significantly associated with terminal MWM performance ($R = 0.68$, $p<0.05$). Synaptic density showed similar correlations and validated MWM results. Fibrillar amyloidosis did not correlate with the cognitive outcome neither at baseline nor considering the whole imaging period (all $R < 0.3$). **Conclusions:** Early and longitudinal microglial response seems beneficial for preserving the cognitive performance in PS2APP mice. Fibrillar amyloidosis was in contrast not associated with cognitive performance.

OP-646

[¹⁸F]NEBIFQUINIDE: First *in vivo* experiences of a new third generation TSPO PET tracer

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Introduction & Aim: *In vivo* imaging of the translocator protein (TSPO) has received particular attention as potential biomarker of glia activation, which has been reported in a variety of neurodegenerative disorders. Nevertheless, TSPO PET imaging is still challenging due to the lack of adequate tracers. In detail, high non-specific binding and a single nucleotide polymorphism in the *TSPO* gene, which causes a heterogeneous binding affinity

of the tracers in a genotype-dependent manner, have limited the applicability of TSPO imaging so far. Hence, the aims of this work were the radiosynthesis and *in vivo* evaluation of a new TSPO PET tracer with optimized properties. **Methods:** The affinity of NEBIFQUINIDE towards the TSPO was determined in a competitive experiment using platelets membranes from genotyped subjects (all three genotypes were used: two homozygous and one heterozygous) as described elsewhere [1]. Subsequently, ¹⁸F-labeling at the pyridine moiety was performed using microwave heating. *In vitro* evaluation included affinity to $\alpha 1$ -AGP and log *P* measurements, which were determined using spin desalting columns and a HPLC method, respectively. Subsequently, μ PET/CT studies were performed in C57BL/L mice after injection of approximately 10 MBq of freshly prepared [¹⁸F]NEBIFQUINIDE. After 60 minutes dynamic scan, animals were sacrificed and the activity of the organs of interest was counted. Additionally, the amount of intact tracer in brain, lungs and liver was determined using radio-HPLC. **Results:** No significant difference was found between the *K_i* values of NEBIFQUINIDE for all genotype groups (*K_i* = 6 ± 1 nM). [¹⁸F]NEBIFQUINIDE was successfully synthesized with an uncorrected RCY (end of bombardment) of 32 ± 4 % and a molar radioactivity of 196 ± 26 GBq/ μ mol ($n=3$). Binding to $\alpha 1$ -AGP and log *P* were significantly reduced in comparison to the established TSPO PET tracer (*R*)-[¹¹C]PK11195. Biodistribution experiments revealed significantly higher accumulation of the tracer [¹⁸F]NEBIFQUINIDE in TSPO-rich organs as lungs and heart. Moreover, no significant radiometabolism was found in the selected organs, since more than 93 % of the activity corresponded to intact [¹⁸F]NEBIFQUINIDE. *In vivo* specific binding was demonstrated by displacement of [¹⁸F]NEBIFQUINIDE after injection of cold PK11195. **Conclusions:** The presented results point towards the suitability of the new TSPO PET tracer, [¹⁸F]NEBIFQUINIDE, for additional *in vivo* evaluations in animals models and humans, especially due to the low sensitivity of [¹⁸F]NEBIFQUINIDE towards the TSPO polymorphism. **References:** [1] Owen, D et al; *J Cereb Blood Flow Metab*; 2012; 32:1-5

OP-647

Metabotropic Glutamate Receptor Subtype 5 Is Altered In Lps-induced Murine Neuroinflammation Model And In Brains Of AD And ALS Patients

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Purpose: Neuroinflammation is an important feature in the pathogenesis and progression of neurodegenerative diseases such as Alzheimer's disease (AD) and amyotrophic lateral sclerosis (ALS). Peripheral administration of lipopolysaccharide (LPS) in mice provokes central inflammation. To understand the effects of LPS on mGluR5 expression in the brain, we administered LPS to different mouse strains and performed PET imaging at different time points. Furthermore, the expression level of mGluR5 in neurodegenerative disease was investigated in post-mortem human brains of AD and ALS and compared to controls. **Methods:** C57BL/6 and CD1 mice were injected intraperitoneally with either 10 mg/kg LPS or vehicle. After 1 and 5 days TSPO

and mGluR5 levels were determined by qPCR and PET imaging was performed applying the mGluR5-specific radiotracer [^{18}F] PSS232. Alterations of mGluR5 in human cortical brain regions from AD and ALS patients and controls were analyzed using in vitro autoradiography. Specificity of binding was determined by the non-competitive mGluR5 antagonist, MMPEP. **Results:** Intraperitoneally applied LPS increased TSPO mRNA significantly by 3.6-fold ($p<0.001$) and 2.6-fold ($p<0.001$) in brains of C57BL/6 and CD1 mice, respectively, after 1 day compared to the vehicle-treated groups. mGluR5 mRNA levels increased with significance by 3.4-fold ($p<0.001$) and 1.9-fold ($p<0.001$) in brains of C57BL/6 and CD1 mice, respectively, after 1 day. TSPO (2.3-fold, $p<0.001$) and mGluR5 (1.9-fold, $p<0.001$) mRNA remained significantly increased after 5 days in C57BL/6 but not in CD1 mice. mGluR5 levels in CD1 mice 5 days post LPS challenge were non-significantly elevated by 1.3-fold ($p=0.052$) compared to the vehicle group. Brain-PET imaging with the mGluR5-specific radiotracer [^{18}F] PSS232 confirmed increased mGluR5 levels in striatum (~22%) and hippocampus (~22%) of both mouse strains 1 day after LPS treatment. After 5 days, mGluR5 levels declined to vehicle status in CD1 but remained high in C57BL/6 mice (17% for striatum, 19% for hippocampus). The mGluR5 antagonist MMPEP significantly reduced [^{18}F] PSS232-binding in striatum and hippocampus. To investigate mGluR5 expression in human neurodegenerative disease, we evaluated post-mortem cortical brain slices from AD and ALS patients using in vitro autoradiography. Autoradiograms revealed a ~5.2-fold and ~3.8-fold higher binding of [^{18}F] PSS232 compared to controls demonstrating increased mGluR5 levels in AD and ALS, respectively. Blocking studies with MMPEP diminished [^{18}F] PSS232-binding. **Conclusions:** LPS-induced neuroinflammation increased mGluR5 levels in mouse brains and is dependent on the mouse strain and time point after LPS challenge. We were able to also demonstrate increased mGluR5 levels in human AD and ALS brains in vitro.

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Quantitative Imaging of AMPA Receptors Using Novel ^{11}C -labeled PET tracer for AMPA receptors

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Introduction: AMPA receptor (AMPA) plays important roles such as cortical reorganization, and it is expected to be utilized to various brain diseases: epilepsy or psychological disorders. We have recently developed novel PET tracer for AMPAR, named [^{11}C -K-2]. This study aims at investigating a fully quantitative approach AMPAR with [^{11}C -K-2] based on a kinetic analysis. K-2 was rapidly hydrolyzed at the amide residue (^{11}C -K-2OH) after injection *in vivo* and ^{11}C -K-2OH is a major metabolite which represents the binding of AMPAR *in vivo*. Interestingly, [^{11}C -K-2OH] binds to the cell surface AMPAR. In vitro autoradiographic assay exhibited that K_d value of [^{11}C -K-2OH] is 4.7 nM and B_{max} is 5.5 nM. In this study, the applicability of Logan graphical analysis (LGA) with a reference region is investigated in human. **Method:** 60-min PET dynamic scans were conducted to patients having

mesial temporal lobe epilepsy, and BP_{ND} is computed using LGA where a corpus callosum is the reference region, and t^* , that is the beginning to apply a line regression in LGA, is 30 min after the administration. Then, the amounts of AMPAR in the resected regions are assayed, and they compared with the BP_{ND} ; 10 regions from the 3 patients. **Results:** The time activity curve of K-2 presents a typical reversible binding kinetics, and the LGA has a clear linear relationship. The range of BP_{ND} are from 0.3 to 1.3. In the BP_{ND} images exhibited high signals at the epileptogenic focus. A significant linear regression is observed between the protein amount of AMPAR and BP_{ND} ($r^2=0.58$, $p<0.05$). **Conclusion:** LGA analysis showed that [^{11}C -K-2] exhibited reversible binding kinetics representing cell surface AMPA receptors. Although the dynamic range of BP_{ND} is moderate, cell surface AMPA receptor amount is small and dynamically regulated by the variety of conditions such as activity. Thus, [^{11}C -K-2] is a promising radiotracer to quantitate functional AMPAR in human. Further investigations on the clinical application of K-2 to brain diseases such as epilepsy or psychiatric diseases will be conducted.

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New multimodality PET/SPECT neuroimaging agent for 5-HT_{1A}/5-HT₇ receptors

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Purpose: 5-HT_{1A} and 5-HT₇ receptors are implicated in depression and anxiety. These are highly co-expressed in brain regions as homo and heterodimers and the cross-talk modulates serotonergic signalling. 5-HT₇ receptor alters the expression and signalling of 5-HT_{1A} receptor in central nervous system in depressed conditions. The complex signalling mechanism includes structural reorganizations as dimerization of receptors. Thus, imaging of 5-HT_{1A}/5-HT₇ receptors either dimers or monomers in normal and pathological conditions can be utilized to assess the quantitative and functional aspect of neurological disorders. Here, we report development of a new multimodality ^{11}C -PET/ $^{99\text{m}}\text{Tc}$ -SPECT based radiotracer for targeted non-invasive imaging of 5-HT_{1A}/5-HT₇ neuroreceptors. **Methods:** The mixed affinity ligands ([CH₃]-BTZ-MPP) and (DTC-BTZ-MPP) were designed using benzothiazolone (BTZ) and methoxyphenyl piperazine (MPP) pharmacophores. Docking studies were carried using MD-validated homology models of 5-HT_{1A} and 5-HT₇ receptors. Development of ligands involved multi-step synthesis, wherein all intermediates and final compounds were characterized by $^1\text{H}/^{13}\text{C}$ -NMR, HRMS, HPLC and UV-Vis techniques. Biocompatibility was evaluated by MTT and haemolysis assays. The ^{11}C and $^{99\text{m}}\text{Tc}$ -radiolabeling were carried using $^{11}\text{CH}_3\text{I}$ and $\text{Na}^{99\text{m}}\text{TcO}_4$. The radiolabelling conditions were thoroughly optimized. HPLC profiling and HRMS were used for the characterization of ^{11}C -labeled radiotracer, while ITLC (two solvent system) was employed for analysing $^{99\text{m}}\text{Tc}$ -labelling efficiency. Depressed mice models were generated using long term corticosterone administration. **Results:** Docking studies reflected presence of conserved residues Asp116, Lys191, Ser199, Ile189 and Asp162, Val163, Phe343, Phe344 in active sites of 5-HT_{1A} and 5-HT₇ re-

ceptors. The $\text{LogP}_{\text{o/w}}$ of $[^{11}\text{CH}_3]$ -BTZ-MPP and $[^{99\text{m}}\text{Tc}]$ -DTC-BTZ-MPP were found to be 1.26 and 1.8 respectively, indicating BBB permeation. The intermediates and final compounds were synthesized in more than 90 and 98 % yields. Purity of compounds were ascertained by HPLC and HRMS. No significant cytotoxicity was observed. Non-invasive imaging studies showed appreciable brain uptake. Biodistribution studies reflected maximum brain uptake corresponding to 11.95 ± 0.4 % ID/g and 13.37 ± 1.2 % ID/g at 15 min p.i. in normal and treated mice for $[^{11}\text{CH}_3]$ -BTZ-MPP and 1.38 ± 0.01 % ID/g and 2.06 ± 0.01 % ID/g at 15 min p.i. under similar conditions for $[^{99\text{m}}\text{Tc}]$ -DTC-BTZ-MPP respectively. Significant uptake in hippocampus and cortex indicated affinity and specificity towards 5-HT_{1A}/5-HT₇ receptors. Major radioactivity accumulation of radiotracers in lungs and liver indicated hepatobiliary as major route of excretion. **Conclusion:** A new multimodality PET/SPECT based neuroimaging agent was designed and developed to selectively target 5-HT_{1A}/5-HT₇ receptors. The pre-clinical evaluations exhibited substantial brain penetration and preferred activity accumulation in receptor-rich specific brain regions.

OP-650

Identification And Preclinical Evaluation Of (R)-[¹⁸F]OF-Me-NB1 As A Pet Imaging Agent For The GluN2B Subunit Of The Ionotropic NMDA Receptor

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Aim: Positron emission tomography (PET) imaging harbors potential to guide the development of GluN2B-antagonists in preclinical and clinical development by means of target engagement studies. As part of our programme to develop a fluorinated PET radioligand for imaging the GluN2B subunit of the ionotropic NMDA receptor, we synthesized a number of benzazepine-based derivatives. The most promising compound, codenamed (R)-OF-Me-NB1, was radiolabeled with fluorine-18 and evaluated using *ex vivo* autoradiography, PET imaging and biodistribution. **Methods:** *Ortho*- and *para*-fluorinated derivatives OF-Me-NB1 and PF-Me-NB1 were synthesized and enantiomeric separations were performed by chiral HPLC. Starting from the desmethyl precursors, the respective enantiomers were radiolabeled with carbon-11 and assessed in a preliminary proof-of-concept *in vitro* autoradiography study using rodent brain sections. (R)-OF-Me-NB1 was selected for radiofluorination and subsequent preclinical evaluation based on the exquisite autoradiograms obtained from the carbon-11 labeled version. *Ex vivo* autoradiography, PET imaging, biodistribution and metabolite studies were used to assess the utility of (R)-[¹⁸F]OF-Me-NB1 in Wistar rats. The brain uptake of (R)-[¹⁸F]OF-Me-NB1 in wild-type mice was compared with σ_1 receptor knock-out mice to validate off-target binding to σ_1 receptors. **Results:** All four compounds were radiolabeled with carbon-11 in good radiochemical yields (7–36% decay corrected) and high molar activities ranging from 54 to 220 GBq/ μmol . *In vitro* autoradiography experiments showed that both enantiomers of [¹¹C]PF-

Me-NB1 distributed homogeneously across coronal rodent brain sections. In contrast, the two enantiomers of [¹¹C]OF-Me-NB1 showed an entirely different behavior. While (S)-[¹¹C]OF-Me-NB1 accumulated in all brain regions with considerable σ_1 receptor off-target binding, (R)-[¹¹C]OF-Me-NB1 exhibited high specificity and selectivity for the GluN2B-rich rat forebrain. These findings were confirmed for the radiofluorinated analogue, (R)-[¹⁸F]OF-Me-NB1, which was synthesized via copper-mediated radiofluorination in radiochemical yields of 13–25% and molar activities ranging from 61–168 GBq/ μmol . *Ex vivo* biodistribution studies and PET imaging experiments in Wistar rats indicated an appropriate pharmacokinetic profile and high *in vivo* specific binding using GluN2B-antagonist CP101,606 as a blocking agent, which showed a dose-dependent blockade. Receptor occupancy studies with CP101,606 revealed a D_{50} -value of 7.5 $\mu\text{mol/kg}$. Off-target activity towards the σ_1 receptor was excluded by PET imaging with σ_1 receptor knock-out mice. **Conclusion:** (R)-[¹⁸F]OF-Me-NB1 is a promising radiofluorinated probe that exhibits specificity and selectivity for the GluN2B-containing NMDA receptor complex and enables target engagement studies *in vivo*.

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Characterization of brain glucose metabolism and blood flow after whole brain irradiation in rats: a PET/SPECT study

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Background: Radiation can induce damage to the brain, often presenting as cognitive deficit. This can happen as a consequence of radiotherapy for e.g. brain tumors, and could be due to damage of normal brain tissue in the radiation field. The cellular and molecular pathways that induce this damage are not yet well understood. Using Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT), this study aims to investigate acute and delayed effects of irradiation on glucose metabolism and blood flow in normal rat brain. **Methods:** Male Wistar rats subjected to 25 Gy X-ray radiation and controls (n=8 per group) were submitted to [¹⁸F]-FDG PET or [^{99m}Tc]-HMPAO SPECT imaging. [¹⁸F]-FDG PET scans for assessment of brain metabolism were performed at baseline and at 60 and 90 days after whole brain irradiation. [^{99m}Tc]-HMPAO SPECT scans for assessment of cerebral blood flow were performed at baseline and 1, 3, 5, 9, 60 and 90 days after whole brain irradiation. All groups also underwent the Open Field Test (OFT) to assess motor behavior at baseline and at day 60 and 90. We quantitatively analyzed the scans by calculating SUV_{mean} for predefined volumes of interest. The Generalized Estimating Equations model was used for statistical analysis of the data. **Results:** Irradiated rats showed a statistically significant increase in [¹⁸F]-FDG uptake in the whole brain (14%, p=0,002) and some specific brain regions, such as the limbic system and cerebellum (8–25%, p<0,05), between baseline and day 60. However, no statistically significant differences in uptake between baseline and day 90 were found. In addition, irradiated rats showed a sig-

nificant increase in [^{99m}Tc]-HMPAO uptake in most brain regions, which sustained until day 90 (39–56%), with a peak on day 9. Finally, the OFT showed that irradiated rats moved less ($p < 0.01$) than controls. **Conclusions:** Our study suggests that brain irradiation in rats induces an early delayed increase in brain glucose metabolism at day 60 and acute and early delayed increase in cerebral blood flow, with a peak at day 9. These findings could be related to an increase in energy demand to ensure normal neuronal functioning. The physiological effects are accompanied by changes in motor behavior.

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^{11}C -metoclopramide PET imaging to reveal and quantify the contribution of the P-glycoprotein to the clearance of its substrates from the brain

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Introduction: Currently available PET radioligands have shown the role of the P-glycoprotein (P-gp, ABCB1) in limiting the influx of its substrates from blood into the brain. We developed ^{11}C -metoclopramide, a P-gp substrate which benefits from suitable pharmacokinetic properties in rats such as a substantial baseline brain uptake and the absence of brain-penetrant radiometabolites (Pottier et al., J Nucl Med 2016). ^{11}C -metoclopramide PET imaging was performed in non-human primates, a relevant animal model of the human BBB, to validate pharmacokinetic models and simplified methods to investigate the importance of the efflux clearance role of P-gp at the BBB. **Materials and Methods:** Dynamic PET acquisitions were performed in anesthetized baboons during 60 min after ^{11}C -metoclopramide injection (298 ± 44 MBq). Metabolite-corrected arterial input functions were measured during PET acquisitions. Four animals were scanned in the absence (baseline) and in the presence of the potent P-gp inhibitor tariquidar (TQD). On baboon underwent a third PET experiment where ^{11}C -metoclopramide was co-injected with unlabelled metoclopramide (0.5 mg/kg). Pharmacokinetic modeling was performed using a 1-tissue compartment model to estimate the influx (K_1) and efflux (k_2) rate constants and the total volume of distribution (V_T). The elimination constant of ^{11}C -metoclopramide from the brain (k_e) was estimated from the elimination slope graphically estimated from the log-transformed brain kinetics obtained in the elimination phase (30–60 min). **Results:** TQD did not impact ^{11}C -metoclopramide plasma kinetics. PET images revealed the high baseline brain distribution of ^{11}C -metoclopramide (V_T , 4.33 ± 0.46 mL/cm³), which was homogeneous among brain regions. V_T was significantly increased by P-gp inhibition (8.70 ± 0.52 mL/cm³, $P < 0.001$). A significant 1.28 $\pm$ 0.14-fold increase in K_1 ($P < 0.05$) was observed during P-gp inhibition. The significant 1.64 $\pm$ 0.20-fold decrease in the efflux rate constant k_2 ($P < 0.01$) was consistent and significantly correlated ($P < 0.0001$) with the 1.5 $\pm$ 0.25-fold decrease in the elimination slope k_e ($P < 0.01$). Parameters estimated in the presence of co-injected metoclopramide were similar to those obtained using a tracer dose which suggests the pre-

dominance of non-receptor specific mechanism for ^{11}C -metoclopramide retention in the brain. **Conclusion:** ^{11}C -metoclopramide PET imaging non-invasively revealed that P-gp may act as a detoxifying system and mediate the clearance of its substrates from the brain into the blood. The elimination slope k_e is a convenient parameter to describe and quantify P-gp function at the BBB, especially when arterial blood sampling is not possible. ^{11}C -metoclopramide may be useful tool to investigate BBB function in the context of pathophysiological conditions where deficiency in the clearance of endogenous and exogenous compounds from the brain is hypothesized.

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Wednesday, October 17, 2018, 08:00 - 09:00, Hall Y

Do.MoRe: PET-CT & PET-MR

OP-653

Intraindividual comparison of subsequently performed PET/MRI to PET/CT for whole-body staging: Results of a unicenter trial in 1000 patients

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Purpose: To evaluate and compare the diagnostic potential of subsequently performed 18F-FDG PET/MRI after 18F-FDG PET/CT for detecting and classifying lesions for whole-body staging. **Material and Methods:** In this retrospective analysis, 1002 oncological patients (443 female, 559 male, mean age 57.7 ± 14.4 years) were included. Patients underwent clinically indicated whole-body PET/CT and subsequently whole-body PET/MRI (149.7 ± 49.7 minutes after FDG administration). Indications for hybrid imaging comprise lung cancer (17.8%), gastrointestinal cancer and neuroendocrine tumors (17.2%), gynecologic and breast cancer (14.7%), prostate cancer (14.7%), lymphoma and malignant bone disease (14.4%), melanoma (8.8%), head and neck cancer (8.1%) and cancer of unknown primary (CUP, 4.3%). Reports of all included PET/CT and PET/MRI examinations were assessed for discrepant and / or additional findings in subsequently performed PET/MRI. **Results:** Additional information in PET/MRI was found in 278 / 1002 of the cases (27.7%), distributed across all indication groups. Additional malignant findings were detected in PET/MRI compared to PET/CT in 113 / 1002 patients (11.3%), comprising 25 / 147 in prostate cancer (17.0%), 28 / 178 in lung cancer (15.7%) and 18 / 144 in lymphoma (12.5%). Furthermore, due to the additional information acquired by PET/MRI an unequivocal lesion classification was possible in 111 / 1002 findings (11.1%) compared to PET/CT. PET/MRI induced additional investigations / follow up in 58 / 1002 cases (5.8%). Here, 3 / 58 (5.2%) cases turned out to be malignant, 18 / 58 benign (31.0%) and 37 / 58 unknown (63.8%). A total of 27 / 1002 lesions (2.7%) were not detected in PET/MRI compared to

PET/CT, comprising 10 malignant lesions (lung nodules). **Conclusion:** PET/MRI offers a preferable staging potential to PET/CT, enabling the detection of additional information in 1/3 of the patient cohort comprising 11.3% additional malignant findings. The amount of unnecessary (additional) investigations induced by PET/MRI as well as missed malignant lesions remained considerably low (5.2%, 2.7%).

OP-654

Evaluation and Correction of Halo Artifacts in ^{68}Ga -PSMA PET/MR Imaging of Prostate Tumors.

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Aim: To correct for halo artifacts around the bladder occurring in ^{68}Ga -PSMA PET/MRI by partially subtracting the activity contribution from the bladder before image reconstruction. **Materials and Methods:** Ten datasets with occurring halo artifacts of patients with prostate cancer (68 ± 8 years old, 90 ± 13 kg), which underwent a ^{68}Ga -PSMA PET/MRI examination were selected for this study. PET imaging consisted of a 10 min-listmode acquisition in a Siemens Biograph PET/MR system after 83 ± 26 min of an intravenous administration of 1.8 ± 0.5 MBq/kg ^{68}Ga -PSMA. The acquired data was reconstructed by using the clinical standard settings: OP-OSEM algorithm with resolution modeling (HD-PET); 3 iterations and 21 subsets; matrix size: $344 \times 344 \times 127$; 3 mm FWHM Gaussian filtering. Attenuation correction was performed using a DIXON based MR-AC approach with maximum likelihood estimation of attenuation and activity (MLAA) based correction for truncation artifacts. Absolute scatter scaling was used in the reconstructions. To correct for halo artifacts, the datasets were additionally reconstructed after performing a partial-bladder subtraction (PBS) in projection space. This was done by segmenting the bladder from the NAC PET image, forward-projecting this segmentation to the sinogram space, and comparing the sinogram contribution of the projected bladder versus the projection of the NAC PET image. A partial contribution of the bladder to the sinogram (75%) was then subtracted from the original sinogram. This new sinogram was used in a new reconstruction with the same settings than explained above. The halo-to-background ratio (HBR) was used as figure of merit; the activities in the halo-artifact and background were measured in a spherical 30mm-diameter volume-of-interest (VOI) located within the artifactual region and background, respectively. **Results:** Halo artifacts were observed in all the images reconstructed with MLAA-based AC-map and absolute scatter scaling. The PBS method produced artifact-free PET images in all cases. The mean HBR values obtained in the standard reconstructions were 0.20 ± 0.14 (range 0.0001–0.38), while the HBR values for the PBS method were 1.01 ± 0.27 (range 0.62–1.40). **Conclusions:** The proposed PBS method is able to correct the halo artifacts around the bladder in ^{68}Ga -PSMA PET/MRI of prostate cancer patients. Further patient evaluations are work in progress.

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Multicentre ^{68}Ga Gallium PET/CT performance harmonisation based on the EARL standards

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Aim: The use of ^{68}Ga -labelled peptides has increased over the past years. In multicentre studies, comparability of quantitative PET reads is essential. For this purpose, the EANM Research Ltd (EARL) initiative has provided PET/CT performance standards for ^{18}F -FDG studies. Specifications for ^{68}Ga PET/CT quantification are, however, not yet available. The aim of this study was to evaluate ^{68}Ga PET/CT system performance in a multicentre setting and to assess recovery coefficients (RCs) specifications for ^{68}Ga based on the current EARL standard. **Materials and Methods:** Five centres with 9 PET/CT systems from three major vendors performed ^{68}Ga phantom scans according to the EARL protocol. The NEMA image quality phantom was filled conform EARL with 2.0 kBq/ml in the background and 20.0 kBq/ml in the 6 spheres (diameter range 10–37mm). The phantom was imaged with minimal two bed positions of at least 5 minutes. RCs were determined for the maximum voxel (RC_{max}), average value within the sphere using 50% of the maximum voxel ($\text{RC}_{\text{A50\%}}$) and the highest uptake region of 1.0 cm³ (RC_{peak}). RCs for ^{68}Ga were compared with mean (FDG) EARL specifications for RC_{max} and $\text{RC}_{\text{A50\%}}$. **Results:** The RCs of ^{68}Ga were on the lower limits of the current EARL standards. The relative variation was the largest for the two smallest spheres. The mean RC_{max} for ^{68}Ga was 10% lower compared to mean EARL limits for ^{18}F . Across the spheres, this ranged from a 4% decrease for the 17- and 22mm sphere, to a 18% decrease for the 13 mm sphere. On average, RC_{mean} for ^{68}Ga was 9% lower compared to mean EARL limits for ^{18}F . Across the spheres, this ranged from a 3% decrease for the 22mm sphere, to a 15% decrease for the 13mm sphere. Finally, mean (range) RC_{peak} values were: 0.88 (0.78–1.02) for 37mm sphere, 0.84 (0.75–0.95) for the 28mm sphere, 0.76 (0.65–0.87) for the 22mm sphere, 0.57 (0.41–0.68) for the 17mm sphere, 0.37 (0.26–0.47) for the 13mm sphere and 0.24 (0.18–0.30) for the 10mm sphere. **Conclusion:** ^{68}Ga PET/CT system performance showed RCs at the lower limit of the current ^{18}F EARL RC-curve. This is likely explained by the larger positron range of ^{68}Ga compared to ^{18}F . For practical reasons we recommend to use the ^{18}F approved reconstruction settings and adapt the RC performance specifications to lower values for ^{68}Ga studies. **Research support:** This project received funding from the EU FP7 Programme (FP7/2007–2013) under grant n° 602812.

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Diagnostic Utility of Automated Robotic Arm-Assisted, PET/CT-guided Metabolic Bone Marrow Biopsy for Assessing the Bone Marrow Infiltration in Newly Diagnosed Lymphoma

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Aim: To evaluate the diagnostic utility of automated robotic arm assisted PET/CT guided metabolic bone marrow biopsy for assessing bone marrow involvement in newly-diagnosed lymphoma and its clinical impact on staging and management in these patients. **Materials and Methods:** The study is ongoing since July 2017. A minimum of 20 patients with initially diagnosed lymphoma (both Hodgkin and Non Hodgkin Lymphoma), who satisfy the inclusion and exclusion criteria will be recruited for the study. Each patient undergoes ^{18}F FDG whole-body PET/CT scan. Acquired images are reviewed by two Nuclear Medicine physicians independently and the most accessible ^{18}F FDG avid marrow lesions are selected for the biopsy. Automated robotic arm (ARA) guided PET/CT guided biopsy is then performed under aseptic conditions either on the day of PET/CT acquisition or a subsequent day. If done on a subsequent day, measures like lower activity of the radiopharmaceutical, non-contrast low-dose and CT single-bed PET/CT acquisition are applied to ensure low radiation delivery to the patient. The samples are subjected to histopathological analysis for assessing marrow infiltration at the biopsied site. **Results:** Eleven patients (7 males/4 females, mean age 49.1 years) have been recruited till the end of April 2018 in this ongoing study. Among them, 9 patients have pathologically proven non Hodgkin lymphoma while 2 patients are diagnosed with Hodgkin lymphoma; these diagnoses were made from cytopathologic/histopathologic evaluation of lymph nodes. ARA-assisted ^{18}F FDG PET/CT guided bone marrow biopsy revealed positive pathological findings in 6 patients. Among these, 3 (27.3%) patients revealed lymphomatous marrow infiltration (2 Hodgkin lymphoma, 1 diffuse large B-cell lymphoma), 1 patient had metastatic adenocarcinoma, whereas diagnoses of multiple myeloma and plasmacytoma were unmasked in one patient each. The patient who showed metastatic adenocarcinoma on ARA PET/CT-guided biopsy was detected with synchronous prostatic carcinoma on further evaluation. Hence change in management plan was effected in 6/11 (54.6%) of the analysed patient sample. On applying independent samples t test, no statistical significance was noted between SUVmax values at biopsied sites between lymphoma-positive and lymphoma-negative marrow diagnoses ($p > 0.05$). **Conclusion:** Robotic arm-assisted PET/CT guided biopsy of bone marrow is not only useful in evaluating the lymphomatous involvement of bone marrow in patients with Lymphoma, but also revealing other unknown concurrent pathologies in these patients. However a large-sample study is warranted to confirm these findings.

OP-657

A new PET whole body dynamic acquisition technique: feasibility and comparison to dual point imaging.

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Introduction: In clinical practice, dynamic PET acquisitions are seldom used. One way to account for the kinetics of ^{18}F FDG uptake is the “Dual Time Point Imaging” method (DTPI: 2 acquisitions at 60 and 175 ± 15 min after injection). We propose a new PET whole body acquisition technique which gives a dynamic information, using only one acquisition (“Whole Body Dynamic” WBD) with the same duration as a classical one (“Whole Body Static” WBS). The aims of this study were (1) to check if this new technique gave the same images quality as the WBS and (2) to determine if the dynamic information of WBD was correlated with the dynamic information provided by DTPI. **Subjects and Methods:** WBD consists of 3 successive static whole body acquisitions within the same time as a WBS one (three 50 sec/bed position vs a classical 150 sec/bed position) 60 minutes after a 3 MBq/kg ^{18}F FDG injection. A Siemens Biograph mCT camera was used. **Aim 1:** One WBD and one WBS acquisitions were performed successively in 20 patients (10 WBD first and 10 WBS first). The summed WBD images and the standard WBS images were compared blindly by 2 nuclear medicine physicians qualitatively and quantitatively (SUVmax and SUVpeak on 60 ROIs). **Aim 2:** 20 patients referred for the extension work-up of lung cancer or for characterization of a pulmonary nodule were enrolled for WBD and DTPI. The dynamic uptake was evaluated on 93 ROIs including 40 background (bkg) ROIs (liver and aorta) and 53 tumors ROIs. **Results:** **Aim 1:** The WBD and WBS were equivalent qualitatively (acceptance for clinical read and diagnostic interpretation) and quantitatively (SUVmax and SUVpeak highly correlated on the 60 ROIs: $R^2 = 0.99$ in the two cases). **Aim 2:** The variation of FDG uptake between the 2 acquisitions (DTPI vs WBD), modeled by the slopes, were significantly correlated ($p < 0.01$) whatever the parameter (SUVmax, SUVpeak, SUVmean). The highest correlations were obtained for the SUVpeak: 0.48 for the tumors ROIs, 0.44 for the tumor/liver bkg and 0.61 for the tumor/aorta bkg on the 53 tumors ROIs. **Conclusion:** We demonstrated that WBD acquisition is feasible in clinical practice without impairment of the diagnostic value of classical WBS. The dynamic information obtained additionally during this single acquisition is representative of the one obtained by DTPI.

OP-658

Digital vs Analog PET/CT: Intrapersonal SUV Comparison of Target Lesions and Reference Regions

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Aim: To assess whether digital photon counting technology in digital PET/CT influences the quantification of SUVmax in target lesions and regions of reference compared to analog PET/CT. Such comparison is necessary prior to the simultaneous use of digital and analog PET/CT systems in follow up studies. **Materials and Methods:** 59 patients were studied by dual imaging with digital and analog PET/CT from January to March of 2018; 34 of them underwent first the analog PET/CT imaging and later the digital PET/CT (mean time delay between studies 50.38 ± 16.31 minutes) and 24 patients the other way around (mean time delay between studies 43.71 ± 24.37 minutes). SUV-

max was measured in reference regions (liver and mediastinal blood pool) and target lesions. In the studies with more than one possible target lesion, only the one with the highest SUVmax was included. 7 patients who underwent the analog PET/CT first and 4 who underwent the digital PET/CT first didn't have any target lesions. Statistical analysis was done with IBM SPSS Statistics V25. **Results:** Significant differences were found between total mean SUVmax in target lesions with analog PET/CT (8.22 ± 6.96) and digital PET/CT (9.84 ± 6.23) ($P < 0.001$). Total mean SUVmax in mediastinal blood pool also showed significant differences between analog (2.57 ± 0.59) vs digital PET/CT (2.91 ± 0.36) ($P < 0.001$). No significant differences were found in total mean SUVmax in liver (analog 4.37 ± 2.64 and digital 4.52 ± 3.30). When the analog PET/CT was done first: mean SUVmax in target lesions with analog system was 6.84 ± 5.28 and digital system 9.51 ± 5.45 ($P < 0.001$). Mean hepatic SUVmax with analog 4.96 ± 3.32 and digital 5.17 ± 4.22 ($P = \text{NS}$). Mediastinal blood pool SUVmax with analog 2.51 ± 0.66 and digital 2.79 ± 0.68 ($P < 0.001$). When the digital PET/CT was done first: mean SUVmax in target lesions with digital system was 9.82 ± 7.12 and analog system 9.27 ± 8.20 ($P = \text{NS}$). Mean hepatic SUVmax with digital 3.64 ± 0.65 and analog 3.61 ± 0.72 ($P = \text{NS}$). Mediastinal blood pool SUVmax with digital 3.10 ± 0.52 and analog 2.69 ± 0.48 ($P < 0.001$). Simple linear regression between time delay and mean SUVmax difference in target lesions showed a R^2 of 0.996 when the analog PET/CT was done first and 0.655 when the digital PET/CT was done first. No significant differences between both time delays were found. **Conclusion:** Improved photon counting technology in the digital PET/CT influences significantly SUVmax quantification and thus follow-up studies must be done with the same technology.

OP-659

PET Imaging of Beta-secretase 1 in The Human Brain: Quantification and Test-Retest Examination with [^{18}F]PF-06684511

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Aim: The enzyme beta-secretase 1 (BACE1) is implicated in the pathophysiology of amyloid-beta (A β) accumulation and BACE1 inhibitors are under evaluation for the treatment of Alzheimer's disease (AD). Imaging of the brain BACE1 level is a promising tool for evaluating the effects of BACE1 inhibitors. [^{18}F]PF-06684511 is a PET radioligand (IC₅₀=0.7 nM) developed for in vivo imaging and quantification of BACE1. The aim of this study was to examine the quantification and test-retest repeatability of [^{18}F]PF-06684511 binding in the brain of healthy human subjects. **Materials & Methods:** Eight healthy subjects (7F/1M, 48 $\pm$ 7 y) underwent two PET measurements with [^{18}F]PF-06684511 (122 $\pm$ 22 MBq, mass: 1.0 $\pm$ 0.3 μg) within 5 to 19 days. For technical reasons, PET studies were performed with an ECAT EXACT HR

system in the first 5 subjects and with a HRRT system in the last 3 subjects. PET data were acquired for 123 min with measurement of the arterial input function. Volumes of interest (VOIs) were delineated using the AAL template. Quantification was performed with 1- and 2-tissue compartment modeling (TCM) and with Logan graphical analysis (GA). The outcome measure was the total distribution volume (V_t , mL*cm⁻³). Test-retest repeatability (TRR) was measured as ABS(test-retest)/MEAN(test-retest)*100. **Results:** [^{18}F]PF-06684511 distributed rather uniformly in the brain, with a peak at around 1.8-1.9 SUV at approximately 20 min after injection and a relatively slow wash-out (mean SUV 1.6 at 120 min). The lowest brain uptake was in the cerebellum and the highest in the anterior cingulate cortex and amygdala. [^{18}F]PF-06684511 in the plasma was rather stable, with ~70% of the unchanged radioligand still present at 60 min after injection. The lowest V_t values estimated with 2-TCM were in the cerebellum (test: 4.2 ± 0.9 , retest: 4.5 ± 0.7) and the highest in the amygdala (test: 6.0 ± 1.1 , retest: 6.7 ± 1.2) and anterior cingulate cortex (test: 6.2 ± 1.0 , retest: 6.8 ± 0.8). The TRR of V_t was the lowest in the cerebellum (12 $\pm$ 11%), and the highest in the caudate (20 $\pm$ 10%). As compared to 2-TCM, 1-TCM and Logan GA showed similar TRR but underestimated V_t (max: 9.3 $\pm$ 6.5% in hippocampus). **Conclusion:** These data suggest that [^{18}F]PF-06684511 is a suitable radioligand for brain imaging of BACE1. Due to its slow kinetics, the quantification of [^{18}F]PF-06684511 requires an imaging duration of at least 90 to 120 min. 1-TCM and Logan GA provided outcome measures in close agreement with 2-TCM. The TRR of V_t was similar to that observed for other radioligands without a reference region, such as [^{11}C]PBR28.

OP-660

Multi-centre Evaluation of Variations in Image Contrast and Background Variability in PET/MR Systems

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Aim: Hybrid PET-based imaging systems (PET/CT, PET/MR) are promising diagnostic tools for multi-parametric image analysis and personalized medicine. However, the comparability of PET studies is still a challenge and quantitative readings have been shown to vary significantly between different PET/CT systems. With the introduction of PET/MR, similar variations to those found with PET/CT are likely. The aim of this work is to assess differences in image quality parameters between different PET/MR systems as a first step towards a future harmonization strategy for PET/MR. **Materials and Methods:** In this ongoing study, we collected results from NEMA image-quality (IQ) measurements acquired as part of the acceptance testing of PET/MR systems available in the HYBRID consortium (H2020/MSCA No.764458). To date, this includes data from 1 Philips Ingenuity TF (ToF), 1 Siemens Biograph mMR and 2 GE SIGNA PET/MR systems (ToF). We report mean $\pm$ SD (min-max), contrast recovery coefficients

(CRC) and the range of the coefficients-of-variation (CV) obtained for all spheres of the NEMA phantom images acquired with the different PET/MR systems. In addition, we collected information about routine quality control (QC) procedures followed in the individual centres to identify the needs regarding standardization of QC protocols. **Results:** Cross-calibration measurements were performed regularly for all evaluated systems. QC procedures include vendor-specific daily QC. Mean CRCs were $43.9 \pm 6.6\%$ (36.2–50.0)%, $57.5 \pm 3.8\%$ (53.8–62.9)%, $68.8 \pm 3.1\%$ (66.2–73.3)% and $77.3 \pm 3.4\%$ (80.7–83.0)% for the 10mm, 13mm, 17mm and 22mm hot sphere, respectively. CRCs for the cold spheres were $78.9 \pm 9.1\%$ (87.1–68.1)% and $80.8 \pm 12.7\%$ (92.7–63.6)% for the 28mm and 37mm sphere, respectively. CVs varied between (6.1–6.6)%, (4.7–5.7)%, (3.3–5.1)%, (2.7–4.9)%, (2.2–5.0)%, (2.2–5.1)%, for the 10mm, 13mm, 17mm, 22mm, 28mm and 37 mm background regions, respectively. **Discussion and Conclusion:** In PET/MR, CRC variability of hot spheres in the IQ phantom is in the same range as reported values for a single PET/CT system¹. CRCs of cold spheres increased substantially in systems with ToF, consistent with a previous PET/MR study². CRCs variabilities across the evaluated PET/MR systems were lower than those found in a recent PET/CT multi-centre study³. Given these initial results, a standardization of PET data from different PET/MR systems appears feasible but additional evaluations are needed to confirm this hypothesis and establishing a base for a PET/MR harmonization concept. Efforts on designing novel QC methods for MPI will be addressed in future works. ¹Rausch et al. EJNMMI Physics (2015) 2:26 ²Boellard et al. Med. Phys. (2015) 5961:5969 ³Rausch et al. Nuklearmedizin (2014) 242:248

1607 Wednesday, October 17, 2018, 08:00 - 09:30, Hall 1

Pitfalls & Artefacts 7 - Interactive Clinical Cases:
Oncology: PSMA Therapy

OP-661

Setting the Stage - Where Does PSMA-Directed Radioligand Therapy Fit into the Urooncological Spectrum of Prostate Cancer Therapy

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OP-662

J591-PSMA Therapy and Important Pitfalls

T. Tagawa; Urology, Weill Cornell Medicine, New York, UNITED STATES OF AMERICA.

OP-663

¹⁷⁷Lu-PSMA Therapy in Advanced Prostate Cancer and Corresponding Pitfalls

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OP-664

²²⁵Ac-PSMA Therapy in Advanced Prostate Cancer and Potential Pitfalls

M. Eiber; Klinik für Nuklearmedizin, Technische Universität München, Munich, GERMANY.

1608 Wednesday, October 17, 2018, 08:00 - 09:00, Hall 4

Clinical Oncology - Rapid Fire Session: Women ONLY!

OP-666

Prostate specific membrane antigen expression and role of ⁶⁸Ga PSMA PET/CT in carcinoma breast

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Purpose: Prostate specific membrane antigen (PSMA) apart from its increasing acceptance and role in carcinoma prostate has also been reported to be expressed in several other tumors including the breast cancer. Postulated role of PSMA in the tumor neoangiogenesis has also been described. Aim of our pilot study was to evaluate the role of ⁶⁸Ga PSMA in recurrent carcinoma breast, compare it with ¹⁸F FDG PET/CT and to confirm the expression of PSMA antigen by immunohistochemistry on histopathology samples. **Material and Methods:** Seventeen female patients of invasive ductal carcinoma breast (previously treated with surgery and/or chemotherapy and/or radiotherapy) who had clinical or radiological suspicion of recurrence on whole body (vertex to mid thigh) ¹⁸F-FDG PET/CT were included in the study. Whole body ⁶⁸Ga-PSMA scans (with low dose CT) were performed within 4 days from the ¹⁸F-FDG PET/CT scans. Tracer avidity of the lesions in different organs was compared in both the scans. Immunohistochemistry staining was also done on biopsy/ surgical samples in 11 patients to look for the PSMA antigen expression on tumor cells and tumor neovasculature. **Results:** On immunohistochemical staining, PSMA antigen expression was found in the endothelium of the neovasculature of all 11 tissue samples while tumor cells in none of the patients showed any antibody reactivity. All 17 patients who had evidence of recurrent metastatic disease on ¹⁸F FDG PET/CT showed PSMA expressing lesions in ⁶⁸Ga PSMA PET/CT. On further analysis, ⁶⁸Ga-PSMA showed significantly more number of metastatic lesions in the brain parenchyma (n=16) with high target to background ratio (mean target/background ratio 4.7) as compared to ¹⁸F-FDG (n=10). Furthermore, 70 % of patients with FDG avid bone lesions showed PSMA avidity as well. PSMA avidity was noted in only 50% of patients with FDG avid lung lesions. Follow-up scans in two patients with FDG avid lesions but showing decreased uptake of FDG suggested an inflammatory/infectious etiology. Number of liver lesions detected by ⁶⁸Ga PSMA PET (n=7) was significantly less than that detected by ¹⁸F FDG (n>50). **Conclusions:** This pilot study confirms the expression of PSMA antigen in tumor neovasculature, provides a rationale for exploring the role of ⁶⁸Ga PSMA PET/CT in recurrent metastatic breast cancer and opens a window for radionuclide therapy in breast cancer patients as well.

OP-667

Clinical evaluation of kit based Tc-99m HYNIC-RGD for imaging neo-angiogenesis in breast cancer patients.

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Introduction: RGD (Arg-Gly-Asp) is a peptide targeting $\alpha_v\beta_3$ integrin receptors which are over-expressed during neo-angiogenesis in both endothelial and tumor cells. Radiolabeled peptide based on Arg-Gly-Asp (RGD) sequence have high affinity and selectivity for $\alpha_v\beta_3$ integrin. The purpose is to establish cost effective and non-invasive angiogenesis imaging agent. **Subjects and Methods:** A total of 12 patients (all female patients), of breast cancer before the start of any definitive treatment were enrolled in the study. The lyophilized kit for HYNIC-RGD was incubated with 70 mCi $^{99m}\text{TcO}_4^-$ in water bath at 100°C for 20 minutes. The preparation was allowed to cool at room temperature for 10 minutes. Paper chromatography was performed with Whatman strips using saline and acetone as mobile phase. The strips were scanned using radioTLC Scanner, also the counts were taken in well counter. 20 mCi dose of ^{99m}Tc -HYNIC-RGD was administered to each patient (n=12) through i.v injection. Planar whole body scan was acquired after 2 hours of dose administration on SIEMENS SYMBIA-T16 Gamma camera. ^{99m}Tc -HYNIC-RGD scans were then compared with ^{68}Ga -RGD scans done on same subjects. **Results:** R_f of ^{99m}Tc -HYNIC-RGD was 0.45 and 0.19 with saline and acetone respectively. From the counts obtained in well counter RCP was found to be $\geq 95\%$. Physiological uptake was seen in nasopharynx, salivary glands and gastric mucosa. Tracer showed renal excretion. Intense uptake was observed in breast lesions in all patients. In two patients axillary lymph nodes were also visualized. The lesions seen in ^{68}Ga -RGD scans were also picked up by ^{99m}Tc -HYNIC-RGD. **Conclusion:** ^{99m}Tc -HYNIC-RGD can be labeled with high radiolabeling efficiency and may be used as a promising SPECT radiopharmaceutical for imaging neo-angiogenesis in breast cancer patients. ^{99m}Tc -HYNIC-RGD is cost effective and has less radiation burden as compared to already existing ^{68}Ga -RGD.

OP-668

Interrater agreement when using PERCIST criteria for FDG-PET/CT response monitoring of metastatic breast cancer

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Aim: To examine interrater agreement and reliability of using one-lesion SULpeak as recommended by the PET Response Criteria in Solid Tumors (PERCIST) at repeat FDG-PET/CT imaging following treatment for metastatic breast cancer (MBC). **Methods:** Women with biopsy-verified MBC undergoing FDG-PET/CT response monitoring at our institution from September to December 2017 were eligible. When consent was given, scans were analyzed retrospectively and screened for comparability with regard to a modified standardization set of PERCIST 1.0. Scans were considered non-comparable if matrices at follow-up scans differed from baseline matrices, and/or if liver SULmean reference volume differed more than 20% between scans. High-

est SULpeak was measured according to PERCIST recommendations for one-lesion (most FDG-avid lesion) selected independently for each scan. PET VCAR (Volume Computer Assisted Reading) version 13.0 Ext 2 by General Electric Healthcare was used for analysis. SULpeak was registered by three experienced nuclear medicine physicians (R1, R2, and R3) blinded to each other and scan reports. Agreement and reliability with regard to measured SULpeak values were analyzed using Bland-Altman limits of agreement (LoA) and concordance correlation coefficients (CCC). **Results:** A total of 315 scans from 43 patients were eligible; exclusion of non-comparable scans reduced this number to 187 (59.4%) scans in 37 patients. Scans with lesions indistinguishable from background activity at baseline (n=2) or follow-up (n=66) were excluded, leaving 119 scans for analysis. The largest estimated mean difference in agreement was 0.040 between R1 and R2 (LoA: -0.40; 0.48) with a CCC of 0.997 (95% CI: 0.996; 0.998). The agreement was better between observers R1 and R3 who had a mean difference of only 0.012 (LoA: -0.28; 0.30) and a CCC of 0.999 (95% CI: 0.998; 0.999) compared to a mean difference between R2 and R3 of -0.028 (LoA: -0.38; 0.32) and a CCC of 0.998 (0.998; 0.999). Six patients were outliers, two of those could be explained by selection of different hottest lesions by the observers. All observers agreed on selected metastatic lesions for the remaining four cases, but there was still a difference in measured SULpeak, probably caused by a slightly different semi-automatic segmentation by PET VCAR. **Conclusion:** Semi-quantitative one-lesion SULpeak measurements generated by PERCIST recommendations by means of PET VCAR had a high degree of interrater agreement at repeat FDG-PET/CT imaging of patients with MBC. Thus, SULpeak and derived response categorization may provide a tool for a more standardized therapy response evaluation in this type of cancer patients.

OP-669

Texture analysis of tumour metabolism and perfusion for newly diagnosed breast cancer using dynamic first-pass 18F-FDG PET/CT

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Purpose: Dynamic first-pass 18F-FDG PET/CT allows assessment in a single exam of tumour blood flow (BF) and metabolism. The aim of this prospective study is to characterise and compare, by using texture analysis (TA), tumour perfusion and metabolism heterogeneities according to different breast cancer (BC) phenotypes. **Methods:** We included 216 patients with newly-diagnosed BC addressed to our department for 18F-FDG PET/CT performed after biopsy and before any treatment. A 2-min dynamic acquisition in a prone position, centred on the chest, was performed immediately after intravenous injection of 3 MBq/kg of 18F-FDG. Primary tumour volumes were manually delineated and a tumour parametric BF (in mL/min/g) image was calculated using a single compartment kinetic model. A 2-step static acquisition was performed 90 min after injection and primary tumour metabolic volumes were delineated semi-automatically. Standard PET parameters reflecting

tumour perfusion and metabolism were extracted: BF values (mean, max) and standard uptake values (SUVmean, SUVmax). In addition, texture features derived from first and second order statistics were computed to describe global and local tumour heterogeneities. Patients were divided into three groups based on immuno-histochemical analysis: luminal (HR+/HER2-), HER2 (HER2+) and triple negative (TN) (HR-/HER2-). Non-parametric tests were performed to compare BF and metabolism heterogeneities for each phenotype. **Results:** Global tumour analysis showed that the luminal tumours were less hypermetabolic than the TN tumours (SUVmax TN = 14 ± 6.6 , luminal = 8 ± 5 , $p < 0.001$). In contrast, BF values did not differ significantly between the three phenotypes. Regarding metabolism, local analysis of heterogeneity showed that the luminal tumours were more homogeneous than the HER2 tumours (homogeneity HER2 = 0.12 ± 0.034 , luminal = 0.13 ± 0.036 , $p = 0.014$). Regarding perfusion, the luminal tumours were better ordered than the TN ones (entropy TN = 6.1 ± 1.6 , luminal = 5.4 ± 1.4 ; $p = 0.01$). For TN and HER2 phenotypes, comparison of BF and metabolism heterogeneities highlighted that BF was more homogeneous (homogeneity BF: TN = 0.17 ± 0.06 , HER2 = 0.15 ± 0.05 , metabolism: TN = 0.13 ± 0.06 , HER2 = 0.12 ± 0.034 , $p < 0.001$) and exhibited less contrast (inertia BF: TN = 74 ± 57 , HER2 = 82 ± 60 , metabolism: TN = 115 ± 63 , HER2 = 124 ± 50 , $p < 0.001$). For the luminal phenotype, metabolism appeared less well-ordered (entropy BF = 5.4 ± 1.4 , metabolism = 6.5 ± 1.3 , $p < 0.001$) and with more contrast than BF (inertia BF = 83 ± 49 , metabolism = 107 ± 50 , $p < 0.001$). **Conclusion:** In breast cancer, significant differences were highlighted between BF and metabolism heterogeneities. Local TA between each phenotype brought additional information that was not seen with global analysis of metabolism and BF.

OP-670

Diagnostic performance of dedicated breast PET in opportunistic breast cancer screening; patient based analysis

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Purpose: A dedicated breast PET (dbPET) scanner has been developed, but its diagnostic performance in breast cancer screening remains unknown. The purpose of this study was to investigate the sensitivity, specificity and positive predictive value (PPV) of abnormal uptake on dedicated breast PET (dbPET) for detecting breast cancer. **Methods:** A total of 489 females who underwent dbPET as well as whole-body PET, mammography (MG) and ultrasonography (US) between June 2016 and June 2017 for opportunistic screening purpose were analyzed. Each patients was administrated FDG (3.7MBq/kg of body weight) and underwent a whole-body PET/CT scan about 60 minutes later, followed by dbPET. Two experienced nuclear medicine physicians interpreted dbPET images on consensus using a 3-point grading scale (0: normal, 1: equivocal, but further evaluation needed, and 2: suspicious for breast cancer). Follow-up information, including histopathological findings,

was used as a reference standard, and sensitivity, specificity and PPV was calculated. **Results:** Of 489 females, 87 and 37 females were judged as grade 1 and 2, respectively. As a final diagnosis, 6 primary breast cancers in 5 patients and 1 atypical ductal hyperplasia (ADH) in 1 patient were confirmed histopathologically. In 37 females with grade 2, 4 patients with breast cancer were accurately diagnosed by dbPET, but one patient had two lesions, one of which was missed by dbPET. In 87 patients judged as grade 1, one ADH lesion was diagnosed by dbPET, and there was no breast cancer patient. The dbPET was negative in one patient with breast cancer that was located close to the chest wall, although MG was positive. When we regarded patients with grade 2 as positive, the patient-based sensitivity, specificity and PPV were 80% (4/5), 93.2% (451/484) and 10.8% (4/37) respectively. **Conclusions:** Our preliminary data suggest that the dbPET showed reasonably high sensitivity and specificity with reasonable PPV for screening. It can miss lesions close to the chest wall.

OP-671

Prognostic value of Post-Treatment 18F-FDG PET/CT in Locally Advanced Cervical Cancer patients treated with chemo-radiation therapy and predictors of metabolic response to therapy: do Metabolic Tumour Volume (MTV) and Total Lesion Glycolysis (TLG) play a role?

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Purpose: To investigate the prognostic value of post-treatment 18F-FDG PET/CT scans in locally advanced cervical cancer (LACC) treated with concomitant chemo-radiation therapy (CCRT). The secondary aim was to assess the role as response-to-treatment predictive factors of the following parameters: SUVmax, SUVmean, Metabolic Tumour Volume (MTV), Total Lesion Glycolysis (TLG), age, pathology, FIGO stage and nodal involvement. **Subject and Methods:** Inclusion criteria were: diagnosis of locally advanced cervical cancer; FIGO stage IIA-IVA; full clinical history and follow up data availability; CCRT on the pelvis +/- external beam boost on PET-positive nodes + brachytherapy boost on the tumour as single treatment option; pre- and post-treatment 18F-FDG PET/CT scan performed. Exclusion criterion was: previous surgical treatment of the cervical tumour. Overall 82 patients could finally be enrolled in this retrospective study. By reviewing post-treatment PET/CT scans, according to EORTC criteria, patients were classified as complete metabolic responders (CMR, equivalent to negative post-treatment FDG PET) or non-complete metabolic responders (N-CMR, including partial metabolic response + stable disease + progressive disease). A Kaplan-Meier Analysis was used to evaluate differences in overall survival (OS) between CMR and N-CMR groups. Student's t-test, Pearson's chi-squared test and logistic regression were used to investigate the possible role of PET and clinical parameters as pre-

dictors of metabolic response to therapy. **Results:** we observed a highly significant difference in OS between CMR and N-CMR (log-rank test $p < 0.0001$). Pre-treatment MTV and TLG means values were statistically different in CMR and N-CMR patients ($p = 0.008$ and $P = 0.046$); also frequencies of nodal involvement were statistically different between the two groups ($p = 0.085$). The significant independent predictors of response-to-therapy were MTV ($p = 0.019$; Odds-Ratio = 1.015; 95%CI = 1.002–1.028) and TLG ($p = 0.045$; Odds-Ratio = 1.001; 95%CI = 1.000–1.002) and Nodal involvement ($p = 0.088$; Odds-Ratio = 2.361; 95%CI = 0.879–6.343). **Conclusion:** 18F-FDG PET/CT could have an important role in the restaging process of LACC. Patients with a CMR after CCRT showed a better OS as compared to N-CMR patients: therefore these patients may benefit from more aggressive or additional treatments. In our cohort of patients pre-treatment MTV and TLG and nodal involvement were predictors of response-to-therapy.

OP-672

Does HIV status impact on nodes visualized on ^{18}F -FDG PET/CT in patients with invasive cervical carcinoma?

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Introduction: The synergistic deleterious impact of cervical cancer and HIV infection make these two entities a raging scourge of the under-privileged society, particularly in young productive women. Despite the established role of [18F] 2-fluoro-2-deoxyglucose (FDG) PET/CT in cervical cancer imaging, inflammatory and infectious lesions may hinder accurate interpretation. With the emergence of FDG PET/[CT] facilities in sub-Saharan Africa, we aim to differentiate these two entities with the aid of simple PET positive node characteristics. This could prove beneficial regarding management. **Subjects and Methods:** We analyzed a total of one hundred and eighty-four F-18 FDG-PET/CT studies performed both pre-and post-treatment in 92 patients with locally advanced cervical cancer (FIGO stages IIB to IIIB). HIV positive patients constitute half of the study population. Qualitative (symmetry) and semi-quantitative (SUVmax) metabolic PET metric as well as CT nodal size and CT score (based on nodal size on axial images, focal defects and extra-capsular spread) were assessed in different nodal sites and were compared between HIV positive and negative patient groups. Correlation between CD4 count level and positive lymph nodes on the PET/CT scan was also assessed in HIV- infected participants.

Results: There was higher median SUVmax in the pelvic lymph nodes of HIV-positive patients compared with negative both on pre-treatment ($p < 0.0001$) and post-treatment ($p < 0.0001$) FDG PET/CT scans using the Mann Whitney test. Overall, we found that the qualitative and quantitative metabolic PET metric studied performed poorly in differentiating cancer of the cervix from reactive adenopathy. However, the median CT nodal size is higher in cervical ($p = 0.027$) and thoracic ($p = 0.05$) lymph nodes of HIV positive patients compared to the other group. There was negative correlation between CD4 count and FDG uptake on pre-treatment FDG PET/CT scans with moderate correlation

in the abdominal nodes ($r_s = -0.5138$, $p = 0.006$). **Conclusion:** Differentiating metastatic lymphadenopathy from reactive adenopathy in HIV-infected patients can be challenging without histopathologic confirmation. In this study, only the nodal size on the CT component of the PET/CT seems to be a potential parameter to differentiate the possible nature of the visualized lymph nodes in the neck and thoracic regions, especially on baseline PET/CT scans.

OP-673

Prognostic role of ^{18}F -FDG PET/CT in patients with cervical cancer treated with Chemo-Radiation Therapy and simultaneous integrated boost (SIB) to positive nodes

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Background/Aim: The recommended standard care in advanced cervical cancer is concurrent chemoradiotherapy followed by brachytherapy. To date there is no agreement about the type of imaging for restaging/surveillance after radiation treatment (RT). We assessed if routine use of ^{18}F -FDG PET/CT (FDG-PET) could be useful in patients treated with RT with radical intent. **Patients/Methods:** We retrospectively evaluated nineteen patients (mean age 57 years) with cervical carcinoma (17 squamocellular, 2 adenocarcinoma) candidate to curative RT. The most representative stage (58%) was IIB, lesion size ranged from 3 to 9.5 cm. Patients underwent FDG-PET respectively prior to RT for staging and target volume definition and post-RT to evaluate treatment response. Images were evaluated in a qualitative and semiquantitative way (SUVmax value and % of variation as ΔSUV). PET results were compared to follow-up data (f-up). We applied Volumetric Modulated Arc Therapy (VMAT) in 8 of the cases and Tomotherapy in 7 patients; 4 patients were treated with 3D-conformal RT. The primary tumor and regional lymphatics at risk were treated with definitive EBRT to a dose of 50.4 Gy/28 fractions. Cervix was then boosted with BRT-HDR with an additional dose of 24–30 Gy/4–5 fractions. In 10/19 pts with positive nodes was performed a Simultaneous Integrated Boost (SIB) to a total dose of 59.36 Gy/28 fractions. A concurrent cisplatin chemotherapy was delivered. **Results:** Regarding primary lesions, FDG-PET post-RT detected complete response (CR) in 9 of the patients, partial response in 7 (PR), disease progression (PD) in 2 and stable disease (SD) in one. F-up was negative in all patients with CR and in 4 with PR. One patient with SD, 2 patients with PD and one patient with PR had distant progression; the remaining 2 patients with PR had persistent local disease. A $\Delta\text{SUV} \geq 35\%$ in primary lesion was strictly related to disease free interval. With regard to nodes treated with SIB, FDG-PET assessed 7 CR and 1 PD (confirmed by f-up) and 2 PR (no evidence of disease at f-up). **Conclusion:** CT-RT, delivered with SIB in selected positive -node patients, was an effective treatment in advanced cervical cancer, with high percentage of CR at follow-up data (respectively 63% on primary cancer and 70% on nodes). FDG-PET was a powerful tool to assess response to

therapy, well-related to patient prognosis, potentially impacting clinical decision making. A $\Delta\text{SUV} \geq 35\%$ could be routinely used as a predictor of outcome.

OP-674

Clinical and prognostic value of 18F-FDG PET/CT in recurrent endometrial carcinoma.

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Purpose: Endometrial carcinoma (EC) is a common gynecological cancer with an overall good prognosis, except of cases of advanced EC or in presence of recurrence. Conventional imaging (CI) and tumor marker have limited accuracy for detecting recurrence in these patients. The aim of this retrospective study was to assess the diagnostic performance, the prognostic value and the impact on therapeutic management of 18fluorine-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) in a large sample of patients with suspected recurrent EC. **Subjects and Methods:** we retrospectively evaluated 157 patients who had undergone surgery with/without adjuvant therapy for histologically proven EC. All patients underwent restaging 18F-FDG PET/CT for suspected recurrence. Comparable CI (contrast-enhanced CT and/or magnetic resonance imaging) was available for 150 patients. The PET images were analyzed visually and semi-quantitatively by measuring the maximum standardized uptake value body weight (SUVmax). A combination of clinical follow-up/imaging follow-up and/or histopathology (when available) was taken as reference standard. PFS and OS were computed using Kaplan-Meier curves **Results:** Seventy-nine patients (50.3%) had positive 18F-FDG PET/CT (average SUVmax 13.1) showing the presence of at least one hypermetabolic lesion consistent with local recurrence or metastatic lesion, while the remaining 78 (49.7%) were negative. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 18F-FDG PET/CT were 96%, 99%, 99%, 96%, 97% respectively and were higher compared to CI (97%, 62%, 72%, 96% and 80%). CI and PET/CT were concordant in 120 patients and discordant in 30 patients. After a mean follow-up period of 39 months, relapse or progression of disease occurred in 58 (37%) patients with an average time of 22.1 months and death occurred in 37 (23%) patients with an average time of 27.6 months. A positive 18F-FDG PET/CT was significantly associated with shorter PFS and OS compared to unremarkable PET/CT scan, both at 3-year (PFS 37% vs 91% $p < 0.001$; OS 54% vs 98% $p < 0.001$) and 5-year (PFS 27% vs 77% $p < 0.001$; OS 40% vs 92% $p < 0.001$). Instead, SUVmax was not correlated with outcome survival. PET/CT results had a significant impact on therapeutic approach in 33 patients: avoiding unnecessary therapies in 28 cases and modifying therapeutic choice in 5 cases. **Conclusions:** 18F-FDG PET/CT showed a good diagnostic performance in patients with suspected recurrent EC, superior than conventional imaging, and showed an important prognostic value in assessing the rate of PFS and OS. Moreover, PET/CT allowed for a change in treatment decision in about 20% of cases.

OP-675

Radiomics in vulvar cancer: first clinical experience using 18F-FDG PET/CT images

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Purpose: Positron emission tomography/computed tomography with 18F-fluorodeoxyglucose (18F-FDG-PET/CT) is mainly used for lymph node staging in the preoperative workup of vulvar cancer. In recent years, there is a growing interest to extract quantitative imaging features, a field also known as radiomics, to predict the biological behaviour of malignant tumours, response to therapy and prognosis. The aim of this study was to investigate whether radiomic features derived from preoperative 18F-FDG-PET/CT images could predict both tumour biology and prognosis in women with invasive vulvar cancer. A novel approach for identification of non-redundant imaging features out of the dataset was achieved by means of principle component analysis (PCA). **Subjects & Methods:** Patients were retrospectively included when they had an unifocal primary tumour of >2.6 cm in diameter, had received a preoperative 18F-FDG-PET/CT scan followed by surgery and had at least 6 months of follow-up data. A volume of interest was drawn semi-automatically on the primary tumour in each PET image, followed by the extraction of 83 radiomic features. Reduction of features containing mutual information was achieved by applying PCA. The identified features were compared with histopathology using non-pairwise group comparison and linear regression. Univariate and multivariate Cox regression analyses were used to correlate the identified features with progression-free survival (PFS) and overall survival (OS). Survival curves were estimated using by the Kaplan-Meier method. **Results:** Between June 2013 and December 2016, 40 women fulfilled the inclusion criteria and were included. PCA revealed four unique radiomic features, i.e. SUV_{max} , local entropy, maximum 3D diameter and Moran's I. These features were not statistically significantly associated with histopathological characteristics such as grading, depth of invasion, lymph-vascular space invasion and the presence of metastatic lymph nodes. No statistically significant correlation was found between the identified features and PFS. However, Moran's I, a measure of global spatial autocorrelation, was sta-

tistically correlated with OS ($p=0.03$). In multivariate Cox regression, extracapsular involvement of the metastatic lymph nodes and Moran's I were independent prognostic factor for PFS and OS in this cohort. **Conclusion:** Our data show that PCA might be usable as a method to identify unique imaging features from a large set of features suitable for further analysis. Although the identified features poorly predicted tumour biology, Moran's I was found to predict patient prognosis. Because of the low incidence of vulvar cancer, a large multicenter study is required to establish the clinical relevance of the observed findings.

OP-676

First-in-Human Study with ^{18}F -AzaFol for Folate Receptor Targeted PET: An Interim-Analysis of the PET_FOL_1 Phase-I Trial

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Introduction/Aim: The folat-receptor α (FR α) has been found overexpressed in different cancer entities and has become a valuable target of several antineoplastic treatments such as monoclonal antibodies, small molecule-/antibody-drug conjugates or vaccinations. Despite the promising therapeutic activity in the early clinical development stages, some of these drugs have ultimately failed in phase-III trials presumably due to variable levels of FR α -positive lesions. The aim of this on-going study is the assessment of the specificity of ^{18}F -AzaFol, a novel FR-targeting PET tracer, for detection of receptor-positive lesions to facilitate better patient selection. **Materials and Methods:** This multicentric phase-I trial (NCT03242993) is evaluating ^{18}F -AzaFol in patients with histologically confirmed ovarian (OC) and non-small cell lung cancer (NSCLC) in terms of tracer uptake (SUV_{max} , SUV_{mean} , ROC analysis), change of overall staging and lesion detection rate. Primary endpoints also include an estimation of gained overall information and confidence changing/adapting this therapy based on imaging results as well as comparison with the immunohistochemistry findings for FR α (IHC) from biopsy specimen. The secondary objective was the calculation of the tissue distribution (dosimetry). Patients received 1 mg folic acid intravenously prior to the injection of ^{18}F -AzaFol (< 600 MBq). **Results:** The interim analysis included 10 of the 36 planned patients. We observed an IHC positivity in 29% (2/7) of NSCLC and 100% (3/3) of OC patients. Although inter- and intratumoral heterogeneity was one of the main findings, all IHC-positive patients showed an ^{18}F -AzaFol uptake in the majority of the lesions. In two patients with negative IHC no uptake was observed in any of the lesions. ^{18}F -AzaFol-PET/CT enabled the detection of additional lesions in comparison to the standard-of-care imaging performed prior to study entry. In one patient with NSCLC (adenocarcinoma) several new bone lesions were found and in two further patients with NSCLC

additional subcutaneous metastases were identified. Incidental findings were a ^{18}F -AzaFol-avid recurrent meningioma and diffuse bone marrow uptake in two patients. Dosimetry revealed a mean dose of 0.01837 mSv/MBq corresponding to an effective dose of 6.0 mSv (5.1 - 6.9 mSv, which is comparable to ^{18}F -FDG. No drug related adverse events were reported. **Conclusions:** The first clinical data of ^{18}F -AzaFol-PET have proven specificity to identify FR α -positive tumors by PET-CT. ^{18}F -AzaFol is well tolerated and holds the potential to influence overall staging in FR α -positive tumors.

1701 Wednesday, October 17, 2018, 10:00 - 11:30, Plenary Hall

CME 14 - Physics / Dosimetry: Quantitative Multimodality Imaging

OP-677

Advances in SPECT/CT Quantitation

B. Hutton; Institute of Nuclear Medicine, London, UNITED KINGDOM.

OP-678

Advances in PET/CT Quantitation

D. Visvikis; National Institute of Health and Clinical Science, Director Research INSERM, Brest, FRANCE.

OP-679

Advances in PET/MRI Quantitation

B. Sattler; University Hospital Leipzig, Department for Nuclear Medicine, Leipzig, GERMANY.

OP-680

Advances in Radionuclide Image Based Dosimetry

Y. Dewaraja; University of Michigan, Department of Radiology, Division of Nuclear Medicine, Ann Arbor, UNITED STATES OF AMERICA.

1702 Wednesday, October 17, 2018, 10:00 - 11:30, Hall 2

Joint Symposium 27 - Cardiovascular / EACVI: The Potential of Dual Isotope Imaging in Nuclear Cardiology

OP-681

Coronary Artery Disease

A. M. Scholtens; Meander Medisch Centrum, Amersfoort, NETHERLANDS.

OP-682

Viability

O. Gämperli; Zurich University Hospital, Zurich, SWITZERLAND.

OP-683

Cardiac Sarcoidosis

R. Slart; Department of Nuclear Medicine and Molecular Imaging,

University of Groningen, University Medical Center Groningen, Groningen, NETHERLANDS.

OP-684

Cardiac Innervation

C. Rischpler; Klinik für Nuklearmedizin, Universitätsklinikum Essen, Universität Duisburg-Essen, Essen, GERMANY.

1703 Wednesday, October 17, 2018, 10:00 - 11:30, Hall 3

Joint Symposium 28 - Oncology / ESTRO: PET/CT for Radiotherapy Planning

OP-685

Esophageal Cancer - The Radiation Oncologist's Point of View

E. Troost; Universitätsklinikum Carl Gustav Carus, Department of Radiotherapy and Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiooncology-OncoRay, Dresden, GERMANY.

OP-686

Esophageal Cancer - The Nuclear Medicine Physician's Point of View

A. Loft Jakobson; PET & Cyclotron Unit 3982, Rigshospitalet, Copenh. Univ. Hosp., Center for Diagnostic Investigations, Copenhagen, DENMARK.

OP-687

Rectal Cancer - The Radiation Oncologist's Point of View

K. Haustermans; Cancer Institute, University Hospitals Leuven Department of Radiation Oncology, Leuven, BELGIUM.

OP-688

Rectal Cancer - The Nuclear Medicine Physician's Point of View

L. Leccisotti; Fondazione Policlinico Universitario Agostino Gemelli, PET/CT Centre, Rome, ITALY.

1704 Wednesday, October 17, 2018, 10:00 - 11:30, Hall 5

CTE 7 - Interactive: Technologists / Thyroid: Thyroid Imaging and Therapy

OP-689

The Role of 99mTc MIBI Scintigraphy in Thyroid Nodules Diagnostics

T. Bogović-Crnčić; Clinical hospital centre Rijeka, Department of nuclear medicine, Rijeka, CROATIA.

OP-690

PET Imaging of Thyroid Diseases

A. Piccardo; Ente Ospedaliero "Ospedali Galliera, Genova-I", Genoa, ITALY.

OP-691

Radioiodine Ablation in Differentiated Thyroid Cancer - An Update

S. Kusačić-Kuna; Clinical hospital Zagreb, Zagreb, CROATIA.

1705 Wednesday, October 17, 2018, 10:00 - 11:30, Hall X
M2M: Radiochemistry is Cool!

OP-692

Purification of ^{155}Tb produced at CERN-MEDICIS for applications in nuclear medicine

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Introduction: A quartet of terbium isotopes (^{149}Tb , ^{152}Tb , ^{155}Tb and ^{161}Tb) has been identified as promising isotopes for use in therapeutic, diagnostic or theranostic nuclear medicine. Terbium-161 can be produced by neutron irradiation of a ^{160}Gd target followed by its subsequent beta decay¹. The other terbium isotopes are mainly produced at the CERN-MEDICIS facility by proton-induced spallation of a tantalum target followed by the mass-separation and isolation of desired radionuclides²⁻⁴. Gamma-emitting polyatomic impurities, such as $^{139}\text{Ce}^{16}\text{O}$ in a ^{155}Tb sample, are produced but not separated in this process which emphasises the need for further radiochemical separation before their application in nuclear medicine. The aim of this study was to develop a rapid and effective separation scheme that is capable of successfully isolating the desired terbium from the cerium impurities. **Methods:** Separation of terbium from cerium impurities has been studied using stable element standards in nitric acid on various ion-exchange (AG1, Bio-Rad) and extraction chromatography resins (UTEVA, TK100 and TEVA, Triskem International). The effect of cerium oxidation with sodium bromate has been studied to encourage selective adsorption of the tetravalent Ce(IV) impurity over the desired Tb(III) product. The rate of adsorption to the resin and the rate of cerium oxidation have also been studied in order to find the optimum conditions for rapid separation. Inductively coupled plasma mass spectrometry (ICP-MS) and HPGe gamma-spectrometry have been used to quantify the quality of the separations achieved. **Results and Conclusions:** The process has been optimised to provide a rapid radiochemical separation to afford a high radiochemical yield. All resins performed best at high nitric acid concentrations and separation was dependent on the selective oxidation of cerium from Ce(III) to Ce(IV). Separation using a mixed resin bed (AG1, UTEVA and TEVA) successfully removed a 31% cerium-139 impurity with an excellent terbium-155 recovery (>90%). This method allows for radiologically pure ^{155}Tb solutions to be prepared which are suitable for pre-clinical applications, SPECT phantom studies and primary standardisation. **References:** 1. S. Lehenberger et al., *Nucl. Med. Biol.*, 2011, **38**, 917-924. 2. C. Müller et al., *Nucl. Med. Biol.*, 2014, **41**, e58-e65. 3. C. Müller et al., *J. Nucl. Med.*, 2012, **53**, 1951-1959. 4. B.J. Allen et al., *Appl. Radiat. Isot.*, 2001, **54**, 53-58.

OP-693

A dual generator concept to yield ^{226}Th : an isotope of interest for targeted alpha therapy

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Introduction: Thorium-226 ($t_{1/2}=30.6\text{m}$) is an isotope of interest for targeted alpha therapy (TAT). It decays via a four alpha decay chain to long-lived ($t_{1/2}=22.3\text{ y}$) ^{210}Pb with a 111 keV γ -line (3.29%) that can be used for SPECT imaging; thus providing theranostic capabilities. A generator concept is necessary to provide a consistent supply of ^{226}Th from its parent ^{230}U (20.23 d) [1]. Furthermore, ^{226}Th needs to be supplied in a form that is amenable to direct labeling with the chelate; minimizing the amount of time required for its preparation for use. Uranium-230 is best obtained by the proton irradiation of thorium targets to obtain ^{230}Pa (17.4 d), which partially decays to ^{230}U . To yield a consistent supply of ^{226}Th , a dual generator concept was developed: first to yield ^{230}U from the decay of ^{230}Pa , and second, to separate ^{226}Th from decay parent ^{230}U . **Methods:** Protactinium-230 used in this work was obtained from Oak Ridge National Laboratory as a side product from the production of ^{225}Ac [2]. An extraction chromatography resin approach was used for both the design of a $^{230}\text{Pa}/^{230}\text{U}$ generator, and a $^{230}\text{U}/^{226}\text{Th}$ generator. Uranium-230 and its decay product ^{226}Th were first sorbed on a solid phase in acid media. Uranium-230 was then eluted in acid as ^{226}Th remained on the stationary phase. In a third step, ^{226}Th was eluted from the resin in acidic media. **Results:** The $^{230}\text{Pa}/^{230}\text{U}$ generator provided ^{230}U in high radiochemical yield and purity (>99.9%). The $^{230}\text{U}/^{226}\text{Th}$ generator yielded approximately 90% of the ^{226}Th with a >99.5% recovery of parent ^{230}U for each elution cycle. Thorium-226 was obtained with high radiochemical purity (>99.9%). Multiple elutions have been performed successfully with consistent radiochemical yields and purities. **Conclusions:** A dual generator system was successfully designed and tested to provide a dependable supply of ^{226}Th . Uranium-230 can be reliably supplied from a $^{230}\text{Pa}/^{230}\text{U}$ generator. The $^{230}\text{U}/^{226}\text{Th}$ generator, in turn, provides ^{226}Th in high radiochemical yield and purity and in a form that is amenable to direct labeling with chelates for use in targeted alpha therapy. **Acknowledgments:** This research was funded by the United States Department of Energy, Office of Science via a grant (FOA LAB 14-1099) from the Isotope Development and Production for Research and Applications subprogram in the Office of Nuclear Physics. **References:** [1] Radchenko, V. et al., *Radiochim Acta*. **2016**, 104, 291–304 [2] Radchenko, V. et al., *J Chromatogr A*. **2015**, 1380, 55–63

OP-694

Evaluation of the *in vitro* and *in vivo* characteristics of the novel ^{89}Zr octacoordinated chelator DFO-cyclo* compared to the hexacoordinated DFO

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Introduction: The current “gold standard” chelator to label antibodies with ^{89}Zr for immunoPET is desferrioxamine (DFO). Preclinical studies have shown that the ^{89}Zr -DFO complex is partly unstable *in vivo*, resulting in release of ^{89}Zr and subsequent accumulation in mineral bone tissue. This bone uptake may prevent the detection of bone metastases, and hampers accurate estimation of the radiation dose to the bone marrow in dose planning for radioimmunotherapy. Therefore, there is a need for a more stable ^{89}Zr chelator. Here we report DFO-cyclo*, a preorganized extended DFO derivative enabling octacoordination of the metal, and investigate the stability of its ^{89}Zr complex over the unsaturated hexacoordinated ^{89}Zr -DFO complex *in vitro* and *in vivo*. **Materials & Methods:** DFO-cyclo* was prepared by coupling of a cyclic hydroxamate group to DFO. Trastuzumab was conjugated with DFO-cyclo*-pPhe-NCS or DFO-pPhe-NCS and radiolabeled with ^{89}Zr . Stability of the labeled antibody conjugates was evaluated in human plasma and in PBS with a 1000-fold molar excess of EDTA or DFO at 37°C up to 7 days. The immunoreactive fraction, IC_{50} and internalization capacity of ^{89}Zr -DFO-cyclo*-trastuzumab or ^{89}Zr -DFO-trastuzumab were evaluated *in vitro* using HER2-expressing SK-OV-3 cells. The *in vivo* distribution of ^{89}Zr -DFO-cyclo*-trastuzumab and ^{89}Zr -DFO-trastuzumab was investigated in mice with subcutaneous SK-OV-3 xenografts by *ex vivo* tissue analyses and PET/CT imaging. **Results:** Labeling efficiencies exceeded 99% and specific activities > 150 MBq/mg were obtained for both ^{89}Zr -DFO-cyclo*-trastuzumab and ^{89}Zr -DFO-trastuzumab. When challenged with an excess of EDTA or DFO at 37°C for 7 days, ^{89}Zr -DFO-cyclo*-trastuzumab showed significantly higher stability than ^{89}Zr -DFO-trastuzumab: $99 \pm 1\%$ vs. $61 \pm 1\%$, and $55 \pm 3\%$ vs. $44 \pm 3\%$, respectively. Immunoreactive fractions of 65% and 61% and IC_{50} values of 2.89 nM and 2.93 nM were found for ^{89}Zr -DFO-cyclo*-trastuzumab and ^{89}Zr -DFO-trastuzumab, respectively. Internalization after 2 h was significantly higher for ^{89}Zr -DFO-cyclo*-trastuzumab ($26.6 \pm 1.1\%$) compared to ^{89}Zr -DFO-trastuzumab ($22.4 \pm 1.5\%$) ($p < 0.005$). Bone uptake (%ID/g) was significantly lower for ^{89}Zr -DFO-cyclo*-trastuzumab compared to ^{89}Zr -DFO-trastuzumab in knee ($3.6 \pm 0.4\%$ vs. $5.9 \pm 0.6\%$), femur ($2.2 \pm 0.2\%$ vs. $3.4 \pm 0.3\%$), and sternum ($3.5 \pm 0.4\%$ vs. $4.5 \pm 0.4\%$) at 72 h after injection ($p < 0.005$). Tumor uptake and blood clearance did not differ significantly. **Discussion/Conclusion:** ^{89}Zr -DFO-cyclo*-trastuzumab shows improved *in vitro* and *in vivo* stability compared to conventional ^{89}Zr -DFO-trastuzumab. In immunoPET, less bone uptake, improved bone metastasis detection and improved radioimmunotherapy dose planning may be achieved using DFO-cyclo*.

OP-695

Labelling and evaluation of different AAZTA and DATA^{5m} derivatives with ^{64}Cu

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Introduction: Copper-64 ($T_{1/2} = 12.7$ hours; β^+ , 0.653 MeV [17.8 %]; β^- , 0.579 MeV [38.4 %]) provides perfect imaging properties for positron emission tomography (PET) as well as for radiotherapy. With its longer half-live compared to typical PET isotopes it is

flexible for use with small molecules and longer blood retaining molecules like antibodies or other larger constructs. The wide range of chelators which have been used with copper allows a great understanding of its coordination chemistry and makes it one of the most promising metals for PET. In this study the interesting hybrid ligands DATA and AAZTA, reported to have excellent complex formation parameters with trivalent metals such as ^{68}Ga , ^{44}Sc and ^{177}Lu , respectively, were labelled with ^{64}Cu . DATA/AAZTA-complexes with ^{64}Cu would provide a very interesting tool for labelling and imaging of proteins because of the long half-life and the possibility to label and conjugate the ligand at mild conditions (RT, pH = 5.5). **Methods:** Different derivatives based on DATA and AAZTA were labelled with ^{64}Cu . The chelates were synthesized as previously published. After purification with HPLC, 10 nmol of each compound were labeled in ammonium acetate buffer (pH = 5.5) with 10 to 30 MBq of ^{64}Cu . Reactions were followed by two-system TLC (citrate and ammonium acetate/MeOH) as well as HPLC. Stabilities of the ^{64}Cu -complexes were determined in vitro in human serum and PBS buffer at different times (2 h, 4 h, 12 h, 24 h, 48 h) **Results:** All tested derivatives were radiolabeled with a radiochemical yield of >95 %. Within 4 h stabilities of > 95% were observed in HS and PBS. **Conclusion:** We were able to provide first results for ^{64}Cu -labeling of DATA and AAZTA and their derivatives. Radiochemical yields of >95% at RT and PH = 5.5 were observed. Next ^{64}Cu -DATA/AAZTA-conjugates radiopharmaceuticals based on octreotides and PSMA inhibitors as well as antibodies and their fragments will be investigated.

OP-696

A Dual Reporter Iodinated Labeling Reagent for Cancer PET Imaging and Fluorescence-guided Surgery

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Introduction: The combination of early diagnosis and complete surgical resection of malignant tumor is the best modality to treat cancer. An iodine-124 fluorescein based dual modality labeling reagent, ^{124}I -Green, would become a generic tool to conjugate a PET and a fluorescent reporter to any cancer specific antibody in one step. The resulting antibody conjugate would allow both cancer diagnosis with positron emission tomography (PET) and fluorescence-guided surgery. **Methods:** The radiosynthesis of ^{124}I -Green was achieved with an improved one-pot three-component radioiodination reaction. The carcinoembryonic antigen (CEA) specific antibody A5B7 was conjugated with ^{124}I -Green. The EC_{50} of the dual labeled A5B7 and the native antibody was measured. CEA-expressing human colorectal carcinoma SW1222 cells were stained with the dual labeled A5B7. A blocking experiment was carried out by co-incubating with the native A5B7. The biodistribution, PET/CT and *ex vivo* fluorescence imaging of the dual labeled A5B7 was performed in the SW1222 xenograft bearing mice (n=3) at 24, 48, and 72 h post intravenous injection. **Results:** The ^{124}I -Green was obtained in excellent radiochemical yields of 92±5% (n = 4). The

EC_{50} of the dual labeled A5B7 towards CEA was 22 nM similar to the native A5B7 (26 nM). The SW1222 cells stained with the dual labeled A5B7 emitted green fluorescence that was largely blocked by the native A5B7. High tumor uptake of the dual labeled A5B7 around 20.21±2.70, 13.31±0.73, and 10.64±1.86 %ID/g (n = 3) was observed at 24, 48, and 72 h post intravenous injection, respectively. The SW1222 xenografts were clearly visualized by both PET/CT and *ex vivo* fluorescence imaging with excellent target to background contrast. **Conclusion:** We have developed a generic dual PET and fluorescence labeling reagent, ^{124}I -Green. It enabled a one-step installation of the iodine-124 fluorescein dual reporters to any cancer targeting antibody. Excellent tumor to background contrast in both PET/CT and *ex vivo* fluorescence imaging was achieved with the dual labeled A5B7. The encouraging results warrant further studies towards translation of the ^{124}I -Green to the PET cancer imaging and fluorescence-guided surgery.

OP-697

Development of the first ^{18}F -labeled PET radioligand for imaging 5-HT_{1B} receptors: [^{18}F]AZ10419096

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Aims: The serotonin 1B receptor (5-HT_{1B}R) has been studied in humans with positron emission tomography (PET) using ^{11}C -labeled PET radioligands. Carbon-11 ($t_{1/2}$ = 20.4 min) has limited utility for PET because of its short half-life. An effective PET radioligand for 5-HT_{1B}R labeled with fluorine-18 ($t_{1/2}$ = 109.8 min) would expand the feasibility for investigations on 5-HT_{1B}R to PET centers without an on-site cyclotron. [^{11}C]AZ10419096 ([N-methyl- ^{11}C]6-fluoro-N-(3-fluoro-4-morpholinophenyl)-8-(4-methylpiperazin-1-yl)-4-oxo-4H-chromene-2-carboxamide) is a recently developed full antagonist radioligand with desirable PET imaging characteristics (Lindberg *et al.*, *Nucl. Med. Biol.* 2017, 54, 34). AZ10419096 has two aryl fluoro substituents, that present opportunities for labeling with fluorine-18. Due to the electron-rich nature of the fluoroaryl groups, direct $\text{S}_{\text{N}}\text{Ar}$ with [^{18}F] fluoride ion was not viable for labeling. Therefore, we explored a recently developed radiofluorination methodology that uses cyclotron-produced [^{18}F] fluoride ion with a boronic ester precursor in the presence of $\text{Cu}(\text{OTf})_2(\text{py})_4$ and is reportedly successful on electron-rich aryl rings (Tredwell *et al.*, *Angew. Chem. Int. Ed.*, 2014, 53, 7751). **Materials and Methods:** The 3-chloro analog of AZ10419096 was treated with pinacolo-diboron, $\text{Pd}_2(\text{dba})_3$ and tricyclohexylphosphine to obtain the corresponding 3-boronic ester precursor. [^{18}F]AZ10419096 was obtained by treating the boronic ester with [^{18}F] fluoride ion in the presence of $\text{Cu}(\text{OTf})_2(\text{py})_4$ in DMF for 10 min at 120 °C. The radioligand was isolated with semi-preparative HPLC and formulated in saline. In a PET experiment, [^{18}F]AZ10419096 (316 MBq; 243 GBqμmol⁻¹) was intravenously administered to cynomolgus monkey (5.5 kg) and brain distribution of radioactivity was followed for 123 min. Venous blood was sampled at different times during the PET

scanning for radio-HPLC analysis of plasma radiometabolites. Binding potential (BP_{ND}) of [^{18}F]AZ10419096 was evaluated by a simplified reference tissue model (SRTM) using the cerebellum as a reference region. **Results:** [^{18}F]AZ10419096 was obtained for intravenous administration in useful activity and molar activity. In the PET experiment, brain radioactivity uptake rapidly peaked at 2.1 SUV at 10 minutes and showed clear wash-out down to 0.6 SUV at 120 minutes. BP_{ND} was high in occipital cortex (1.4) and globus pallidus (1.5), known as 5-HT_{1B} receptor rich regions. At 60 min after radioligand injection, 50% of radioactivity in plasma represented unchanged radioligand. 60% of the radioligand was protein bound. **Conclusion:** [^{18}F]AZ10419096 is the first ^{18}F -labeled PET radioligand to image 5-HT_{1B}R *in vivo* in monkey brain and shows potential to be the first useful ^{18}F -labeled PET radioligand for studying human 5-HT_{1B}R.

OP-698

Automated Synthesis Of 5- ^{18}F fluoro-tryptophan Via Deoxyfluorination Of A Phenol-derived Ru-coordinated Complex

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Aim: The development of innovative and improved fluorination techniques targeting electronrich centers in small molecules has always been a very active field in PET radiochemistry. This is due to the inherent importance of fluorine, either in medicinal chemistry (e.g. enhance biological activity, improve metabolic stability or alter physicochemical properties) and in PET imaging (through the β^+ emitter radioisotope ^{18}F), together with the generally unsatisfactory results obtained when resorting to electrophilic [^{18}F]fluorination strategies (i.e. lack of regioselectivity, limited molar activity and reduced yields). In the last decade, several late-stage [^{18}F]fluorination approaches enabled the access to a high range of [^{18}F]fluorobenzene-derivative radiotracers. However, not all of them have the ability to be practically translated in radiochemistry modules. Here, is reported the automation of a recent late-stage [^{18}F]fluorination strategy: the deoxy[^{18}F]fluorination of phenols via Ru π -complexes⁽¹⁾. As proof of concept, the synthesis of 5- ^{18}F fluoro-tryptophan, a radiotracer with potential for mapping indoleamine (IDO1) and tryptophan 2,3-dioxygenases (TDO2), two biomarkers which expression is increased in the microenvironment of some tumors⁽²⁾, was automatized using one of the latest commercial research synthesis modules. **Methods:** Firstly, it was performed a non-automated optimization for the deoxy[^{18}F]fluorination step of a Boc- and *tert*-butyl protected 5-hydroxytryptophan whose benzene ring was previously activated by π coordination to a ruthenium complex. Subsequent hydrolysis was performed to yield the amino acid moiety. These procedures were translated for automation taking into account the particularities and constraints (i.e. limitation of volumes, fluid trajectories, arrangements...) of the selected module (Synthra RNplus). The optimal findings were then

programmed to achieve 5- ^{18}F fluoro-tryptophan in a fully automated way. The purified product was obtained by semi-preparative radioHPLC and reformulated into a physiological saline solution. **Results:** To date, 5- ^{18}F fluoro-tryptophan has been repetitively achieved both manually ($n=12$) and automated ($n=4$), which reinforces the robustness of this deoxy[^{18}F]fluorination method. After a total time of 90 min., a stable final product with radiochemical purity $\geq 95\%$ was attained in moderate yields of up to 10%, being adequate for pre-clinical studies. Furthermore, the obtained data forecast an interesting margin of progression and improvement for application to the labeling of other compounds containing electronrich structures non-compatible with aromatic nucleophilic fluorination. **Conclusion:** Here we demonstrate the suitability of this late-stage deoxy[^{18}F]fluorination strategy to be automated in order to achieve the radiolabeling of phenol-derived Ru-coordinated complexes to routinely produce [^{18}F]fluorobenzene-containing tracers such as 5- ^{18}F fluoro-tryptophan. **References:** (1)Beyzavi M.H. *et al.*, *ACS Cent.Sci.*, 2017, 3(9):944–948; (2)Tang T. *et al.*, *Nucl.Med.Biol.*, 2017, 51:10–17.

OP-699

3D Printed Automated Synthesizer for Radiometal Pharmaceutical Preparations. Routine Production of ^{68}Ga -PSMA-11

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Aim: To design, build and test an Automated Synthesis Unit (ASU) manufactured via 3D printing and engineered to perform automated radiometal chelations with the push of a button. The design should include a purification/reformulation step and produce a sterile, pyrogen free solution suitable for injection. To use the clinical production of ^{68}Ga -PSMA-11 as an example. **Materials and Methods:** All designs were drawn using Autodesk® AutoCAD® 2015. While test prints were done using an XYZ DaVinci Duo 2.0 dual nozzle printer with either Polylactic Acid (PLA) and/or Acrylonitrile Butadiene Styrene (ABS) filaments, the final prints were performed using a Stratasys Printer with ABS. Rotating valves and syringe drivers were 3D printed in nylon at Shapeways.com. High torque motors (180 ° rotation) and linear actuators (50 mm drive) were used for valve turning and syringe loading/dispensing operations. The ASU is controlled by a 24 channel USB servo miniMaestro® controller which is capable of sequenced automation. The temperature was controlled by a CN-142 thermostat with an attached K-type thermocouple. A syringe pump was included to the design to automate ^{68}Ge / ^{68}Ga generator elution. A modified ITG peptide labeling cassette was used for testing. The final reaction mixture is purified using a C-18 Sep-Pak Plus Lite, and eluted in an 8% ethanol solution in saline suitable for injection (3.6 ml total volume). **Results:** The ASU was manufactured for less than 1500 USD. All materials performed as expected and a full sequence was programmed into the miniMaestro® controller totaling 15 minutes for a complete synthesis, including generator elution. Several tests were run “cold” to ensure the proper functioning of the ASU. Three consecutive ^{68}Ga -PSMA-11 batches were produced as sterile, pyro-

gen free solutions ready for injection with a final average synthesis yield of 90.7 ± 0.6 % and $>99\%$ radiochemical purity. Only 0.5 ± 0.2 % was found in the waste vial (with $\geq 99\%$ of the eluted ^{68}Ge), 6.6 ± 0.5 % was not eluted from the C-18 and 2.2 ± 0.2 % was retained in the $0.22 \mu\text{m}$ filter. **Conclusions:** A 3D printed ASU for radiometal pharmaceutical preparations was designed, manufactured and tested in the production of ^{68}Ga -PSMA-11. The ASU has shown to be robust and reliable for routine clinical use. No leakage of liquids or radioactivity was found. The 3D printed ASU is a practical, lower cost alternative to commercially available ASUs. 3D printed ASUs may allow for inexpensive purpose built units to accommodate a wide variety of radio synthetic schemes.

1706 Wednesday, October 17, 2018, 10:00 - 11:30, Hall Y

Do.MoRe: Miscellaneous Topics in Dosimetry

OP-700

A Pediatric Library Of Phantoms For Renal Imaging Incorporating Waist Circumference, Renal Volume, And Renal Depth

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Objective: Presently, when administering radiopharmaceuticals to pediatric patients for diagnostic nuclear medicine studies, the recommended minimum administered activity is typically assigned as a function of patient body mass. These guidelines are obtained through expert consensus to yield diagnostic quality images. Previous work has shown that body morphometry is an important factor when minimizing injected activity while maintaining diagnostic quality images. The present study focuses on developing a library of pediatric phantoms accounting for variability in patient waist size, renal volume, and renal depth. The objective of this study is two-fold. First, to develop a robust methodology to generate a library of computational phantoms accounting for waist size, renal depth and volume. Secondly, to assess the dosimetric differences using current guidelines versus new guidelines tailored to patient morphometry for $^{99\text{m}}\text{Tc}$ -DMSA renal studies. **Methods:** To assess dependence of waist circumference the UF/NCI anthropomorphic 1-year, 5-year, 10-year, and 15-year reference male and female phantoms were scaled between their 5th and 95th percentile waist circumferences at each age according to the CDC NHANES databases. To accurately model renal depth, cohort of 175 patient CT image sets were sampled between the ages of 1 and 15 years in which renal depth was measured as well as waist circumference. Using this data, a linear model was developed to estimate kidney depth as a function of waist circumference. To accurately model kidney size, previous work was used giving renal volume and

length as a function of body mass. Monte Carlo radiation transport was performed on the library of computational phantoms using PHITS and biokinetic models for $^{99\text{m}}\text{Tc}$ -DMSA; allowing organ doses to be calculated given the injected activity. **Results:** A library of pediatric male and female phantoms was created which represents a current population waist circumference, renal depth, and renal volume for pediatric patients of various ages. Organ level dosimetry was assessed and effective doses were computed using current guidelines as well as new guidelines optimized for local anatomy. Preliminary results show potential dose savings using injected activity informed by patient anatomy over strictly using patient body mass. **Conclusions:** This study presents a methodology for creating computational phantoms capturing patient variability about the area of diagnostic interest. Additionally, the phantoms in this study can be used to create guidelines for pediatric nuclear medicine studies optimized for the expected anatomy accounting for both radiation dose and image quality.

OP-701

Dosimetry-Based Tandem High-Dose ^{131}I -MIBG Therapy For Paediatric Patients With High Risk Neuroblastoma

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Aim: Tandem high-dose therapy based on two administrations of ^{131}I -meta-iodobenzylguanidine (^{131}I -mIBG) represents the treatment of choice for children with neuroblastoma (NB) for increasing palliation and progression-free survival, especially in patients who have undergone previous chemotherapy treatments. In recent years, as also established by the European Union regulation, radiation dosimetry has become a basic requirement for establishing therapies on a patient-specific basis especially in paediatrics. The present study aims to report the results of patient's dosimetry in order to investigate absorbed doses for whole-body (WB), red-marrow (RM) and tumours in children affected by NB. **Materials and Methods:** Eight patients with relapsed/refractory NB treated with ^{131}I -mIBG between 2016 and 2017 were included, giving in total 14 treatments as two patients were treated once. Absorbed doses to WB and RM were calculated according to MIRD and EANM guidelines, collecting WB data and blood samples at 0.5-h, 6-h, 24-h, 30-h, 48-h, 72-h and 144-h after the administration. The WB absorbed dose resulting from the first administration was used to determine the second activity to be administered to reach a total WB absorbed dose of 4 Gy. According to MIRD approach, tumour absorbed doses were calculated individually for both therapeutic administrations collecting five static images; tumour volumes were evaluated by means of SPECT, CT and MRI images. **Results:** A dosimetry-based high-dose ^{131}I -mIBG therapy of children with

NB has been successfully established and routinely performed in our institution. The injected activity by administration was from 6610 to 11100 MBq (median: 8963 MBq), resulting in WB doses ranging from 1.04 to 2.44 Gy (median: 1.57 Gy) and in RM doses from 0.72 to 2.16 Gy (median: 1.13 Gy). The WB and RM absorbed doses per unit activity lie between $0.11 \div 0.36$ Gy/GBq and $0.07 \div 0.32$ Gy/GBq respectively, varying to a factor of 3. The cumulated activity in the blood contributes from approximately 10 to 20% to the RM absorbed dose. The tumour absorbed doses show a high variability (between 10 and 80 Gy) mostly depending on administered activities, tumour's uptakes and bio-kinetics. **Conclusion:** For treatment of neuroblastoma, the WB and RM absorbed doses could be prescribed individually in order to perform both palliation for avoiding prolonged patients' hematologic toxicity and myeloablation in curative setting. This is especially true in paediatrics where a highly heterogeneous and heavily pre-treated patient population has to be treated; dosimetry is suggested with the intent of administer as high as possible treatment activities.

OP-702

Dosimetric evidences of 131I-MIBG treatment in High Risk Neuroblastoma in VERITAS protocol

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Neuroblastoma is an aggressive pediatric tumour that can be treated by high doses of 131I-MIBG. After treatment, patients are hospitalised in shielded rooms until dose rate decreases under a stated level. Recently, a new protocol for HR-NBL (High Risk - Neuroblastoma) was proposed in poor responders induction chemotherapy patients. In such protocol (named VERITAS) two 131I-MIBG administrations are planned in a lapse of time of two weeks (TANDEM) in order to reach a final absorbed dose of 4Gy total body. Activity to be administered is based on patient weight in first administration, dosimetric evaluation is performed on MIRDose model by means of dose rate measurements in preset geometry and, from calculated dose, second administration activity is then calculated. At our hospital, three patients were treated following VERITAS protocol and according to TANDEM dosimetric rules. An activity of 444MBq/kg (A1) was administered in first treatment and absorbed dose (D1) was calculated according to MIRDose scheme: $D = \bar{A} * S$ (Gy), where $S = 1.9e-06 * 70 * Wt - 0.918$ (Gy/MBq*h) and Wt is patient weight (kg). $\bar{A}$ was calculated by means of exposure rate at 1m from patient measured by ionization chamber Victoreen 450P. First measurement was done at the end of radiopharmaceutical administration before voiding bladder; following measurements were done in AP and PA position in order to average possible fluctuations for at least 4 times per day, taking into account time of each acquisition. A plot of averaged dose rate as a function of time was done and a curve was outlined which area is $\bar{A}$. D1 was then calculated as stated above and, considering that 4 Gy is desired total amount of dose to be delivered in whole treatment, the second 131I-MIBG activity to be administered, A2, necessary for achieving D2, was simply calculated by: $A2 = D2 / D1 * A1$, being $D2 = 4Gy - D1$. For all patients, first administration

of 131I-MIBG involved an absorbed dose greater than 2Gy (ranging from 10% to 15%). On the other hand, dosimetry in the first phase (D1) proved to be an excellent predictive tool since absorbed dose (D2) was always as expected in such a way that, at the end of treatment, total absorbed dose was around 4Gy (7%). No organ dosimetry was however performed even if, in order to assess red marrow toxicity, blood sample could be collected in future treatments to calculate, from gamma spectrometry, cumulated activity and related absorbed dose.

OP-703

LuISA - Lu-177-PSMA intelligent szintigraphy application

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Aim: After application of a radiopharmaceutical for radionuclide therapy, it is essential to determine the absorbed dose. Particularly with regard to repeated therapies, reliable and standardize dosimetry is mandatory to achieve optimal tumour control with minimal side effects. The lesion dose and the dose in organs-at-risk are usually calculated 'manually'. The aim was to create a semi-automatic software-tool for use in clinical routine for standardized dose-calculation across series of radionuclide therapies. **Methods:** We developed a GUI-based software-tool in Matlab (MathWorks) which allows semi-automated dose assessment in serial whole-body-scans with minimal user interaction. The user selects one scan of a series and draws a ROI on the structure of interest. The software marks this scan as reference template and automatically registers the remaining scans to this reference. Then, the ROI is transferred to the remaining images. The counts measured in this ROI across several time-points are automatically converted into an activity by a patient-specific calibration factor. A fitting curve to the data is determined with a fit-function selected by the user. The activity is plotted against time as time-activity-curve. Time-integral and residence-time are calculated and from that - if mass is known - the achieved dose. It is also possible to create a report and store the data in a SQL-database. To evaluate the performance of this tool, the results were validated with a series of Tc-99m filled NEMA-phantom-scans and serial whole-body-scans in patients treated with Lu-177-PSMA. The quality of the image registration was validated by phantom measurements. The weighted-centroids of the ROI's permit a quantitative analysis of the registration quality. To verify translation and rotation by the registration-algorithm, the phantom was placed in different positions. **Results:** The weighted-centroids deviated by a few pixels when adjusting the registration parameters. The quality of registration could be shown by comparing the physical half-life of Tc-99m (6.01h) with the calculated half-life from time-activity-curves of all active NEMA-spheres. Although the phantom was rotated by 45° in some scans the half-life was calculated up to 6.0h (+/-0.2h). Residence-time obtained from patient measurements accorded well (~5% deviation) to results of Lu-177-PSMA therapies evaluated manually in the past. **Conclusion:** We could show that co-registration, transferring a ROI on each image of a series and calculating a well-matching fit-function for the time-activity-curve lead to convincing results. Due to this rapid semi-au-

tomatic dose evaluation, dosimetry in clinical routine can be performed individually and within a reasonable time for each patient.

OP-704

Dosimetric analysis reveals favorable potential for the short-ranged particle emitter ^{161}Tb for radionuclide therapy of metastatic prostate cancer

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Introduction: Treatment of metastatic prostate cancer with radiolabeled prostate specific membrane antigen (PSMA)-targeting ligands have shown encouraging results with visual confirmation of treatment response and PSA decrease. Despite these results metastatic regrowth occurs after treatment. The aim of this study was to analyze the absorbed doses required to achieve complete remission for different radionuclides and varying metastatic scenarios. In addition to the analysis of the clinically used radionuclides ^{90}Y , ^{131}I , ^{177}Lu , and ^{225}Ac , the low-energy electron emitter ^{161}Tb was analyzed due to its proposed potential for treatment of small tumors. **Method:** The required absorbed tumor dose (D_{req}) for obtaining a metastatic cure probability (MCP) equal to 0.9 was adopted by Monte Carlo simulation of the metastatic dissemination process. In the model tumors were assumed to have a Gompertzian growth, were able to disseminate metastases and to disseminate and grow into each other. The metastatic detection limit was set to a diameter of 7 mm. Tumor absorbed fractions were pre-calculated with the Monte Carlo code PENELOPE, or the in-house developed code for alpha emission. To evaluate treatment response, the biological effective dose was calculated with a α/β -value of 1.5 Gy and repair half-life of 1.9 h. α was derived from recently published data on external irradiation of localized primary tumors. For alpha particles the relative biological efficacy was set to 5. The activity concentration in a simulated metastatic distribution was iteratively increased until MCP=0.9 was reached. **Results:** Low metastatic formation rates generated large detectable metastasis, as is the case with oligometastases, and increasing formation rates resulted in a metastatic distribution seen in superscan patients. Even if the total metastatic burden was 4-6 times higher in the oligometastatic scenario, the abundance of small tumors in the superscan scenario caused D_{req} to increase 19-38 % in situations with equal number of detectable metastases. The D_{req} for ^{90}Y and ^{131}I was considered to be too high (600-2200 Gy) to be considered an alternative for treatment of metastatic disease. For ^{177}Lu the D_{req} was between 370-590 Gy, which might be an option when the tumor uptake is high. Considerably lower D_{req} was obtained for ^{225}Ac and ^{161}Tb , 200-300 Gy and 130-200 Gy, respectively. **Conclusion:** The simulation demonstrated that superscan patients are more challenging to cure than patients with oligometastases. Based on this dosimetric analysis of MCP, the short ranged electrons emitted by ^{161}Tb could be a valuable contribution to targeted radionuclide therapy using PSMA ligands.

OP-705

Antecedent clinical imaging optimisation and activity measurements for theragnostic terbium isotopes

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Aim: Theragnostic isotope combinations utilising diagnostic imaging for predicting molecular radiotherapy absorbed doses offer the possibility of individualised treatment optimisation[1]. Constrained access to these isotopes prior to clinical adoption often means clinical imaging protocols for potential new isotopes are poorly optimised. Additionally, underlying activity standards and radionuclide calibrator factors are often unavailable, leading to a lack of harmonisation in clinical trial data - ultimately reducing the predicative power of such trials. CERN-MEDICIS is a dedicated facility for medical applications which provides exotic radionuclides to support pre-clinical investigations. This gives a unique opportunity to establish optimised imaging protocols and primary radioactivity measurements at an earlier stage of development, ensuring maximum diagnostic potential is available for future clinical-trials and establishing the traceability needed to meet legislative requirements. A quartet of terbium (^{65}Tb) isotopes has recently been identified with the potential to provide unique theragnostic treatment strategies combining alpha- and beta- therapy with SPECT and PET imaging[2]. In this work we report on the first clinical phantom imaging studies of ^{152}Tb , ^{155}Tb , ^{161}Tb and accompanying activity standards and nuclear data measurements underpinning future clinical use of these isotopes. **Materials and Methods:** Samples of ^{152}Tb and ^{155}Tb were collected at CERN-MEDICIS and ^{161}Tb from a high-flux nuclear reactor at Institut-Laue-Langevin. The samples were imaged using GE-Discovery-670 and Mediso-AnyScan-SCP systems. Data was acquired in 'list-mode' enabling retrospective projected SPECT images to be produced. Experimental SPECT/CT data was combined with validated Monte Carlo simulations to optimise collimators and energy windows. New primary activity standardisations were performed using liquid scintillation techniques and calibration factors for the NPL secondary standard ionisation chamber were determined. Gamma spectrometry measurements of decay schemes and half-lives were performed. **Results and Conclusions:** The first isotope-specific photopeak and scatter imaging energy windows for ^{155}Tb (86.5, 105.3, 180.1, 262.3, 163.3 keV) and ^{161}Tb (25.7, 48.9, 74.6 keV) will be presented. The effect of applying these energy windows, calculated using a minimization method applied to data from a full MC simulated SPECT acquisition, to clinical imaging systems

will be discussed. New primary activity measurements and calibration factors for the NPL secondary standard ionisation chamber are presented. The potential for quantitative imaging of the terbium isotope quartet provided by this unique combination of results will be discussed. The impact of these new measurements on future applications of terbium in a clinical setting will be considered. [1]U. Eberlein et al., JNM 58:97S-103S(2017) [2]C. Müller et al, JNM 53:1951-1959(2012)

1709 Wednesday, October 17, 2018, 10:00 - 11:30, Hall 6
Neuroimaging: Dementia

OP-706

Assessment Of 18F-florbetaben Amyloid PET Imaging In Patients With Suspected Alzheimer's Disease And Isolated Increases Of Tau-proteins In The CSF

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Cerebrospinal fluid (CSF) analysis of patients with suspected Alzheimer's disease (AD) may lead to ambiguous results with especially increases of Tau proteins but normal amyloid- β concentration. The aim of this study was to assess, in a natural setting, the rates with which an excess in amyloid brain uptake was documented by ¹⁸F-florbetaben PET in such patients with isolated increases of Tau proteins in the CSF, and the further impact on medical management. **Methods:** This prospective study (NCT02556502) included 37 patients (73 $\pm$ 9 years, 19 women) with suspected AD but with isolated increases of Tau and/or phospho-Tau proteins in the CSF (normal A β 42 concentration and A β 42/A β 40 ratio). These patients were referred to a ¹⁸F-florbetaben PET which clinical impact was assessed according to the subsequent changes: 1) in a confidence score for AD diagnosis graded as low, intermediate or high by an expert group and 2) in the medical management with cholinesterase inhibitor drugs. **Results:** Ten among the 37 PET examinations (27%) were positive for AD. The additional knowledge of PET data was associated: 1) with high rate of changes of the confidence score for AD (46%) with a marked decrease in the proportion of patients setting at an indeterminate level (43% to 3%, $p < 0.001$), and 2) with therapeutic changes in 12 patients (32%), a cholinesterase inhibitors treatment being introduced in 9 among the 10 positive PET patients and stopped in 3 among the 27 negative PET patients. **Conclusion:** In patients with suspected AD and abnormal CSF levels of Tau-proteins but not of amyloid- β , excess in amyloid brain uptake is however document by ¹⁸F-florbetaben PET in more than a quarter of cases, an information that leads to significant changes in medical management.

OP-707

Agreement between T and N PET staging in patients with suspected Alzheimer's Disease: a FDG/Flortaucipir PET study

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Aim Temporo-parietal cortex hypometabolism is a well established PET marker of neurodegeneration (N) with a high diagnostic accuracy and prognostic value in patients with suspected Alzheimer's Disease. In recent years, PET radiotracers specific for tau deposits have been tested, showing an in vivo distribution consistent with the topographical distribution of tau pathology (T) expected in AD. Individuals with a clinical impairment usually have a Braak stage 3 or higher. Aim of this study is to assess the concordance of the two markers in a clinical population investigated for suspected AD, to estimate the potential clinical added value of tau markers in classifying patients. **Methods:** 37 patients were included, 22 of whom were amyloid positive. 3 individuals were cognitively normal at neuropsychological evaluation, 24 with mild cognitive impairment, 10 with a major cognitive disorder. The N status (N+ vs N-) was estimated on the basis of FDG PET images, spatially normalized and normalized to global intensity, compared with a reference normal database and subsequently visually interpreted as normal (N-), AD-like (N+) or pathological for a non-AD degenerative process (7 individuals, excluded from subsequent analyses). T staging was based on Flortaucipir cortical distribution 75 to 105 minutes post administration, scored visually in Braak stages, from 0 to 6, and considering T+ individuals showing neocortical tracer deposition (Braak stage 3 or higher). The presence of an association between the two indices was tested using a chi square and the level of agreement was estimated calculating the kappa score. **Results:** There was a significant association between a tau PET distribution indicating a Braak stage 3 or higher and the presence of an FDG PET AD-like pattern ($p = 0.047$), however with a poor agreement between the two measures (kappa score = 0.37). **Conclusion:** The presence of hypometabolism and the presence of neocortical tau deposits are significantly associated. The limited agreement between the two measures suggests that T and N markers provide complementary information for patient staging across the AD spectrum. Funding Swiss National Science Foundation (SNSF) grant number 320030_169876; Horizon 2020 (667375 : CoSTREAM) and Segre Foundation.

OP-708

Predicting Cognitive Decline Due To Alzheimer Disease in MCI Subjects by FDG-PET: A Prospective Multicenter Study

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Purpose: We aim to explore the utility of FDG-PET for predicting the development of Alzheimer's disease (AD) dementia in a large population of patients with amnesic mild cognitive impairment (a-MCI). **S- Methods:** We studied 188 subjects over 65 years, 44 cognitively normal (CN) and 144 with a-MCI (Petersen's

criteria, 2004), recruited at 19 centers (Spain, Italy, Sweden and France) in longitudinal trial (AB255). All were clinically assessed (neuropsychological evaluation and neurological examination) at baseline and during the follow up at 12 and 24 months. Structural-MRI, FDG-PET, and APOE genotyping were performed in all subjects at baseline. An amyloid-PET study (11C-PIB) was additionally carried out in a subset of 59 subjects. An individual voxel-based analysis (Arbizu, et al. Eur J Nucl Med Mol Imaging, 2013) was used for FDG-PET evaluation. The parameters AD-index (similarity between each individual z-score map and the AD pattern); MCI-index (similarity between each individual z-score map and the posterior cingulate map); and AD conversion score (computation of age, gender, MIC-index, MMSE-score and APOE4 genotype), were explored according to the clinical diagnosis at baseline and at 24 months (stable-CN, stable-MCI, converted-MCI to AD). Besides, we analyzed the correlation between these parameters and PIB-PET A β -positivity (SUVR $\geq$ 1.4). Descriptive values (Mean, SD, Median, IQR) are reported, and differences were explored using the Mann-Whitney-U test. **Results:** At baseline, FDG-PET risk parameters were found to be significantly higher in a-MCI subjects compared to CN: AD-index 43,36 (61,35) vs. 0,25 (1,85), $p<0.001$; MCI-Index 2,15 (13,3) vs. 0,0 (0,08), $p<0.001$; AD-Conv-Score 0.3202 (0,47) vs. 0.0876 (0,04), $p<0.001$. At 24 months, the differences were: AD-index 13,2 (31) stable-MCI vs 26 (89,95) converted-MCI ($p<0.001$), and vs. 0,3 (1,90) stable-CN ($p<0.001$); MCI-Index 0,9 (10,8) stable-MCI vs. 4,5 (30,85) converted-MCI ($p<0.006$), and vs. 0 (0,1) Stable-CN ($p<0.001$, respectively); AD-Conv-Score 0,2683 (0,36) stable-MCI vs. 0,4087 (0,63) converted-MCI ($p<0.006$), and vs. 0,0893 (0,04) stable-CN ($p<0.001$). The subgroup of 11C-PIB positive subjects, showed significantly higher values respect to 11C-PIB negative: AD-Index_A β + (45.08 $\pm$ 58.39) vs. A β - (10.5 $\pm$ 33.28, $p=0.002$), MCI-index_A β + (2.12 $\pm$ 8.68) vs. A β - (8.99 $\pm$ 12.58, $p=0.001$), and AD-Conv-Score_A β + (0.3840 $\pm$ 0.259) vs. A β - (0.1331 $\pm$ 0.162, $p=0.001$). **Conclusions:** FDG-PET parameters obtained at the baseline in a-MCI subjects can be useful to identify in an appropriate way those subjects at higher risk of progression to AD dementia in 24 months. Subjects with higher risk of conversion according to FDG-PET parameters, exhibit a higher cortical A β burden. Therefore, further analysis in an individual bases to establish the usefulness of FDG-PET in the clinical setting are warranted.

OP-709

The value of combining molecular and structural imaging biomarkers with psychometric data in a system for predicting neurological decline validated by a 3 year outcomes study

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Objectives: A computer-based application for providing decision support in dementia, including predictions of cognitive decline based on imaging and other biomarkers, was developed by an EU framework-7 funded “PredictND” consortium. Here, this application was used with baseline PET and MRI imaging

and psychometric scores to predict the cognitive trajectory of 222 amnesic mild cognitive impairment (aMCI) subjects. The prognostic indication was tested against known 3-year outcomes for these subjects. **Methods:** In this study, the system was trained with data from 244 cognitively normal subjects and 241 probable AD (pAD) subjects. The imaging data consisted of structural information derived from T1 3D MRIs and composite standard uptake value ratios (SUVRs) derived from [¹⁸F]flutemetamol PET amyloid images, together with psychometric scores. The validation dataset comprised the same imaging/psychometric metrics [FG(H1) [BC(H2) [BC(H3) derived from 222 subjects at baseline obtained from GE Healthcare’s GE067-005 study. The subjects in this study were cognitively assessed by a clinical adjudication committee every 6 months to test for conversion to pAD. The baseline image data were stratified in a separate post-hoc analysis into four groups where their amyloid status (A-, A+) and their neuronal injury status (N-, N+) determined by threshold of hippocampal volumes. The system computed a Disease State Index (DSI) for each subject and these were compared against a Kaplan-Meier survival (non-conversion to AD) analysis which computed the survival fractions (SF) for the four (A,N) combinations. **Results:** Low computed DSI values predicted a high survival (non conversion to dementia) fraction (A-,N- group) and high values predicted a low survival fraction (A+,N+ group). The DSI’s were also concordant with the (A+,N-) and (A-,N+) outcomes: (A- N-) 83 subjects with a median DSI of 0.16 (DSI-1 = 0.84) and a Kaplan-Meier Survival Fraction of 0.86 (A- N+) 42 subjects with median DSI of 0.43 (DSI-1 = 0.57) and a Kaplan-Meier Survival Fraction of 0.53 (A+ N-) 40 subjects with median DSI of 0.5 (DSI-1 = 0.5) and a Kaplan-Meier Survival Fraction of 0.46 (A+ N+) 40 subjects with median DSI of 0.91 (DSI-1 = 0.09) and a Kaplan-Meier Survival Fraction of 0.12. **Conclusions:** In this study, the use of the PredictND tool, which incorporates T1 MRI results, SUVRs from amyloid PET imaging, and psychometric data, provided DSI values that accurately predicted clinical status 3 years later. This study demonstrates that the predictive system provides accurate and useful prognostic information for patients at risk of AD dementia.

OP-710

Neuronal Injury Biomarkers for Assessment of Cognitive Reserve in Alzheimer’s Disease

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Introduction: The model of cognitive reserve has been extensively investigated in patients with Alzheimer's Disease (AD). Many factors could be identified as being influencing or predictive for a higher cognitive reserve. Neuronal injury correlates with cognitive decline in AD with [^{18}F]-fluorodesoxyglucose positron-emission-tomography (FDG-PET), structural MRI and total tau in cerebrospinal fluid ($\text{CSF}_{\text{t-tau}}$) as the most important biomarkers of neuronal injury according to the A/T/N-classification. The aim of this study was to compare neuronal injury biomarkers with the cognitive performance and further cognitive development to evaluate their potential to predict the individual cognitive reserve. **Subjects & Methods:** In 110 mild cognitive impaired and demented subjects (age 71 ± 8 years) with a final diagnosis of AD dementia were assessed at baseline by mini-mental-state-examination (MMSE), FDG-PET, MRI and $\text{CSF}_{\text{t-tau}}$. Using partial correlation, we tested first for each neuronal injury marker the correlation with MMSE, controlled for age, gender and leukoencephalopathy. Next using multiple regression analysis, we calculated the expected MMSE score based on neuronal injury markers and covariates (MMSE_{NI}). The residuals of the partial correlation for each biomarker and the difference between MMSE_{NI} and MMSE_{CU} were correlated with the cognitive outcome of patients at clinical follow-up (27 ± 13 months). **Results:** FDG-PET correlated highly with MMSE_{CU} ($R = -0.49$, $p < 0.01$), whereas hippocampal atrophy in MRI ($R = -0.15$, $p = 0.14$) and $\text{CSF}_{\text{t-tau}}$ ($R = -0.12$, $p = 0.22$) showed only weak correlations. High neuronal injury relative to cognitive performance was associated with more pronounced cognitive deterioration at follow-up for the residuals of FDG-PET ($R = -0.40$, $p = 0.005$) and the combined model ($R = -0.43$, $p = 0.04$). **Conclusions:** The residuals in the correlation of neuronal injury in FDG-PET and cognitive performance represent the individual cognitive reserve in patients with AD and may allow a prediction of an individual's clinical course. Thus, the individual cognitive reserve should be considered as a covariate in therapeutic trials.

OP-711

Characterization of disease-specific covariance patterns of neurodegeneration in FTLN-variants

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Aim: Frontotemporal lobar degeneration (FTLD) is the most common form of dementia after Alzheimer's disease and covers a whole spectrum of clinically separable diagnoses, including

the behavioral variant (bvFTD) as well as the non-fluent (nfvPPA), semantic (svPPA) and logopenic (lvPPA) variants of primary progressive aphasia. Our primary goal here was to characterize disease specific metabolic patterns usable in an automated, data-driven diagnostic approach to help in the early classification to a specific clinical diagnosis. **Materials and Methods:** FDG PET was performed in a total of 102 patients with FTLN at 10 different German centers (bvFTD: $n=55$, nfvPPA: $n = 19$, lvPPA: $n = 15$ and svPPA: $n= 13$). Clinical diagnosis was confirmed by clinical follow-up of at least one year after the PET scan. The data was supplemented by a set of 24 healthy controls of similar age and gender from the ADNI-database. All files were spatially normalized and voxel-wise T-tests were performed to compare FTLN variants against healthy controls. Secondly, a group-wise scaled subprofile modelling/principal component analysis (SSM/PCA; according to Eidelberg et al. Trends Neurosci 2009) was performed to identify covariance patterns with respect to a sample of healthy controls. **Results:** Areas of strongest hypometabolism in the voxel-wise T-test were bilateral frontal cortex for bvFTD, left temporo-parietal cortex and precuneus for lvPPA, temporopolar cortex (left >> right) for svPPA and left centro-mesial and perisylvian frontolateral cortex for nfvPPA. Similar regions were also identified as main components explaining a relevant amount of variance in the group-wise SSM/PCA approach. **Conclusion:** Typical patterns of neurodegeneration were characterized in a cohort of 109 patients with clinically confirmed FTLN. Group-wise combinations of the components identified in the SSM/PCA method seem to be suitable to characterize disease specific patterns for bvFTD, lvPPA, nfvPPA and svPPA in an automated, data-driven approach. Once validated, these patterns can be used to score the respective expression strength in individual patients with respect to healthy controls and thereby assist in differential diagnosis of suspected FTLN.

OP-712

Determination of FTD Candidates in an MCI-SNAP Cohort by PET Amyloid and MRI Structural Analysis

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Introduction: GE Healthcare conducted a 3-year outcome study in which 232 patients with amnesic Mild Cognitive Impairment (aMCI) underwent baseline amyloid PET imaging with [^{18}F]flutemetamol to determine time to conversion to dementia in relation to baseline amyloid status. Conversion was determined by an independent clinical adjudication committee (CAC) which reviewed the results of 6-monthly neuropsychiatric testing for up to 36 months. While amyloid positivity was a significant and independent predictor of conversion, a fraction (23%) of the amyloid-negative subjects (suspected non-Alzheimer's pathology - SNAP) also converted in the 3-year study window. In a post hoc analysis, we determined the number of these amyloid negative subjects who were candidates for Frontotemporal Dementia (FTD) based on their right-hemisphere temporal pole to occipital lobe cortical thickness. **Methods:** In this analysis, the subjects' [^{18}F]flutemetamol PET Standard Uptake

Value Ratio (SUV_Rcr) was quantified using Cortex ID™ with a composite cortical region. The subjects were divided into amyloid positive and negative by the mean +2SD of age-equivalent healthy controls. The MRI images were analysed using Freesurfer v6.0 to extract the ratio between the temporal pole cortical thickness (T) and the lateral occipital region cortical thickness (O) with regions defined by the Desikan/Killiany atlas. A threshold of healthy T/O ratio was obtained from the mean-2SD and used to classify subjects with decreased temporal pole cortical thickness for the commonly affected right hemisphere. **Results:** Of 232 subjects in the longitudinal aMCI study, 222 had MRIs suitable for analysis. Of these, 101 were amyloid positive and 121 were negative. The amyloid negative subjects did not have apparent AD pathology in imaging and this group were analysed by cortical thickness analysis in Freesurfer. There were 32 subjects who had a T/O ratio below the established threshold. Of these potential FTD candidates, 12 converted to dementia within three years. **Discussion:** Non-AD pathologies including cerebrovascular disease, α -synucleinopathy, argyrophilic grain disease, TDP-43 proteinopathy and primary age-related tauopathies are common with advancing age. However, only FTD has preferential decreased temporal pole cortical thickness. Therefore, it is possible that the 32 subjects classified as below T/O cortical thickness threshold were subjects either with probable FTD (n= 12) or aMCI with positive FTD imaging biomarker (n=20).

1710 Wednesday, October 17, 2018, 10:00 – 11:30, Hall 28

Bone & Joint - Featured Session: Bone & Joint Hybrid Imaging

OP-713

Recent Publications in Bone SPECT/CT - An Overview

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OP-714

Diagnostic Validity of Combined Triphase Bone Scintigraphy and SPECT/CT in the Diagnosis of Non-Traumatic Osteonecrosis of Knee

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Purpose: To assess the diagnostic validity of Triphase bone scintigraphy and SPECT/CT (CBS) in the diagnosis of non-traumatic osteonecrosis of the knee in comparison with MRI. **Subjects and Methods:** Consecutive patients who fulfilled all the following inclusion criteria were prospectively included in the study: 1) connective tissue disorders with or without the history of steroid or cytotoxic drug therapy; 2) clinical suspicion of osteonecrosis; 3) no prior history of trauma; and 4) normal radiograph of the knees. All patients underwent triphase bone scintigraphy on Siemens Symbia T6 with 25 mCi of Tc-99m labeled Methylene DiPhosphonate (MDP). The protocol included flow

and tissue phase images of bilateral knees, and whole body images during tissue and delayed phases. Regional SPECT/CT was acquired in delayed phase. The scans were reported by a trained nuclear medicine physician, who was blinded to history and MRI findings, as positive and negative for osteonecrosis. MRI of the knee region was done with a median gap of 17 days from CBS. MRI scans were reported by a trained Radiologist. CBS results were compared with MRI findings for assessment of diagnostic validity. The study was approved by Institute Ethics Committee.

Results: A total of 90 knee joints in 45 patients were included for analysis. There were 41 females and 4 males with mean age of 34.6 years (10.6). CBS detected osteonecrosis in 25 (27.7%) out of 90 knee joints whereas MRI detected osteonecrosis in 27 out of 90 knee joints (30%). CBS detected 8 additional sites of osteonecrosis in 5 patients (6 in distal tibia and 2 in the head of the femur). Sensitivity, Specificity and diagnostic accuracy of CBS were 92.6%, 95.2%, and 94.4% respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 89.3% and 96.77% respectively. There was good agreement between CBS and MRI in the detection of osteonecrosis (Cohen's kappa coefficient - 0.86, positive and negative percent agreement - 92% and 95% respectively). **Conclusion:** Combined Triphase bone scan and SPECT/CT (CBS) showed good performance compared to MRI in the detection of osteonecrosis of the knee. Since whole-body imaging was part of the method, additional distant sites of osteonecrosis could be detected.

OP-715

High efficacy of skeletal SPECT/CT in detecting active pain generators in patients with persistent/recurrent lumbar pain and inconclusive conventional imaging

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Introduction: Despite recent advances in lumbar spine stabilization surgery (LSSS), there is a high number of patients complaining of persistent/recurrent lumbar pain after LSSS. Conventional imaging is commonly performed in assessing potential lumbar pain generators, but it remains equivocal in approximately 20% of cases. Purpose: The purpose of this study was to assess the diagnostic performance of ^{99m}Tc-HDP SPECT/CT in identifying potential pain generators in patients with persistent/recurrent lumbar pain after LSSS but in which conventional diagnostic imaging was inconclusive. **Methods:** A total of 187 patients (median 56 years old, 70 male) with persistent/recurrent lumbar pain following LSSS who underwent ^{99m}Tc-HDP SPECT/CT after inconclusive conventional (X-ray and/or CT) imaging were included in the study. Tracer uptake on SPECT/CT, as indicator of ongoing osteoblastic activity, was assessed within the lumbar spine stabilization segment (SS) and at adjacent segments (AS); uptake intensity was graded as i) high, $\geq$ iliac crest uptake, ii) mild, $\geq$ non-diseased vertebrae but $<$ iliac crest uptake or iii) negative. MRI was performed using standard protocol. assessed the AS features of AS in 73 patients were correlated with SPECT/CT results. **Results:** In 160/187 (85.0%) patients, SPECT/

CT showed positive mild-to-high avid changes within the LSSS region. 56.7% of patients had uptake within the SS, while 54.0% had abnormal activity in AS (39% high AS uptake vs. 15% mild AS uptake, $p < 0.05$). Although positive SS findings were common at < 2 years (70.3%) and decreased with time after LSSS, there were still 21.7% of patients with positive SS findings > 6 years after surgery. A high AS activity was noted in 28.4% of patients already < 2 years post-LSSS, suggesting early/accelerated degeneration post-LSSS. This further increased to 60.4% after > 6 years post-LSSS ($p < 0.05$). Positive SPECT/CT findings at SS were more frequent in patients with ≥ 3 stabilized segments ($p < 0.05$), while SPECT/CT findings at the AS did not. Overall, positive SPECT/CT guided the therapy in 64% of cases which included root injections or re-do surgery at active sites and/or adjacent sites. **Conclusion:** Skeletal SPECT/CT is a sensitive diagnostic tool to identify osteoblastic activity which may be a pain generator in patients with persistent/recurrent pain after lumbar surgery in which conventional imaging was inconclusive.

OP-716

Additional diagnostic value of SPECT/CT over SPECT in condylar hyperplasia using visual and quantitative analysis

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Introduction: Condylar hyperplasia (HC) is characterized by exaggerated and progressive unilateral (rarely bilateral) growth of the mandibular condyles that causes facial asymmetry, dysfunction and often pain. Diagnosis is clinical with structural imaging. Bone scintigraphy is the gold standard for assessing increased condylar activity, providing a guide for treatment. SPECT/CT provides anatomical information improving localization with possible diagnostic impact. The aim of the study is to evaluate the additional value of bone SPECT-CT over SPECT in the diagnosis of active HC using qualitative and quantitative analysis. **Methodology:** Forty-six patients (9–56 years, mean 24, 36 female) who concurred with clinical data of mandibular asymmetry and suspicion of HC were included. Bone scintigraphy was performed with 99mTc-MDP with SPECT-CT of the skull in a GE Infinia Hawkeye 4 gamma camera. Symmetrical circular areas of interest (ROIs) were drawn on the condyles in SPECT images and elliptical ROIs oriented to the axes of the condyles in SPECT-CT. The percentage of uptake for each condyle was quantified (normal value $< 55\%$). Clinical and imaging follow-up and/or histopathology were used as reference. Diagnostic accuracy was calculated for SPECT and SPECT/CT. **Results:** Thirty-three of the 46 patients showed increased condylar uptake in SPECT with visual analysis and 37 with quantification (21 right condyle, 14 left condyle and 2 bilateral). Thirty-one were female. In SPECT-CT 27 patients were positive in the visual analysis and 32 in the quantitative one. The 6 patients with positive SPECT and negative SPECT/CT in the visual analysis presented uptake in the temporomandibular joint. Only 5 patients had surgical treatment, 3 of them positive on SPECT (1 with HC and 2 with degenerative

changes) and 2 negative (1 of them with HC confirmation). In the other patients, the final diagnosis was based on clinical/imaging follow-up, with HC confirmed in 28 of them. Sensitivity, specificity, PPV, NPV and accuracy for SPECT were 83%, 50%, 76%, 62% and 72% in the visual analysis and 85%, 33%, 78%, 44% and 72% in the quantitative analysis. Values for SPECT-CT were 90%, 94%, 96%, 84% and 91% in the visual analysis and 94%, 92%, 97%, 86% and 94% in the quantitative one. **Conclusion:** SPECT-CT images allow increasing the diagnostic accuracy in active HC with respect to SPECT. The impact is greater in the specificity due to the ability to recognize inflammatory-degenerative joint uptake. Quantification could further increase diagnostic accuracy in SPECT/CT.

OP-717

Prospective evaluation of the application of ¹⁸F-NaF PET/CT imaging in melorheostosis

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Purpose: Melorheostosis is a rare, benign, hyperostotic disease of the long bones, with no sex predilection, typically occurring in late childhood or early adulthood, which can lead to substantial functional morbidity, depending on the sites of involvement. The typical radiographic appearance of melorheostosis consists of cortical and medullary hyperostosis of the affected bones, resembling a “dripping candle wax”, while soft-tissue ossifications are rare features of this uncommon disorder. Aim of the current study was to prospectively evaluate the efficacy of ¹⁸F-NaF PET/CT imaging in targeting melorheostotic lesions. **Subjects & Methods:** Thirty unrelated adults with radiographic appearance of melorheostosis were prospectively evaluated with whole-body ¹⁸F-NaF PET/CT studies. PET/CT scans were obtained after intravenous injection of 2.72–3.26 mCi of ¹⁸F-NaF (¹⁸F-sodium fluoride). PET images from the vertex of the skull to the plantar surface of the feet were acquired on dedicated PET/CT scanners, 58 to 70 minutes after the radiotracer injection, while a non-contrast, low dose, non-diagnostic CT scan was performed for attenuation correction and co-registration purposes. **Results:** All skeletal and extra-osseous melorheostotic lesions demonstrated intensely elevated ¹⁸F-NaF activity co-localizing with areas of increased attenuation on CT. In addition, disease-related areas with low-level increased hyperdensity on CT, could be confidently identified on ¹⁸F-NaF PET/CT allowing the diagnosis of early-stage melorheostotic abnormalities. **Discussion/Conclusion:** ¹⁸F-NaF PET/CT is the optimal in vivo imaging modality for the assessment and monitoring of melorheostosis burden. The unique quantitative capabilities offered by PET-imaging, together with the detailed morphological char-

acterization provided by the multisection CT component and the vastly superior resolution in comparison to conventional gamma camera imaging, suggest that ^{18}F -NaF-PET/CT should be employed in the work-up of patients diagnosed with this rare bone disorder.

OP-718

Quantitative analysis of F18-FDG uptake in the shoulder for the diagnosis of frozen-shoulder (adhesive capsulitis)

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Purpose: In this study we explore the benefits of F18-FDG PET/CT as a non-invasive, diagnostic marker for the frozen shoulder syndrome. Frozen shoulder syndrome is characterized by reduced mobility and pain of the shoulder caused by inflammatory contracture of the joint capsule leading to a painful restriction of the movement. While the condition often reverts itself after some years, a number of patients are subjected to surgical treatment to accelerate recovery. Clinical diagnosis is based on movement restriction, but in the first phase of the condition movement can be normal and the condition can be interpreted as impingement syndrome, which does not involve the shoulder capsule and which is treated differently. However, since inflammation is present one could expect to find ^{18}F -FDG accumulation in the joint during a PET/CT scan. **Method:** A blinded study was carried out where 20 patients with either frozen shoulder or impingement syndrome underwent F18-FDG PET/CT before surgery (200MBq, 1h rest). The data was analyzed qualitatively by experienced nuclear medicine physicians as well as quantitatively by placing regions of interest (ROI) around both shoulders and analyzing the standard uptake values (SUV). The patients' other shoulder was used for vice versa comparison and normalization. The analysis was done without knowing which clinical group the patients belonged to or the results of the arthroscopic viewing. Finally, results from quantification and visual interpretation were compared to the 'gold standard' which were the surgeons actual findings and diagnosis during the surgical procedure. **Results:** Patients with a confirmed frozen shoulder show increased SUV uptake, both seen in the visual observation and the ROI analysis.. Both physicians' assessments were in good agreement with each other with a kappa-value of 0.74. Comparing the PET-FDG examination with the surgical diagnosis, we observed a sensitivity of 85% and a specificity of 93% for the physicians evaluation as well as 77% sensitivity and 96% specificity for the quantitative analysis. Combining these two methods we gained 100% sensitivity and 92% specificity. **Conclusion:** Using a blinded study design, we have shown that ^{18}F -FDG PET/CT is a sensitive method for non-invasive diagnosis of frozen shoulder. The best results reducing the level of false negative is obtained by combining both a visual evaluation by FDG-PET trained physicians and a computer assisted determination of significantly increased SUV uptake in the shoulders ro-

tator cuff. This method is relevant in cases where there is doubt about the diagnosis frozen shoulder.

1801/1804 Wednesday, October 17, 2018, 12:15 - 13:15, Plenary Hall

Plenary 4: Highlights Lecture

OP-719

Highlights Lecture

K. Herrmann; Universitätsklinikum Essen, Dept. of Nuclear Medicine, Essen, GERMANY.

OP-720

Highlights Lecture

F. van Leeuwen; Leiden University Medical Center, LUMC, Leiden, NETHERLANDS.

Scientific e-Poster Walks

111 Sunday, October 14, 2018, 08:00 - 09:00, Hall A

e-Poster Walk 1 - Clinical Oncology: All Around Oncology

E-PW001

Whole-Body ^{18}F -FDG PET/MRI With ADC Mapping to Detect Malignant Transformation of Peripheral Nerve Sheath Tumours in Patients With Neurofibromatosis Type 1

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Purpose: To evaluate the combined diagnostic value of simultaneous PET/MRI imaging in patients with neurofibromatosis type 1 (NF1), suspect of malignant transformation. **Methods:** Between July 2017 and February 2018, 11 consecutive NF1 patients (8 women and 3 men, mean age 35.7 years, range 18 to 65) presenting an “at-risk” phenotype underwent whole-body PET/MRI for detection of malignant transformation of peripheral nerve sheath tumours. PET imaging was performed 1 h after 4 MBq/kg ^{18}F -FDG injection with simultaneous whole-body MR diffusion-weighted imaging at 3 Tesla ($b = 50, 400, 800 \text{ s/mm}^2$) on a Biograph mMR (Siemens, Erlangen, Germany). Metabolic metrics (SUVmax, MTV, TLG, tumour/liver ratio [T/L]) and tissue cellularity (ADCmean, ADCmin) were measured. ROC analysis was used to determine the optimal cut-off for these variables to distinguish benign from transformed lesions and Fisher’s exact test was employed to classify categorical variables. **Results:** A total of 20 lesions showed increased FDG uptake. Pathological examination was performed in patients who had clinical manifestations (pain, neurological deficit, tumour growth) or lesions with SUVmax >3.5 . In the 14 documented lesions, pathology revealed 5 benign neurofibromas, 7 dysplastic neurofibromas and 2 sarcomatous transformations. Median SUVmax was 1.95 (range, 1.59–3.41), 5.06 (range, 3.04–6.97) and 6.09 (range, 4.76–7.41), respectively. Median ADCmean was $1.93 \times 10^{-3} \text{ mm}^2/\text{s}$ (range, 1.54–2.27), $1.74 \times 10^{-3} \text{ mm}^2/\text{s}$ (range, 1.20–1.89) and $1.44 \times 10^{-3} \text{ mm}^2/\text{s}$ (range, 0.91–1.96), respectively. A significant negative linear relationship was found between SUVmax and ADCmean ($y = -3.9x + 10.3$, $R^2 = 0.47$, $P = 0.001$). The optimal cut-off values for detection of malignant transformation were, in decreasing order of area under the ROC curves, a T/L ratio >1.78 , SUVmax >3.41 , TLG >7.73 , ADCmean $\leq 1.96 \times 10^{-3}$, MTV $>19.52 \text{ cm}^3$, mm^2/s , ADCmin $<1.31 \times 10^{-3} \text{ mm}^2/\text{s}$. Diagnostic performances to distinguish benign neurofibromas from dysplastic/malignant tumours were $P = 0.0003$ for T/L ratio, $P = 0.00007$ for SUVmax, and $P = 0.04$ for ADCmean. **Conclusion:** In this preliminary study, we confirm that intensity of ^{18}F -FDG uptake is predictive of malignant transformation. Whole-body MRI is the reference standard to identify nerve sheath tumours and their extent in NF1 and ADCmean characterization shows prom-

ising results to distinguish benign from dysplastic/malignant in a PET/MRI one-shot setting.

E-PW002

Quantitative SPECT/CT for differentiation between enchondroma and low grade chondrosarcoma

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Objective: As management and prognosis are different between enchondroma and low-grade chondrosarcoma, differential diagnosis is very important. Although various clinical and radiological clues have been proposed for differential diagnosis, it is not easy to distinguish both diagnoses, which is difficult to even by pathological examinations. The objective of this study was to evaluate the efficacy of quantitative SPECT/CT in differential diagnosis of the chondroid bone tumors in the long bone.

Material and Methods: We retrospectively reviewed the patients with pathologically diagnosed as enchondroma or low-grade chondrosarcoma of long bone who had SPECT/CT scan from July 2015 to February 2018. Maximum standard uptake value (SUVmax) were measured from SPECT/CT images, and we statistically analyzed the differences in the values between enchondromas and low-grade chondrosarcomas. **Results:** A total of 16 cases were investigated. There were 9 females and 7 males. Mean ages of 8 patients with enchondromas and the rest of patients with low-grade chondrosarcoma were 48 and 45 years. Median main lengths were 3.2 cm in enchondroma and 6.15 cm in low-grade chondrosarcoma. Median follow-up period was 12 months. Mean SUVmax were 12.6 in enchondroma and 24.2 in low-grade chondrosarcoma. Mann-Whitney U test demonstrated that differences in SUVmax between enchondromas and low-grade chondrosarcomas were statistically significant ($p = 0.009$). The area under the ROC curve for SUVmax was 0.893 ($p = 0.001$). Using a cut-off value of SUVmax of 16.63, the sensitivity and specificity were 87.5% and 100% for discriminating chondrosarcoma. **Conclusion:** While it is still challenging to distinguish enchondroma and low-grade chondrosarcoma in the long bone, quantitative SPECT/CT might facilitate differentiation of the diagnoses. Further studies on more cases with longer follow-up period should be mandatory.

E-PW003

Predicting Pathological Invasiveness in T1 Non-Small Cell Lung Cancer using Deep Learning Algorithm on Chest CT and ^{18}F -FDG PET/CT

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Purpose: To evaluate the ability of deep learning algorithm to predict invasiveness of T1 stage non-small cell lung cancer (NS-

CLC) using computed tomography (CT) and positron emission tomography (PET)/CT images. **Methods:** A total of 468 patients with NSCLC smaller than 3 cm, resected at our institution from 2008 to 2015 were enrolled. NSCLCs were classified as either noninvasive or invasive according to the pathological reports. Noninvasiveness was defined as the absence of nodal involvement, vascular invasion, and lymphatic invasion. Preoperative chest CT images were used to train and validate the deep learning algorithm. A deep 3D convolutional neural network (CNN) was trained using 5-fold cross-validation method. To normalize input data, we rescaled CT image to let one voxel size be represented as (1mm, 1mm, 1mm). Input cube size was (32mm, 32mm, 32mm). Horizontal flip and vertical flip augmentation were applied and max-pooling and dropout layer were used to avoid overfitting. Receiver operating characteristic (ROC) curves and areas under the curve (AUCs), accuracy, sensitivity and specificity were used to assess the performance of 3D CNN. Maximum standardized uptake values (SUVmax) of primary tumors were obtained from 373 preoperative ^{18}F -fluorodeoxyglucose PET/CT images. We added tumor size and SUVmax as external features to the 3D CNN model and evaluated the performance of the combined model using XGBoost classifier. **Results:** 157 out of 486 samples (33.5%) were invasive. A subsample group composed of 10% of the data (32 noninvasive and 16 invasive samples) was retained for the validation set. The 3D CNN showed an AUC of 0.834, 75.0% accuracy, 75.0% sensitivity, and 75.0% specificity. The AUC, accuracy, sensitivity, and specificity were 0.873, 83.3%, 87.5%, 81.3%, respectively, when size alone was added to the 3D CNN model; 0.924, 81.3%, 81.3%, 81.3%, respectively, when SUVmax alone was added to the 3D CNN model. When both tumor size and SUVmax were added to CNN model, the AUC, accuracy, sensitivity and specificity were 0.928, 83.3%, 87.5%, 81.3%, respectively. **Conclusion:** A hybrid CNN-XGBoost model using CT and ^{18}F -FDG PET/CT images showed good diagnostic performance for the predicting pathological invasiveness in patients with T1 NSCLC.

E-PW004

The Risk Factors For Occult Lymph Node Metastasis And Recurrence By F-18 FDG Uptake In Clinical N0 Esophageal Squamous Cell Carcinoma Patients

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Aim: To investigate the relationship between fluorine-18 fluorodeoxyglucose (^{18}F -FDG) uptake of primary tumor and occult lymph node metastasis (OLM) and recurrence in clinical N0 esophageal squamous cell carcinoma (ESCC) patients. **Materials and Methods:** Our study population comprised of 132 patients (109 men and 23 women) with clinically N0 ESCC based on CT and ^{18}F -FDG PET/CT before operation. The median age was 66 (range, 50–80) years. The PET parameters of primary le-

sion (maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV), total lesion glycolysis (TLG), SUVpeak and maximum SUV corrected for lean body mass (SULmax)) were measured. Threshold of 40% of the maximum peak activity within primary lesions was used to delineate the MTV. Patients were classified into two groups using the cutoff value, namely, those with low and high values of all PET parameters using ROC analyses. The relationship among PET parameters, clinicopathological variables and OLM was investigated using Fisher exact test, chi-square test and logistic regression analyses. The Cox proportional hazard model was used to evaluate the effects of PET parameters and clinicopathological variables for relapse free survival (RFS) while adjusting for potential confounding factors. RFS was evaluated by Kaplan-Meier methods, and the difference in survival between subgroups was analyzed by log-rank test. **Results:** The incidence of OLM was 43/132 (32.5%). The each optimal threshold of SUVmax, MTV, TLG, SUVpeak and SULmax max was 3.05, 5.52, 6.6, 2.86, and 2.69 respectively. On univariate analysis, all PET parameters were associated with OLM, and multivariate logistic regression analyses showed that SUVmax, TLG, SUVpeak and SULmax were significant risk factors for OLM (SUVmax: hazard ratio (HR)=0.21, $P=0.002$, TLG: HR=3.410, $P=0.006$, SUVpeak: HR=3.087, $P=0.01$, SULmax: HR=3.424, $P=0.007$), however, MTV was not. With adjustment for several clinicopathological variables, Cox regression analysis showed that SULmax, age, clinical stage (cStage), and venous invasion were significantly associated with RFS (SULmax: HR=3.991; $P=0.032$, age: HR=0.375; $P=0.009$, cStage: HR=4.536; $P=0.002$, venous invasion: HR=9.549, $P<0.001$). SUVmax, SUVpeak, MTV and TLG had no significant association with RFS. On the Kaplan-Meier survival curves, the patients with SULmax $\geq$ 2.69, cStage IIA and venous invasion showed significantly worse prognosis than those with SULmax $<$ 2.69, Stage I and non-venous invasion ($P<0.001$ for all). **Conclusion:** SUVmax $\geq$ 3.05, TLG $\geq$ 6.6, SUVpeak $\geq$ 2.86 and SULmax $\geq$ 2.69 may be significant risk factors for OLM, and SULmax $\geq$ 2.69, venous invasion and cStage max may be significantly associated with RFS in clinical N0 ESCC patients.

E-PW005

The predictive value of early evaluation during radiotherapy with 18F-FDG PET/CT and Epstein-Barr virus DNA concentration for treatment outcome in nasopharyngeal carcinoma patients

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Aim: The prognostic value of 18F-FDG PET derived parameters with Epstein-Barr virus (EBV) DNA titer obtained during radiotherapy in patients with nasopharyngeal carcinoma (NPC) has not been evaluated. The aim of this prospective study is to investigate the predictive value of the interim PET parameters and EBV DNA titer to definitive chemoradiotherapy in NPC. **Materials and Methods:** Sixty patients with NPC were prospectively enrolled. Participants underwent 18F-FDG PET/CT before and during concurrent chemoradiotherapy (CCRT). The plasma EBV

DNA titer was measured along with PET/CT. Change of EBV DNA titer and parameters derived from PET/CT during CCRT were analyzed according to treatment response, recurrence-free survival (RFS), and overall survival (OS). **Results:** The total lesion glycolysis (TLG) reduction ratio during CCRT was the independent unfavorable risk factor for treatment response ($p = 0.002$). Of the patients with a reduction ratio of $TLG \leq 0.6$, 56% did not achieve complete remission after treatment. On multivariate analysis, TLG reduction ratio ≤ 0.6 predicted for a decreased RFS ($p = 0.003$) and a detectable EBV DNA titer during CCRT, TLG reduction ratio ≤ 0.6 , and the elder age were associated with the poorer OS ($p = 0.037$, 0.009 , and 0.016 , respectively). A scoring system with a range from 0 to 2–3 was developed according to the 3 independent prognosticators for OS. Patients with a score of 1 and 2–3 had poorer survival outcome compared with those with a score of 0 ($HR = 4.756$, $p = 0.074$ and $HR = 18.973$, $p = 0.001$, respectively). **Conclusion:** Our preliminary data indicate that the reduction ratio of TLG or the EBV DNA titer acquired during radiotherapy are early predictive biomarkers for ultimate response or long-term prognosis after the definitive treatment. These early biomarkers enable identification of patients at risk of treatment failure at an early time point, permitting treatment individualization and consideration of alternative strategies such as adjuvant therapy.

E-PW006

Whole-Body PET/MRI for Multiple Myeloma Staging: Impact of ^{18}F -FDG uptake and MR Sequence Design on Focal Lesion and Bone Marrow Infiltration Assessment

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Purpose: To study the combined performance of simultaneous ^{18}F -FDG PET/MRI with dedicated whole-body MR sequences for focal lesion (FL) detection and bone marrow infiltration (BMI) evaluation in multiple myeloma at staging. **Methods:** Between June 2017 and April 2018, 29 consecutive patients were referred for initial staging of a (previously untreated) monoclonal gammopathy. One hour after injection of 4 MBq/kg ^{18}F -FDG, PET/MRI acquisitions (Biograph mMR, Siemens, Erlangen, Germany) consisted of conventional whole-body T1-weighted spin-echo and T2-fat suppressed Dixon-weighted images (CWB-MRI), and simultaneous dedicated whole-body MR sequences, including multi-slice diffusion-weighted (WB-DWI), 3D isotropic dynamic contrast-enhanced (WB-DCE) and 3D-T1 weighted imaging combined with PET (T1-PET). MRI images were interpreted by 2 observers according to Salmon-Durie plus classification, with measurement of the ADC-mean and mean contrast enhancement (CEmean). PET images were interpreted by 2 observers according to IMAJEM criteria (Moreau, JCO 2017) as FL (focally increased tracer uptake within bones), diffuse BMI (homogeneous skeletal uptake >liver or

heterogeneous uptake regardless of intensity) and extramedullary disease (FDG-avid soft tissue uptake not contiguous to bones), and SUVmax was recorded. Each patient was then allocated a specific staging on CWB-MRI, CWB-MRI+WB-DWI, CWB-MRI+WB-DCE, CWB-MRI+PET, and PET/MRI. **Results:** PET diagnosed FL in 10 patients ($SUV_{max}=6.1\pm 4.3$; range, 3.0 to 16.6), including 4 patients with 1–4 FL, 3 with 5–20 FL and 3 with >20 FL, and diffuse BMI in 7 patients ($SUV_{max}=4.1\pm 0.4$; range, 3.7 to 5.0). Compared to CWB-MRI, PET/MRI detected 36 additional FL among 9 patients and upstaged 8 of them; 5 patients from MGUS to stage-I multiple myeloma, 1 from MGUS to stage-II, 1 from stage-I to stage-II, and 1 from stage-I to stage-III. Detection of additional FL did not modify staging in 2 patients. In addition, dedicated whole-body MR sequences significantly impacted assessment of BMI. Compared to CWB-MRI, WB-DWI upstaged 7 patients and downstaged 8, and WB-DCE upstaged 16 patients and downstaged 4. In 1 patient bone marrow was considered normal on CWB-MRI and WB-DWI but severe on WB-DCE and PET. Finally, we noted a high prevalence of associated extramedullary diseases on PET: multiple lymph nodes in 10 patients, 1 breast cancer, 1 cholangiocarcinoma, 1 colon polypus, 1 thyroid nodule and 3 abnormal pituitary uptakes. **Conclusion:** Whole-body PET/MRI with dedicated MR sequences modifies initial staging of patients with a monoclonal gammopathy. Longitudinal follow-up will evaluate the prognostic value of these modifications.

E-PW007

Predicting the outcome of Peptide Receptor Radionuclide Therapy (PRRT) for the treatment of neuroendocrine tumours using PET-CT

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Background: The use of radiolabelled peptides for the imaging or therapy of patients with Neuroendocrine Tumours (NET) is standard practice. The primary aim of this research was to see if there was any predictive value in the pre-therapy ^{68}Ga (^{68}Ga)-DOTANOC PET-CT studies of NET patients that could be used to determine the likely outcome of ^{90}Y (^{90}Y)-DOTATATE Peptide Receptor Radionuclide Therapy (PRRT). **Method:** Standardised Uptake Values (SUVs) of 93 spinal lesions were measured in the pre-therapy and post-therapy PET-CT studies over 38 patients. Spinal lesions were considered as they were well delineated in PET due to the low uptake of somatostatin receptor radiotracer in healthy bone. The relationship between the pre-therapy SUVs (SUV_{mean} and SUV_{max}) and the overall change in SUV between the pre-therapy and post-therapy images were considered using an adapted PET Response Criteria in Solid Tumours (PERCIST) criteria. The relationship between the pre-therapy splenic SUVs and the reported clinical outcomes were also investigated, as the spleen has a high expression of somatostatin receptor cells in both healthy and diseased tissue. **Results:** A Kruskal-Wallis test showed that the overall response of the tumour had a significant correlation with the pre-therapy SUV_{mean} ($p < 0.001$). A pairwise comparison showed that there was a significant difference between the lesions that demon-

strated a complete response to treatment and the other three groups (partial response $p=0.005$, stable disease $p=0.001$ and progressive disease $p<0.001$). There was also a significant correlation between lesion pre-therapy SUV_{max} and the overall response of the lesions, and a significant correlation between the ratio of the $SUV_{mean}/SUV_{background}$ and the overall response. There was no correlation between any of the pre-therapy SUV indicators for the spleen and the overall clinical response. **Discussion:** Pre-therapy SUVs could be used to predict the response of spinal lesions to PRRT, although the overall clinical response needs to be considered in conjunction with the response of lesions. A limitation of this project is the perceived loss of uptake of smaller spine lesions due to the partial volume effect, where the SUVs of smaller lesions could be corrected using ^{68}Ga recovery curves. This work must be extended to consider the response of NET lesions across other organs. The spleen SUVs were found not to be a good indicator of overall response, although the effect of partial splenectomy procedures on the SUV results is unknown.

E-PW008

Use Of ^{223}Ra -dichloride In Mcrpc Patients At The Early Onset Of Castration Resistance: Is Early Introduction Useful?

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Purpose: To date there is no precise indication for the best timing to use ^{223}Ra -dichloride in mCRPC patients compared to other chemotherapeutic or biological lines. Purpose of this study is to evaluate mCRPC patients treated at the early onset of castration resistance with ^{223}Ra -dichloride without other previous treatment. **Materials and Methods:** ^{223}Ra -dichloride (55KBq/Kg lq4w) was administered to 149 consecutive mCRPC symptomatic patients in our Nuclear Medicine Unit in 28 months. Among these patients, 36 received ^{223}Ra as first line treatment, at the time of assessment of castration resistance. Some Baseline and "At the End of ^{223}Ra treatment" (ATE) values were recorded: PSA, tALP, Complete blood counts. Pain response during treatment was assessed by the Brief Pain Inventory Numeric Rating Scale (BPI 0-10 Scale) and Narcotic Score (NS)(considering medication type and medication frequency). Moreover, follow-up time, age, Gleason, BMI and ECOG Performance Status were analyzed. **Results:** 36 patients (mean age 74 years) treated at the early onset of castration resistance with ^{223}Ra -dichloride, received 189 ^{223}Ra cycles. Among these patients, 6 pts were still receiving ^{223}Ra therapy at the time of analysis. Therefore, we evaluated 30 pts: 23 (76.6%) completed the 6 scheduled administrations, 7 patients (23.4%) discontinued ^{223}Ra treatment for death or progression disease. The mean follow-up time was 13.9 months (2-31 months) from the start of ^{223}Ra therapy. The Gleason mean value was 8 (7-10) and ECOG PS was 0 in 14 pts, 1 in 15 pts and 2 in 1 pt. Mean BMI was 26.8. Baseline PSA mean value was 109.2 ng/ml (0.5-384.7) while ATE PSA mean value was 76.97 ng/ml (0.02-335). Baseline tALP mean value was 309.9 U/l (57-1219) whereas ATE tALP mean value was 127.3 U/l (43-391). Furthermore, Baseline Hemoglobin mean value was

12.53 g/dl (10.3-14.6) instead ATE Hemoglobin mean value was 11.8 g/dl (9.2-14.3). Finally, Baseline Platelets mean value was $225 \times 10^3/ml$ (110-345) while ATE Platelets mean value was $199.7 \times 10^3/ml$ (99-287). Patients had a Baseline BPI mean value of 4.9 (2-10) with mean NS of 3.2 (0-21), while at ATE BPI mean value was 3.6 (0-9) with mean NS of 2.4 (0-16). **Conclusion:** In patients treated at the early onset of castration resistance, ^{223}Ra -dichloride therapy proved to be effective, preserving bone marrow reserve. In addition, both PSA and tALP decreased as well as pain. Using ^{223}Ra -dichloride as first line therapy in mCRPC patients with only bone metastases, could represent a useful medical choice.

E-PW009

The Value of Repeated PET/CT Imaging and Quantitative analysis to define true progression and improve response assessment during Nivolumab treatment: preliminary results from a retrospective, single centre study

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Aim: Nivolumab is an immune checkpoint inhibitor used for cancer treatment. However, Response assessment (RA) by means of PET/CT remains challenging, as available criteria are not yet harmonised in clinical practice. We retrospectively investigated the role of repeated PET/CT and quantitative analysis in patients(pts) on Nivolumab treatment referred for RA. **Methods:** Pts referred for RA during Nivolumab treatment (September2015-May2018) were evaluated. Inclusion Criteria were a pre Nivolumab PET/CT(S0) and 2 PET/CT(S1-S2) within first 12 cycles of treatment(CYN). Response was initially defined qualitatively by experienced Nuclear medicine physicians: Disease-Progression(DP), Stable-Disease(SD), Partial-Metabolic-Response(PR), Complete-Metabolic-Response(CR). The Volume and SUVmax variations of the most intensely FDG avid malignant lesion (XLesion) at S0 were recorded. Volume reduction $\geq 25\%$ was recorded as volumetric response, SUVmax reduction $\geq 25\%$ was recorded as SUV response. Validation of results, when available, was obtained by means of follow-up PET/CT scans (FUS). **Results:** Overall, 40pts were included(range 26-83, median 60) for a total of 221 PET/CT scans. Primary malignancy was Lung (24/40 pts), Melanoma (10/40 pts), Lymphoma (6/40 pts). S1 scans (S0-S1 mean interval: 3.4 CYN. Range: 1-8 CYN) demonstrated DP in 9/40pts, SD in 6/40pts, PR in 23/40pts, CR in 2/40pts. SUV response of XLesion was associated with PR-CR pts ($p<0.01$) and occurred in 16/40pts. Volumetric response was associated with PR-CR ($p<0.01$) and occurred in 17/40pts. Inflammatory findings on S1 were identified in 25/40pts. S2 scans (S0-S2 mean interval: 6.6 CYN. Range: 3-11 CYN) demonstrated DP in 8/40pts, SD in 6/40pts, PR in 20/40pts, CR in 6/40pts. SUV response of XLesion was associated with PR-CR pts ($p=0.01$) and occurred in 30/40pts. Volumetric response was not associated with PR-CR ($p=0.4$) and occurred in 27/40pts. Inflammatory

findings on S1 were identified in 25/40pts. FUS was available in 30pts (mean follow up 14 months). Tumor Control (CMR, SD or PR) on FUS was achieved in 21/30pts(70%). FUS demonstrated DP in 7/30pts, SD in 2/30pts, PR in 5/30pts, CMR in 14/30pts, Immune-related Progression in 2/30pts. S1 and S2 were concordant in 18/30pts, discordant in 12/30pts. Compared to FUS, S1 mis-interpreted response with a higher rate (12/30,40%) than S2 (3/30,10%)($p = 0.015$). Five pts had pseudo-progression in S1, then corrected by FUS. **Conclusion:** Qualitative analysis identified tumour response with good accuracy, however quantitative analysis may prove beneficial to Response assessment. Repeated follow up PET/CT scans are useful to improve accuracy in identifying patterns of progression or response in patients being treated with Nivolumab.

E-PW010

Prediction of Immune-Checkpoint-Inhibitor therapy effectiveness by evaluation of bone marrow activity modifications: an FDG-PET/CT Study

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Background: Immune-checkpoint-inhibitor therapy (ICIT) is a very promising approach in patients with metastatic melanoma. However, up to 60% of patients fail to respond to this treatment. Higher lymphocytes counts have been linked to longer survival. As the production of blood elements is connected to the bone marrow function, we planned this study to analyze bone marrow glucose metabolism on 18F-FDG-PET/CT (PET/CT) images. **Methods:** 30 patients with metastatic melanoma were retrospectively recruited. Each patient underwent a PET/CT before the ICIT start (PET1) and a second PET/CT after 4 ICIT cycles (PET2). 15 of those were responders and 15 non-responders, according to PERCIST criteria. In each patient, a computational software was employed to segment the bone spongiosa in the CT images automatically; mean FDG uptake was analyzed on the corresponding area on the co-registered PET images. Uptake was then normalized for background activity, to obtain a target-to-background ratio (TBR). **Results:** Responders had a higher TBR in the baseline PET when compared to non-responders (1.68 ± 0.62 vs. 1.16 ± 0.37 , $p < 0.01$). Moreover, responders showed an increase in TBR after the 4 ICIT cycles (mean TBR increase: 0.4 ± 0.44 , $p < 0.001$ vs. baseline). This increase was particularly pronounced when considering axial skeleton only ($p < 0.001$). Conversely, non-responders didn't show any variation. **Conclusion:** These data suggest that a valid bone marrow function is required for ICIT effectiveness. Computational analysis of PET/CT data might help in identifying the best candidates for ICIT.

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Sunday, October 14, 2018, 11:30 - 13:00, Hall A

e-Poster Walk 2 - M2M: PSMA - e-Walk to Success?

E-PW011

Determining the Effect of Androgen Deprivation Therapy (ADT) on Prostate Specific Membrane Antigen (PSMA) Expression Levels in Patient-Derived Xenografts Using PSMA PET agent [18]F-DCFPyL

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Introduction: Prostate specific membrane antigen (PSMA) is overexpressed in nearly all prostate cancers (PCa). PSMA PET imaging has shown differential uptake pattern in response to androgen-deprivation therapy (ADT). ADT is the first line of therapy for most PCa and a robust information on the relationship between PSMA and ADT can be helpful to extrapolate more reliable information from PSMA-PET scans. The purpose of this work is to evaluate the effect of ADT on PSMA expression by using 18F-DCFPyL (FDC) a PSMA-PET agent to image genomically characterized patient-derived xenograft (PDX) models LuCAP167 (castrate resistant, CR) and LuCAP136 (castrate sensitive, CS). These PDX models represent the heterogeneity of human PCa and therefore the results obtained with these models will provide more reliable and clinically translatable information in comparison to using conventional cancer cell lines. **Methods:** FDC was synthesized by coupling DCFPyL with 2,3,5,6-tetrafluorophenyl-6-[18F]fluoronicotinate. Control and ADT treated PDXs (degarelix, 25mg/Kg, s.c) were imaged 1h post-injection of FDC (100 μ Ci, i.v) at baseline (0 day), day 7, 14, and 21. Post-ADT caliper measurements of the tumor were performed on the same schedule. At day 21 biodistribution [%injected dose/g (%ID/g)] was performed following imaging with FDC. Tumors were also histologically analyzed (H & E, PSMA, and AR). **Results and Discussion:** Difference in the growth rate between the control and treated LuCAP136 tumors were observed but no difference in the uptake (%ID/g) of FDC between the two groups were observed at Day 21. The tumor:blood(T:B) ratios further confirmed no changes in PSMA levels between the two groups. LuCAP167 treated mice showed a 33% decrease in tumor uptake (%ID/g) when compared to control tumors at Day 21. Similarly, the LuCAP167 treated group showed ~ 2-fold decrease in T:B compared to the control group indicating a decrease in PSMA. Although both LuCAP136 and 167 were androgen positive but the ADT had a different effect on PSMA levels in these tumor types. Since the PDX tumor models are well characterized, a deeper analysis might provide further information that results in varying PSMA levels post-ADT. **Conclusion:** The results indicate that PSMA expression in PCa may be either modified or remain unaltered post-ADT and change in PSMA may serve as an indi-

cator of PCa progressiveness. Additional studies using other PDX models will help establish a better understanding of the correlation between PSMA expression and response to ADT.

E-PW012

Prostate cancer bone metastasis model for preclinical evaluation of radiotherapeutics

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Bone metastases cause high mortality in bone metastatic castration-resistant prostate cancer (mCRCP) patients. Several targeted radionuclide and combination treatments for prostate cancer are in development after approval of radium-223 dichloride (Xofigo®) for the treatment of mCRPC. The aim of the study was to evaluate the growth of LNCaP human prostate cancer cells in bone of NMRI nude mice in order to widen the range of drug candidates that can be tested in this model. Previously used NOD.scid mice have a defect in the DNA damage repair system that sensitizes them to radiation and DNA damage repair inhibitors. Male NMRI nude mice (Janvier, France) aged 6–8 weeks were inoculated with 2×10^6 LNCaP cells (ATCC, VA, USA) into the tibia, modeling tumor growth in bone. The mice were randomized to treatment groups based on serum prostate specific antigen (PSA) levels and cancer-induced changes in bone (bone lesions) evaluated by X-ray imaging at 6 weeks after inoculation of cancer cells. The mice were treated intravenously with 300 kBq/kg of radium-223 dichloride (Ra-223 dichloride, Oak Ridge National Laboratory, TN, USA) or citrate buffer at 6 and 10 weeks. During the study, the tumor growth was followed by PSA and the bone formation marker serum PINP measurements, and X-ray imaging. The study was terminated 12 weeks after inoculation of the cancer cells. Bone volume was analyzed *ex vivo* by micro-computed tomography (μ CT) and tumor and bone areas were evaluated by histology. Ra-223 dichloride was well tolerated in NMRI nude mice. A tumor take rate of 50% was observed at 6 weeks based on evaluation of PSA and bone lesions. The LNCaP tumors induced osteoblastic-mixed bone lesions and Ra-223 dichloride reduced the progression of these lesions and decreased serum PSA levels. The μ CT imaging showed better preserved bone architecture and decreased serum PINP levels. Histological evaluation showed increased fibrotic areas and changes in tumor cell morphology in Ra-223 dichloride treated mice. Based on histological evaluation about 50% of Ra-223 dichloride treated mice were tumor free at the end of the study. In conclusion, NMRI nude mice can be used in the prostate cancer bone metastasis model utilizing LNCaP cells. This model is of high importance when assessing efficacy of different radiotherapeutics as mono- or combination treatments against bone metastases. Ra-223 dichloride was successfully validated as a standard-of-care reference compound.

E-PW013

Peripheral ganglia of the rat: A tumor-free model to evaluate PSMA-specific PET-tracers

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Aim: Prostate-specific membrane antigen (PSMA) is highly expressed in prostate carcinoma (PCa) cells and represents an excellent target for imaging. PSMA-specific PET ligands are usually evaluated in tumor xenograft mouse models. Disadvantages of this approach are immunodeficiency of the mice, erratic tumor growth and inhomogeneous PSMA expression. Moreover, the binding properties are strongly affected by tumor size due to the hindered intratumoral tracer distribution. The aim of this study was to develop a tumor-free model using the peripheral ganglia of the rat as PSMA expressing tissues for the evaluation of PSMA-specific PET tracers. **Methods:** Healthy male rats were injected i.v. with different PSMA-selective tracers: [¹⁸F]DCFPyL (14–71 MBq; n=6), [¹⁸F]DCFPyL (23–64 MBq) + PSMA inhibitor 2-PMPA (23 mg/kg; n=3), [Al¹⁸F]PSMA-HBED-CC (25–54 MBq; n=3) and [⁶⁸Ga]PSMA-HBED-CC (13–51 MBq; n=3). Rats were measured in a Focus 220 or Inveon PET/CT scanner 60–120 min p.i. In addition, dorsal root ganglia were histologically examined using immunostaining with an antibody against PSMA (YPSMA-1, Abcam). **Results:** [¹⁸F]DCFPyL accumulated in all peripheral ganglia (trigeminal ganglion, sympathetic ganglia, dorsal root ganglia). The sympathetic superior cervical ganglion (SCG) was used as a reference structure sufficiently remote from bones, which highly accumulate [¹⁸F]F-produced in case of tracer defluorination. Background was measured dorsal from the cervical spine. Mean [¹⁸F]DCFPyL uptake in SCG was 20.2 ± 5.8 %ID with a signal-to-noise ratio of 6.7 ± 2.6 . Bone uptake was low (12.4 ± 4.3 %ID). When the PSMA-inhibitor 2-PMPA was co-injected, mean SCG uptake was significantly reduced to 4.6 ± 1.8 %ID. [⁶⁸Ga]PSMA-HBED-CC showed a significantly higher uptake in the SCG (41.0 ± 3.4 %ID), a slightly lower signal-to-noise ratio (4.5 ± 0.1) and comparable bone uptake (18.5 ± 0.6 %ID). Due to the high β^+ -energy of ⁶⁸Ga, the images appeared slightly blurry. For [Al¹⁸F]PSMA-HBED-CC, the mean SCG signal was significantly higher compared to [¹⁸F]DCFPyL (36.8 ± 9.5 %ID); signal-to-noise ratio was 4.5 ± 0.1 %ID. Unfortunately, this tracer suffered from fast defluorination *in vivo* as indicated by considerable radioactivity uptake in bones (122.8 ± 50.2 %ID). Immunohistochemistry confirmed high PSMA expression in the peripheral ganglia, which was restricted to satellite glial cells. **Conclusion:** In this study the suitability of tracer uptake in peripheral ganglia of healthy rats for the evaluation of PSMA-selective ligands was demonstrated. This peripheral ganglia rat model is highly advantageous owing to its low price, constant availability and compliance with the 3R-principles (replacement, reduction, refinement) of animal welfare.

E-PW014

Tumor models for PET-imaging of prostate and breast cancer targeting prostate-specific membrane antigen (PSMA) and gastrin-releasing peptide receptor (GRPr)

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Introduction: PSMA and GRPr are considered attractive targets for imaging and therapy of prostate cancer (PC) due to their high expression on the surface of cancer cells. GRPr has been also been suggested for imaging breast cancer (BC), while on the contrary BC is considered negative for PSMA. The chelator N,N'-bis[2-hydroxy-5-(carboxyethyl)benzyl]ethylenediamine-N,N'-diacetic acid (HBED-CC), was linked to H₂N-Lys(Ahx)-NH-CO-NH-Glu, ⁶⁸Ga-**1** (⁶⁸Ga-PSMA-11) and a GRPr antagonist, H₂N-4-amino-1-carboxymethyl piperidine-[(R)-Phe⁶, Sta¹³]BN(6-14), ⁶⁸Ga-**2**^{1,2}. Both tracers were *in vitro* tested in PC: PC-3, LNCaP, in BC: T47D, MDA-MB-231 and in the *PSMA*-transduced and *PSMA*-overexpressing PC-3⁺, T47D⁺ and MDA-MB-231⁺ cell lines. In addition, a GRPr probe for fluorescence-based flow cytometry (FACS), **3**, was synthesized by the replacement of HBED-CC with Alkyne-BDP-FL (Jena Bioscience®). **Methods:** PSMA was overexpressed in PC-3, T47D and MDA-MB-231 cell lines by means of lentiviral transduction which was subsequently confirmed by western blot analysis in the respective cell lysates. **1** and **2** were synthesized, radiolabeled (⁶⁸Ga-**1** and ⁶⁸Ga-**2**) and tested for total cell bound radioactivity over time (0-90 min) according to published methods¹⁻³. FACS analysis with **3** was also performed on T47D⁺ (PSMA⁺), T47D^{Mock} (vector only) and T47D (wild type) cell lines. **Results:** After 45 min of incubation time maximum cell binding of ⁶⁸Ga-**1** and ⁶⁸Ga-**2** (PSMA and GRPr specific, respectively) was achieved. *PSMA* transduction increased the amount of total cell-bound ⁶⁸Ga-**1** and ⁶⁸Ga-**2** in all cell lines tested. More specifically in comparison to the control cells ⁶⁸Ga-**1** was **100x** higher in MDA-MB-231⁺, **10x** in PC-3⁺ and **4x** in T47D⁺. Resulting cell-bound radioactivities were approximately 80 %, 13 % and 2.5 % of total added, respectively. For PSMA control LNCaP cells it was 66 %. Surprisingly, PSMA transduction also increased the binding of the GRPr ligand, thus bound ⁶⁸Ga-**2** was **2x** higher than the controls for MDA-MB-231⁺, PC-3⁺ and T47D⁺. Resulting cell-bound radioactivities were 3 %, 30 % and 9 % respectively. These observations have been also confirmed by FACS using **3** in T47D and T47D⁺. **Conclusion:** The amount of cell-bound ligands ⁶⁸Ga-**1** (PSMA) and [⁶⁸Ga]**2** (GRPr) was increased after transduction of PSMA in all PC and BC cell lines studied, indicating a possible interaction between the two receptors. Such interactions between GRPr and PSMA would be of high impact for the future development of novel radiopharmaceutical treatment strategies addressing tumor heterogeneity. Further studies are currently underway to prove this hypothesis. ¹Eder M, et al. *Eur.J.Nucl.Med.Mol.Imaging*.(2008).35(10):1878-1886 ²Liolios C, et al. *J.Med.Chem*.(2018).61(5):2062-2074 ³Liolios C; et al. *Bioconjug.Chem*.(2016).27(3):737-751

E-PW015

Specific Modulation of radioactive uptake of PSMA-based

tracers in prostate carcinoma by androgen receptor inhibitors

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Introduction/Purpose: In the last few years radioligands, targeting the Prostate-specific-membrane-antigen (PSMA), become more important in treatment and diagnosis of prostate carcinomas. The eligible group of patients is at the same time commonly treated with androgen receptor inhibitors such as abiraterone, therefore understanding of the mutual influences is of high importance. The aim of the study is to investigate the effects of abiraterone and VPC-13566, which targets the binding function 3 of the androgen receptor, on the uptake of [⁶⁸Ga]Ga-PSMA-11 and the cell growth within LNCaP-cells. **Methods:** LNCaP-cells were seeded 98 hours before starting the experiment in fibronectin-coated plates. The hormone addition was started 72 hours respectively 48 hours before with abiraterone (10μM) and VPC-13566 (10 and 15μM). At the beginning the cells were incubated for 90 minutes at 37°C with [⁶⁸Ga]Ga-PSMA-11 (final activity 370kBq/mL). After incubation, uptake was terminated by ice-cold PBS, followed by washing twice with PBS. The remained cells were dissolved twice with an ice-cold solution of 2%-Triton dissolved in PBS. Both fractions treated with Triton were collected and the radioactivity measured with the help of a gamma counter. To determine the effects on the cell growth, further cells were seeded, treated in the same way, but instead of incubating with the radioligand, labeled with DAPI. Cell count ratios were calculated from the different fluorescent emission intensities. **Results:** The results indicate for VPC-13566 a significant decline of the uptake of [⁶⁸Ga]Ga-PSMA-11 in LNCaP-cells for all utilized concentrations and incubation times. Compared to the untreated LNCaP-cells the uptake decreased about 40%±10% for a final VPC-13566-concentration of 10μM and an incubation period of 48 hours. This effect becomes stronger for longer time scales of incubation and higher concentrations. The trend of the uptake shift through the influence of VPC-13566 remains unchanged after having included the cell ratios of the treated cells compared to the untreated ones in the calculation. In case of abiraterone a decline of the uptake for the final concentration of 10μM could be observed as well. **Conclusion:** This preliminary study shows for the LNCaP-cell-line a dependence of the uptake of [⁶⁸Ga]Ga-PSMA-11 and the cell growth on the presence of abiraterone or VPC-13566. Therefore, an improvement of the coordination of ⁶⁸Ga-PSMA-PET-diagnostics, anti-androgen therapies and ¹⁷⁷Lu-PSMA-treatment seems to be necessary. However, further experiments and studies, especially *in vivo*, are required to confirm this initial findings.

E-PW016

Preclinical evaluation of PSMA specific tracers using autoradiography and uptake analysis

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Introduction: Prostate specific membrane antigen (PSMA) is (over)expressed in 90–100% of prostate cancer (PCa) cases and its expression is highly correlated with disease progression. This makes PSMA an excellent target for PCa imaging and therapy, using PSMA-targeting radiotracers. Today, various PSMA specific tracers, including the small molecule inhibitors PSMA-617 and PSMA-I&T, are being used successfully for PCa imaging and therapy. However, since PSMA is not solely expressed in PCa, therapeutic use requires careful evaluation of efficacy combined with maximal protection of PSMA-expressing organs. The aim of this study is to compare the binding affinity and binding of PSMA-617, PSMA-I&T and JVZ-007 for human tumor-, salivary gland- and renal tissue using in vitro autoradiography and uptake experiments in various models. **Materials and Methods:** To determine IC50 values, LNCaP cells were incubated with ^{177}Lu -labeled tracers (PSMA-617, PSMA-I&T and nanobody JVZ-007) with or without an excess of unlabeled PSMA-617, whereafter the membrane-bound and the internalized fractions were measured. Furthermore, cryosections of different PSMA-positive patient derived xenografts were incubated with ^{177}Lu -labeled PSMA-tracers together with increasing concentrations of unlabeled PSMA-617. Additionally, cryosections of healthy human salivary gland and renal tissue were incubated with ^{177}Lu -labeled PSMA-tracers with or without an excess of the same unlabeled tracer. **Results:** Autoradiography blocking experiments revealed an IC50 value of 2.64E-9M and 2.69E-9M for PSMA-617 when blocking ^{177}Lu -PSMA-617 or ^{177}Lu -PSMA-I&T, respectively. This indicates a similar binding affinity of these radiotracers. JVZ-007 could not be blocked by PSMA-617, which was confirmed in *in vitro* uptake studies. These results suggest that JVZ-007 binds to a different epitope of the molecule than PSMA-617 and PSMA-I&T. Furthermore, autoradiography experiments on various PSMA-positive xenografts resulted in similar binding of PSMA-617 and PSMA I&T, 6.4–7.6% and 7.19–9.49% respectively. JVZ-007 on the other hand showed a clearly lower binding of 0.047–0.23%. Autoradiography on kidney and salivary gland tissue revealed a tumor/kidney and a high tumor/salivary gland ratio of 27.03 and 23.68 for JVZ-007, as compared to 3.18 and 4.10 for PSMA-617, and 2.65 and 4.92 for PSMA-I&T, indicating that JVZ-007 is highly tumor specific. **Conclusion:** Our results show that small molecule inhibitors PSMA-617 and PSMA-I&T had similar binding characteristics, while the PSMA nanobody JVZ-007 had a significantly lower binding. This novel nanobody also showed a clearly lower binding to kidney and salivary gland tissue compared to PSMA-617 and PSMA-I&T. This observation may have major implications for the toxicity of PSMA-targeted radionuclide therapy and requires further investigation.

E-PW017

Automated synthesis of [^{68}Ga]Ga-PSMA HBED for compassionate use in France : Experience in Centre Jean Perrin Cancer institute

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Purpose/Introduction: The Prostate Specific Membrane Antigen (PSMA) inhibitor conjugated with the HBED-CC (PSMA-HBED) chelating agent has been developed for radiolabelling with gallium-68, a positron-emitting isotope ($T_{1/2}=68$ min). This [^{68}Ga]Ga-PSMA radiopharmaceutical allows PET-CT imaging of prostate carcinoma cells with overexpression of PSMA. In France, compassionate use of PSMA-HBED is allowed by current regulations since 2016 but subject to a specific authorization by National Health Authority (ANSM) for small-scale preparations of radiopharmaceuticals, requiring submission and expertise of a product dossier. **Subjects & Methods:** The manufacture of [^{68}Ga]Ga-PSMA was performed in an automated synthesis module miniAIO (TRASIS). The gallium-68 generator (GalliaPharm®, Eckert&Ziegler) is eluted with 5 mL of 0.1 M HCl solution and the eluate is directly collected into the reaction vial previously loaded with 10 μg of PSMA-HBED dissolved in 1 mL of acetate buffer 0.7 N. The reaction takes place at 120 °C for 2 min, then 95°C for 5 min. After labelling, [^{68}Ga]Ga-PSMA was retained on a HLB purification cartridge and rinsed with saline. Desorption of [^{68}Ga]Ga-PSMA is achieved by washing with ethanol followed by saline. The final product is formulated for intravenous injection by passing through a 0.22 μm sterilizing filter. All criteria affecting synthesis yield were evaluated. Radiochemical purity of final product was performed using validated radio-HPLC method and must be higher than 95%. Finally, the stability of [^{68}Ga]Ga-PSMA was studied over a period of three hours. **Results:** 26 runs of [^{68}Ga]Ga-PSMA synthesis were carried out over a period of 6 month: 9 performed for the validation process in order to complete the product dossier intended to ANSM and 17 for routine clinical use after the agreement was delivered. Mean complexation yield was 86 % decay corrected. The mean percentage of activity in the waste vial and cartridge were 5.8% and 3.6% respectively. Total synthesis time was approximatively 15 minutes and the radio-HPLC method allows a short time of analysis ($t_r=4.6\pm0.5$ min) compatible with the clinical use. The radiochemical yields were greater than 99%. [^{68}Ga]Ga-PSMA solution is stable at least for 3 hours after manufacturing without decrease of the radiochemical purity. **Discussion/Conclusion:** Trasis method of production of [^{68}Ga]Ga-PSMA was adapted with success in our Radiopharmacy with a reliable synthesis process. In France, this compassionate use of [^{68}Ga]Ga-PSMA is actually the only opportunity to access this radiotracer for patients with prostate carcinoma.

E-PW018

Production of ^{68}Ga -PSMA-HBED-CC for clinical use: synthesis module vs kit

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Aim: ^{68}Ga -PSMA-HBED-CC is an urea-based inhibitor of PSMA employed as PET radiopharmaceutical in the staging of prostate cancer. Production of this radiopharmaceutical is generally performed by using automated synthesis module. Recently,

a kit for ^{68}Ga -PSMA-HBED-CC production was introduced and commercially available. Aim of this work was to compare the production of ^{68}Ga -PSMA-HBED-CC performed with synthesis module to kit based production. **Subjects and Methods:** ^{68}Ga -PSMA-HBED-CC production was performed in a synthesis module equipped with single-use cassettes (Modular-Lab Pharm Tracer, Eckert & Ziegler) using the eluate of GalliaPharm generator (Eckert & Ziegler, 1850 MBq). The eluate was purified with a cation exchange column. Reaction with PSMA-HBED-CC (GMP grade, ABX) was carried out at 95°C for 5 minutes in acetate buffer and followed by purification on C18 column. The product was eluted with ethanol, diluted with saline and sterilized by means of 0.22 μm filter. Kit production runs (configuration A, ANMI) were performed by direct generator elution in a vial, reconstitution of precursor with acetate buffer and by adding the solution to the eluate with labeling reaction of 5 minutes at room temperature. The eluate of Galli Eo generator (IRE Elit, 1850 MBq) was also used (kit configuration B, ANMI). **Results:** Synthesis yield with the automatic module was >85% corrected for the decay ($n = 50$) in 20 minutes. Radiochemical purity was >98% (RP-HPLC) and colloids <1% (TLC), pH 5.5, ethanol and residual Ge-68 content complied with European Pharmacopoeia limits. The product was sterile and apyrogenic. Synthesis yield with kit was 99.9% corrected for the decay ($n = 50$) in 10 minutes. Radiochemical purity was >98% (RP-HPLC) and colloids <1% (TLC), pH 4.2 and the product was found to be ethanol free, sterile and apyrogenic. The residual content of Ge-68 complies with the specification of the European Pharmacopoeia. **Conclusion:** Using synthesis module, ^{68}Ga -PSMA-HBED-CC was produced in high yield and high radiochemical purity. However, the use of kit makes all the ^{68}Ga activity coming from the generator available as radiopharmaceutical, with a radiochemical and radionuclidic purity similar to these obtained with synthesis module after purification. Kit labelling has less operational complexity and no presence of additional reagents but those already available in the package. Furthermore, the use of kit speeds up the process, cutting operational times (no need for module and reactive preparation, no eluate and product purification). All these results make the kit a valid alternative for the production of ^{68}Ga -PSMA-HBED-CC for clinical use.

E-PW019

Optimization Of [^{18}F]-FPSMA1007 Synthesis HPLC Free On Fastlab Platform And QC Optimization On GMP PROSPECTC

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Introduction: Over the past years, many different PET agents have been developed to investigating on Prostate Cancer to make the noninvasive approach a reality. Due to the high incidence of this pathology are mandatory to investigate on a fluorine-18 tracer that give the possibility to overcome the gallium-68 tracers limitations. The aim of this study is to optimize production of [^{18}F]FPSMA1007 on GE FASTLAB® module, in a stable high yield with a wide range of inlet activity and setting up a

faster, efficient and EU Pharmacopoeia compliant QC to shorten the time of product realize. **Material&Methods:** The synthesis method is based on one step synthesis using a new precursor commercialized by ABX and is tuned on Ge FASTLab® synthesizer. All the reagents are included on a single use cassette. The [^{18}F]Fluorine was trapped on QMA and eluted with a mixture of $\text{TBAHCO}_3/\text{ACN}$ or $\text{K222}/\text{ACN}/\text{K}_2\text{CO}_3$ and after drying on synthesis reactor, the ABX precursor in DMSO was added to proceed with the nucleophilic [^{18}F]-Fluorination. The reaction mixture was heated at 95°C@10 min after the reaction step the mixture was cooled at 35°C to starting the purification step followed by formulation. The total process takes place on 37 minutes. HPLC analysis was performed on an Agilent 1260 Infinity HPLC with UV and gamma-ray detector. Column 4,6x100 Eclipse Plus C18 3,5 μm (Agilent) in isocratic conditions running CH_3CN and 0.1 % TFA (70/30, run time 15 min). **Results:** Two different elution solution was used to compare the final process yields, at the same time, high activity runs were performed, in different inlet activity range, to evaluating the yield and product stability in final formulation. For stability study a range of 1-2.5 GBq/ml radioactive concentration was evaluated at room and at 40°C for up to 12h. According to final product formula specification the synthesis yield was stable on range 30-50 % at the inlet activity range (55-170 GBq) with a A_m (800-3500 GBq/ μmol) at EOS. The radiochemical purity for all the runs was > 96 % and chemical impurities were < 0.1 mg/V. **Conclusion:** All the synthesis performed by using the K222 elution solution shows slightly lower yield compared to TBA, at the same time any difference, in quality control profile and stability were found, all the products collected were stable and in high chemical/radiochemical purity. The HPLC and TLC methods setup allow to perform a complete purity evaluation on less than 15 min.

E-PW020

Incorporating novel pa-chelates into PSMA-targeting lutetium-177-labeled theranostic compounds provides easier tracer delivery

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The aim of this project is to develop and pre-clinically evaluate theranostic compound molecules targeting PSMA - a validated transmembrane protein highly expressed in metastatic PCa - by using available tumour targeting urea-derived biomolecules, conjugated to novel picolinic acid (pa) - derived chelates named pa-ligands. Unconjugated pa-ligands allowed for high-yield radiolabeling at room temperature. In our studies, we confirmed quantitative radiolabeling at concentrations as low as 10^{-6}M at ambient temperature and relative ligand ratio up to 10:1 and 2:1, depending on the incorporated chelate, compared to 10^{-4}M for ^{177}Lu -DOTA at ambient temperature and 10^{-5}M at 80 °C. Both ^{177}Lu -pypa-PSMA and ^{177}Lu -octapa-PSMA showed exceptional serum stability at 37°C over 8 and 6 days, respectively. Competitive binding affinity assays performed with DCFPyL, for all four of the pa-ligand containing conjugated compounds tested

thus far, confirmed strong PSMA-binding (mean K_i ranges between 0.16–3.4 nM). First *in vivo* studies in mice for both tested PSMA-targeting compounds labeled with ^{177}Lu showed stable accumulation in PSMA-expressing LNCaP tumours ($n=30$) after 1 ($4.0 \pm 0.7\%$ ID/g) and 4 hours ($4.8 \pm 1.15\%$ ID/g) for ^{177}Lu -py-pa-PSMA, and after 1 hour for ^{177}Lu -octapa-PSMA ($4.9 \pm 0.9\%$ ID/g), with low uptake in bone, liver and intestine. Further optimization is underway with modifications of the linker to improve tumour uptake and retention. In conclusion, pa-ligands, offer convenient room temperature labeling, of PSMA targeting compounds, and can make a valuable addition to PSMA targeting radiopharmaceuticals.

411 Sunday, October 14, 2018, 14:30 - 16:00, Hall A

e-Poster Walk 3 - Do.MoRe: Clinical Dosimetry

E-PW021

Application of new ICRP biokinetic models for pharmacokinetic modelling of Radium-223 used for treatment of prostate cancer

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Introduction: ^{223}Ra -Dichloride (^{223}Ra , Xofigo) is a bone-seeking alpha-emitter (physical half-life 11.43 days) and is used as a registered radiopharmaceutical in patients with castration-resistant metastatic prostate cancer. The objective of this study is to apply the new ICRP biokinetic models of ^{223}Ra and its seven decay products to assess their pharmacokinetic behaviour in the human body. The biodistributions of ^{223}Ra and its decay products can be compared to clinical data of ^{223}Ra for the model validation. **Material and Methods:** Starting from the current systemic biokinetic models of the elements radium, radon, polonium, lead, bismuth, and thallium published by the International Committee on Radiation Protection (ICRP), the biokinetic models of ^{223}Ra and its decay products (^{219}Rn , ^{215}Po , ^{211}Pb , ^{211}Bi , ^{211}Po , and ^{207}Tl) until the decay to the stable ^{207}Pb were built and interconnected as independent biokinetic models through their decay constants to ^{223}Ra ; the complete biokinetic models were implemented in the SAAM II computer program. The transfer coefficients of the models were taken from ICRP Publication 71 and 137 or were recalculated because four new model compartments (representing the organs spleen, gonads, trabecular marrow and cortical marrow) had to be added to the biokinetic model of the parent nuclide ^{223}Ra . **Results:** This work presents the setup of the biokinetic model chain of ^{223}Ra which describes the sources and sinks of ^{223}Ra and its decay products. The time-dependent biodistributions of ^{223}Ra and its decay products in different organs are presented and compared to available clinical imaging or bioassay data. **Conclusion:** The linked independent biokinetic models of ^{223}Ra and its daughter nuclides may help to predict their distribution in patients after administration of the radiopharmaceutical Xofigo, and could later on be used for dosimetric assessments.

E-PW022

Prognostic impact of dosimetry calculation in bone metastases treated with 223Radium (Xofigo) in the therapeutic management of patients with metastatic castration-resistant prostate cancer

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Aim: To develop the methodology to quantify the activity of ^{223}Ra in bone metastases, calculate the absorbed dose and individually evaluate the effectiveness of treatment. **Materials and Methods:** Prospective study of 7 patients treated in 2017 with ^{223}Ra (31 doses). Absorbed dose (Gy) of more intense uptake foci, half-life of ^{223}Ra in the lesion (days) and DRBE (relative biological effectiveness (RBE) models in the RBE-weighted dose) were calculated from whole body planar images and SPECT/CT 48h after the administration of ^{223}Ra and images of relevant regions 7 days after treatment. Analytical and clinical values (such as: improvement, stabilization, deterioration) were registered. **Results:** Patient 1 (6 doses): D_{RBE} 22Gy in sacrum, 8 Gy in right elbow, clinically stable, PSA from 27.15 to 45.42 ng/mL. Patient 2 (6 doses): D_{RBE} 143 Gy in sternum, < 9 Gy in the rest of lesions, clinical improvement, PSA from 24.50 to 71.20 ng/mL. Patient 3 (5 doses): dosimetry evaluation was impossible because of intense bowel uptake, clinical deterioration, PSA from 240 to 289 ng/mL. Patient 4 (5 doses): D_{RBE} 60 Gy in T12, 88 Gy L4, symptomatic improvement, PSA from 13.5 to 17.60 ng/mL. Patient 5 (4 doses, ongoing treatment): D_{RBE} 64 Gy in L1, clinical improvement, PSA from 218 to 91.6 ng/mL. Patient 6 (3 doses): D_{RBE} 46 Gy in T10, < 41 Gy in the rest of lesions, clinically stable, PSA from 96.20 to > 1000 ng/mL. Patient 7 (2 doses, ongoing treatment): D_{RBE} 14 Gy in thoracic and lumbar spine and pelvis, clinical improvement, PSA 0.16 ng/mL. **Conclusion:** Performing images after ^{223}Ra treatment allows us to estimate absorbed dose in bone metastases, that could be an important criteria to stop or continuing this treatment. More intense bone uptake is related with clinical improvement or stabilization of pain, regardless of PSA levels.

E-PW023

Lesion-specific Voxel-wise Absorbed Radiation Dose Estimation Of Bone Metastases In Patients With Prostate Cancer Using Quantitative Bone SPECT/CT Images

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Purpose: Sr-89 and Ra-223 radionuclide therapy is currently used in clinical practice. Lesion-specific dosimetry of bone metastasis may be useful for planning of therapeutic strategy and effect evaluation. We adapted a voxel-based self-absorbed radiation dose estimation method to quantitative bone SPECT/CT image data, reconstructed using the Conjugate gradient reconstruction with tissue zoning and attenuation and scatter corrections applied (CGZAS) algorithm based on CT zone map-

ping (xSPECT bone), for bone targeted radionuclide therapy. We aimed to estimate the absorbed radiation dose for Sr-89 and Ra-223 therapy in bone metastasis of patients with prostate cancer using quantitative bone SPECT/CT. **Subjects & Methods:** Subjects were 62 patients aged 70.5 ± 7.5 years with bone metastasis from prostate cancer who underwent quantitative CGZAS SPECT/CT using Symbia Intevo (Siemens Healthcare Japan Co. Ltd.) about 3 hours after administration of Tc-99m-methylene diphosphonate. We assumed similar uptake rate for the therapeutic radionuclides for bone scan agents, and that the wash-out was negligible, as compared to the half-lives of therapeutic radionuclides in bone metastasis. We obtained self-absorbed voxel-wise S values for Sr-89 and Ra-223 adjusted to the cubic voxel as 256×256 matrix size of CGZAS SPECT images. Spherical volumes of interests were set on bone lesions. Subsequently, average values of doses and metabolic volumes of bone lesions at threshold of 40% of the maximum values were obtained. The median value and range of absorbed radiation doses in the 123 bone metastases in vertebra was calculated. Administered doses were assumed as 2 MBq/kg of Sr-89 and 55 kBq/kg of Ra-223.

Results: The median value and range of averages of estimated absorbed doses considering relative biological effectiveness (D_{RBE}) in bone metastases were 22.7 Gy (0.41–302 Gy) for Sr-89 therapy ($Sr-89 D_{RBE}$) and 6.8 Gy (0.12–90.8 Gy) for Ra-223 therapy ($Ra-223 D_{RBE}$). If Ra-223 was administered 6 times to the patients, the estimated absorbed doses would be 40.9 Gy (0.73–545 Gy). Based on these values, the median and range of metabolic volumes were 14.3 ml (0.6–94.7 ml). Absorbed doses showed no significant correlation with metabolic volumes. **Conclusion:** Lesion-specific absorbed radiation doses of bone metastases from prostate cancer for Sr-89 and Ra-223 radionuclide therapy were estimated by voxel-based method using CGZAS SPECT images. The results indicated a wide range of absorbed radiation doses based on lesions. Lesion-specific estimation of absorbed radiation dose of bone metastasis may be useful in planning for patient-specific therapy and assessing the effects of response to bone targeted radionuclide therapy.

E-PW024

Predictive power of the post-treatment scans after the first or first two courses of treatment with [^{177}Lu]-DOTA-TATE

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Purpose: To evaluate the predictive power of the dose to kidneys after the first course of treatment with [^{177}Lu]-DOTA-TATE for neuroendocrine tumors on the cumulative kidney dose after of 3 or 4 cycles of treatment. Post-treatment scans (PTS) are acquired after each course of Peptide Receptor Radionuclide Therapy (PRRT) with [^{177}Lu]-DOTA-TATE for personalized radiation dosimetry to ensure a cumulative dose to kidneys under a safety threshold of 25 Gy. **Subjects & Methods:** 187 patients who completed treatment with [^{177}Lu]-DOTA-TATE and underwent PTS for dosimetry calculation were included in this retrospective study. The correlation between the cumulative dose to kidneys after the completion of treatment and the dose after the first or two first cycles was studied, and an algorithm for the follow

up of kidney dose is proposed. **Results:** Patients whose dose to kidneys after the first cycle of treatment is below 5.4 Gy can receive four cycles of treatment with a cumulative kidney dose less than 25 Gy ($p < 0.1$). Patients whose cumulative dose to kidneys after the first two cycles is below 11.4 Gy can also receive four courses of treatment safely ($p < 0.1$). If this value is between 14.5 Gy and 15.4 Gy, they can receive 3 cycles safely ($p < 0.1$) but cannot receive 4 cycles without exceeding a cumulative kidney dose of 25 Gy ($p < 0.05$). **Conclusion:** The follow up of kidney dose after PRRT can be simplified with the algorithm presented in this study, reducing by one third the number of post-treatment scans and reducing hospitalization time for more than half of the treatment cycles.

E-PW025

SPECT/CT based dosimetry for ^{177}Lu Lutetium therapy: impact of day 7 measurements on dose calculation for kidney and tumour

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Introduction: Multiple SPECT/CT measurements are used to determine the voxel-based dose to organs under ^{177}Lu -DOTATATE or ^{177}Lu -PSMA-617 therapy. The accuracy of dose calculations depends on the number of available images. In clinical routine, acquisition of images at later time-points (e.g. at day 7 after injection) is often problematic because patients are already discharged from hospital. The aim of the present work was to investigate the impact of this late time-point on tumour and kidney dose calculation. **Methods:** Kinetics of kidney and tumour activity were examined in 43 cycles of ^{177}Lu -DOTATATE therapy (5.2 ± 0.4) GBq and 51 cycles of ^{177}Lu -PSMA-617 therapy (5.8 ± 0.7) GBq. Five SPECT/CT images were acquired after activity administration at approx. 2, 19, 43, 67 and 158 h and co-registered to the latest time-point. Volumes of interest were placed on the reference-CT and transferred to SPECT under consideration of partial volume effects. Time integrated activity coefficient was determined by trapezoidal numerical integration of the time-activity curve over all data points and with a tail fit (bi-exponential for 5 and mono-exponential for 4 data points). Dose was calculated with patient-specific voxel-S-values using STRATOS software (Philips Medical Systems). **Results:** Calculated doses in Gy/GBq (mean, [range]) were 0.9 [0.6; 1.7] for the kidneys and 2.7 [0.5; 8.6] for the tumour for ^{177}Lu -DOTATATE therapy and 0.7 [0.3; 1.3] for the kidneys and 2.8 [0.1; 28.0] for the tumour for ^{177}Lu -PSMA-617 therapy. The approximated tail contributed about 10% to the total dose for the kidneys and 20% for the tumours. By using only four time-points, this portion rises up to around 50% for both, kidneys and tumours. Consequently, calculated dose differs. In 67% of the therapy cycles kidney dose is overestimated by 16.4% [0.1; 70.0] and underestimated by -4.3% [-0.6; -12.5] for the remaining cases for ^{177}Lu -DOTATATE therapy. Whereas in 67% of the cycles the calculated tumour dose is underestimated by -15.7% [-2.0; -65.6] and in 37% of the

cycles overestimated by 35.5% [2.5; 120.7]. For ^{177}Lu -PSMA-617 therapy the kidney dose is underestimated in most cycles (92%) by -16.4% [-1.0;-43.2] and overestimated by 44.4% [0.2; 146.0] in only 8%. In 59% of the cycles the tumour dose is overestimated by 20.4% [0.7; 63.0] and underestimated by -7.4% [-1.1;-22.2] in the remaining cases. **Conclusion:** If only four time-points are used for dose calculation, the estimated tail enlarges clearly and dose results differ significantly by over- and underestimation. In individual cases this deviation can be extremely huge.

E-PW026

An optimal sampling schedule for dosimetry: A simulation study

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Aim: For dosimetry in nuclear medicine, the areas under the time-activity curves (AUCs) for organs at risk and for tumours have to be determined. The used measurement scheme can significantly affect the **AUC**-values and therefore the calculated absorbed dose. In contrast to existing methods for determining an optimal sampling scheme, a general, practical and flexible approach has been developed in this work. **Methods:** A “true” time-activity curve TAC_{true} for the kidneys was determined based on a population study with 5 patients with neuroendocrine tumours (NETs). The most supported function f by the data was a tri-exponential function convoluted with the injection function. The function f , which consisted of 4 adjustable parameters, was further used to compute the activity values at the time points of the sampling schemes. In total, 7560 sampling schemes, each consisting of 5 time points ($t_1, \dots, t_5$), which consider clinical working hours, were investigated. The determined corresponding activity data at these time points were added with multiplicative noise (Gaussian with mean: 0, $SD \in [0.05, 0.1, 0.2, 0.3]$) and fitted with the tri-exponential function f . A fractional standard deviation according to the SD -value of the Gaussian noise was assigned to the data. For each investigated sampling schedule, 10000 replications were performed. The schedule with the lowest Root-Mean-Square Error (**RMSE**) of the determined **AUC**-values to the true value AUC_{true} was defined as optimal. The determined optimal schedules were compared with established schedules (e.g. from literature). **Results:** For $SD=0.2$, the optimal sampling schedule was (7, 8, 32, 80, 100) h with a mean deviation of the **AUC**-values to AUC_{true} of $(-2 \pm 10)\%$. Applying the determined optimal sampling schedules, 4%, 28%, 62% and 76% of the AUCs deviated more than 5% from AUC_{true} for noise levels with $SD=0.05, 0.1, 0.2$ and 0.3 , respectively. In comparison, a measurement schedule from the literature with (1, 2, 4, 24, 48) h and the schedule of (3, 5, 24, 48, 72) h used for the 5 patients showed a significantly higher number of deviations >5% of 50%, 73%, 85%, 88% and 15%, 47%, 71%, 81%, respectively. Late measurement points ($t_5 \geq 100$ h) were generally important for low **RMSE**-values, i.e. for precise and robust measurement schemes. **Conclusion:** A method of determining the optimal sampling schedule for dosimetry, which considers clinical working hours

and measurement uncertainties, has been developed and applied. The simulation study shows that an optimal sampling schedule significantly enhances the accuracy and precision of the determined the **AUC**-values.

E-PW027

Red marrow dosimetry for PRRT: blood versus 3D image based methods of activity measurement

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Red marrow is one of the major organs at risk from Peptide Receptor Radionuclide Therapy (PRRT) with haematological toxicity resulting if excessive irradiation occurs. A widely used dose limit for the red marrow to avoid toxicity incidence is 2Gy. Blood based methods of red marrow dosimetry measuring blood activity concentration as a surrogate for red marrow activity concentration are commonly used for PRRT and other molecular radiotherapy procedures. More recently, image based methods of red marrow activity have been investigated as an alternative method of measuring phar-mo-kinetics of the red marrow. These methods rely on measurement of red marrow activity on 2D or 3D imaging data from a sub-region of marrow to estimate the total red marrow activity. This study reports of the results of blood and 3D image based red marrow dosimetry performed for 10 ^{177}Lu Dotatate patients treated between 2011 and 2016. Time activity curves generated from blood and image based methods are compared, and the impact of these two different measurement methods on red marrow dose due to self-irradiation (‘self-dose’) assessed. 6 blood samples and 4 abdominal SPECT-CT images were acquired per patient post therapy. Image based red marrow activity was measured from the $L_2 - L_4$ vertebra in the lumbar spine on the SPECT images. The effect of being able to use a patient specific estimate of the patient’s red marrow mass was assessed for the image based methods. Patient specific red marrow mass was estimated volumetrically from diagnostic quality CT of the patient’s lumbar vertebrae. An uncertainties analysis was performed for both methods of dose calculation and the magnitude of uncertainties compared, both for the self - dose and at each stage of the dose calculation. Image based red marrow doses resulted in higher red marrow doses than blood based methods. The largest contributor to red marrow dose uncertainty for the blood based methods was the sensitivity factor used to convert counts to activity values, whereas the largest contributor was TAC cumulated activity for the image based methods.

E-PW028

A knowledge-based model to correct I-131 biokinetics modification due to the administration of rhTSH in paediatric patients affected by differentiated thyroid carcinoma

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Aim: Use of ¹²³I-Nal, in combination with recombinant human TSH (rhTSH), has several possible advantages for pre-therapeutic red marrow dosimetry in ¹³¹I differentiated thyroid cancer (mDTC) therapy: it reduces radiation exposure and provides high-sensitivity diagnostic scans. The short physical half-time of ¹²³I and the well-known modification of the biokinetic due to rhTSH administration could be inadequate for dosimetric accuracy. The aim of this study was to introduce a knowledge-based model to correct biokinetics results and to improve the accuracy of the dosimetric results by comparing whole-body (WB) and blood residence time (τ) as calculated during pre-treatment (PT) and in-treatment (IT) dosimetry. **Materials and Methods:** 20 paediatric patients affected by mDTC, during PT phase, underwent an administration of ¹²³I-Nal two days after the administration of rhTSH. ¹²³I biokinetic was studied collecting blood samples and WB images with a time window of [0.5;54] h. During the IT phase patients were administered with a therapeutic activity of ¹³¹I-Nal after four weeks of LT4 replacement with LT3 and two weeks of thyroid hormone withdrawal. In a time window of [0.5;144] h ¹³¹I biokinetic was studied collecting blood samples and measuring WB activities. τ of blood and WB were determined according to EANM guidelines. Cohort has been divided in two groups of ten patients each. Taking into account the percentage difference between PT and IT biokinetics curves of the first group, two correction curves have been obtained (for blood and for WB data). These curves have been used to correct biokinetic data of the other group. To evaluate the impact of a different time sampling, τ values were compared with Wilcoxon paired-samples test and its percentage differences between PT and IT were evaluated using ¹³¹I data both in a restricted time window [0;54] h and entire time window. **Results:** Using the restricted time window, the mean percentage difference of τ_{blood} between PT and IT was -46% (p-value<0.05) while the same difference was about -9% (p-value=0.15) if the correction curve was used. Analogously, τ_{WB} percent difference was -35% (p-value<0.05) and 4% (p-value=0.30) with or without the correction. Using all data-set and the correction curves, the differences between PT and IT residence times increase to -12% (p-value<0.05) for blood and 6% for WB (p-value=0.07). **Conclusion:** τ underestimation in PT dosimetry is mainly due to administration of rhTSH (causing an acceleration of washout phase) and the restricted time window. The method improves the prediction power of PT dosimetry.

E-PW029

Clinical Feasibility of Post-Radioembolization Hepatopulmonary Shunt Fraction Assessment of Yttrium-90 Microspheres using PET/CT

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Aim: To assess the clinical feasibility for estimating Yttrium-90 (90Y) microsphere hepatopulmonary shunt fraction (HPSF) using conventional photomultiplier tube-based PET/CT (cPET/CT) following routine radioembolization and compare with the pre-radioembolization ^{99m}Tc macroaggregated albumin (MAA) HPSF. **Materials and Methods:** In an ongoing Phase I clinical trial, pre-radioembolization ^{99m}Tc MAA HPSF was determined in 11 patients who then underwent routine radioembolization using 90Y glass microspheres (0.7 - 4 GBq) for hepatic malignancies and metastases. Investigational ⁹⁰Y cPET/CT imaging of the lungs and liver was performed in each patient following radioembolization using a total image acquisition time of 21 min. Using the Intellispace Portal workstation (Philips), intra-individual comparison of pre-radioembolization MAA SPECT/CT and post-radioembolization 90Y cPET/CT image quality, intrahepatic radioactivity biodistribution, pre-/post-radioembolization concordance, and volumetric assessment of intrahepatic radioactivity was performed. The pre-radioembolization ^{99m}Tc MAA HPSF was calculated using routine planar scintigraphy approaches. Post-radioembolization 90Y HPSF was estimated using MIMVista (MIM Software). ⁹⁰Y cPET HPSF assessment was performed using ROIs of the lungs and liver and then calculated using the integral radioactivity in lungs with respect to integral radioactivity in lungs plus liver. **Results:** All patients had evaluable pre-radioembolization MAA and post-radioembolization ⁹⁰Y cPET images for qualitative assessment of intrahepatic radioactivity biodistribution. There were no significant qualitative differences in intrahepatic radioactivity biodistribution on pre-/post-radioembolization imaging. Quantitatively, there was also no significant difference in the measured intrahepatic radioactivity volumes (MAA was 1139 +/- 729 mL and 90Y was 1147 +/- 666 mL). On post-radioembolization cPET, there were no instances of significant ⁹⁰Y microspheres shunting outside of the liver or any discrete foci of abnormally increased 90Y activity detected in the lungs. PET estimation of ⁹⁰Y HPSF was consistently and significantly less (cPET was 0.2 +/- 0.3 %) than MAA HPSF (8 +/- 7 %, P < 0.002). **Conclusion:** At present, quantitative cPET assessment of the 90Y microsphere HPSF following liver radioembolization has not been described and likewise no data are available comparing pre-radioembolization MAA HPSF with post-radioembolization 90Y HPSF in these patients. This study demonstrates the clinical feasibility of assessing the 90Y HPSF using cPET/CT in patients following routine 90Y radioembolization. Such cPET-based dosimetric approaches could have both diagnostic and therapeutic implications by identifying subsets of patients with larger or smaller than anticipated HPSFs when compared with pre-radioembolization MAA HPSF. Furthermore, routine assessment of 90Y HPSF with quantitative cPET approaches may provide new insights into intra-hepatic tumor neovascularity and vascular shunting in various hepatic malignancies/metastases.

E-PW030

In-vitro dosimetry of radioactive patches incorporating Rhenium-188 for local radionuclide therapy

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Introduction: Rhenium-188 (Re-188) can be used for local radionuclide therapy of various benign and malignant skin diseases. The aim of this study was to perform in vitro dosimetry of radioactive patches incorporating Re-188 to determine the surface dose delivered, dose rate, depth in skin upto which significant radiation dose is delivered and total radiation dose delivered upto that depth. **Materials and Methods:** TLD 700H chip dosimeters were used for dosimetry of the in-house prepared circular radioactive patches of area 1cm² incorporating 1mCi Re-188 distributed uniformly over the patch. Dosimeters were first standardized which included calibration and selection of dosimeters with uniform response. The selected dosimeter chips were annealed and placed over the surface of the sealed patch for different time intervals i.e. 1, 5, 10, 20, 30, 45, 50 and 60 minutes to determine the dose delivered at the surface and to determine the dose rate. Thermoluminescence (TL) curves were obtained and absorbed dose corrected for weight was determined for each chip. Curves were plotted for time of exposure verses absorbed dose. For determining the depth in skin upto which significant radiation dose will be delivered, and to determine the total radiation dose delivered upto that depth, tissue equivalent material sheets (Lucite) of 1 mm were used. Measurements were done in duplicates using TLD 700H chips. TL curves were obtained for all the chips and graphs plotted for absorbed dose verses the lucite thickness. Percentage drop in dose rate and depth after which dose rate was negligible was determined. Dose delivered at different depths and cumulative dose delivered upto significant depth was found. **Results:** Dose delivered to the TLD chip at the surface of the patch at 1, 5, 10, 20, 30, 45, 50 and 60 minutes was found to be 0.14, 0.7, 1.46, 2.78, 4.11, 6.31, 7.2 and 8.62 Gy respectively and was found to have a linear relationship with respect to the duration of exposure. Dose rate at the surface was found to be approximately 8.6 Gy/hr. The depth upto which significant radiation dose is delivered was found to be 4mm after which it dropped to less than 1%. Total cumulative dose delivered upto 4 mm depth was found to be 14.06 Gy in 1 hr. **Conclusion:** For a circular patch of 1cm² area containing 1mCi of Re-188 activity distributed uniformly, the surface dose rate was found to be 8.6 Gy/hr. The total cumulative dose delivered upto 4mm depth was 14.06 Gy/hr.

511 Sunday, October 14, 2018, 16:30 -18:00, Hall A

e-Poster Walk 4 - Bone & Joint: Scintillating Bone Imaging

E-PW031

Influence Of Clinical Factors On ^{99m}Tc-HMDP Uptake In Normal Lumbar Vertebra: Evaluation Using SUV Corrected By Body Weight, Lean Body Mass, And Body Surface Area

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Purpose: Quantitative assessment of normal bone uptake would be useful to evaluate the risk of osteoporosis as well as to differ-

entiate between normal and pathologic bone uptake. The aims of this study were to evaluate which clinical variables could be associated with normal lumbar uptake and to determine what correction method to calculate standardized uptake value (SUV) is preferable for quantifying bone uptake. **Subjects & Methods:** Quantitative Tc-99m HMDP SPECT/CT data were obtained from 96 cancer patients without any of bone metastasis or recent cancer treatment such as hormonal therapy. SUVs in cancellous bone of the third lumbar vertebral body (L3) were calculated using body weight (SUVbw), lean body mass according to James (SUVlbm1) and Janmahasatian (SUVlbm2) formulations, and body surface area (SUVbsa). The effect of potentially influencing parameters including age, gender, circulation time, estimated glomerular filtration rate (eGFR) and body mass index (BMI) on the SUVs were investigated. **Results:** In multivariate linear regression analyses, high age, female gender and higher eGFR were found to be independent factors associated with decreased SUVs with all correction methods. In addition, higher BMI was associated with higher SUVbw despite the fact that Tc-99m HMDP barely accumulates in fat and soft-tissue. SUVlbm could be well predicted by age, gender and eGFR; the prediction was better for SUVlbm2 ($R^2 = 0.5797$) than for SUVlbm1 ($R^2 = 0.4610$). The effects of age ($\beta = -0.5379$, $p < .0001$) and gender ($\beta = -0.6672$, $p < .0001$) on SUVlbm2 were higher than that of eGFR ($\beta = -0.1802$, $p = 0.023$). A similar tendency was observed for SUVlbm1 (age, $\beta = -0.6324$, $p < .0001$; gender, $\beta = -0.4732$, $p < .0001$; eGFR, $\beta = -0.2032$, $p = 0.024$). **Conclusions:** Tc-99m HMDP uptake values in normal lumbar spine are influenced by age, gender and eGFR. SUVlbm, especially when using Janmahasatian formulation, appears to be preferable for quantifying Tc-99m HMDP uptake to avoid overestimation of bone metabolism in obese patients.

E-PW032

The Relationship Between Bone SPECT-CT And VAS Pain Scores In Patients With Joint Impingement Syndrome

X. Zhang, Q. Luo; Sixth People's Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, CHINA.

Purpose: Osteoarthritis and impingement syndrome was common disease in sport medicine, however, failure in pain alleviation by surgical intervention troubles orthopedists. Hybrid SPECT/CT combines the metabolic and structural information of the ankle. Here, we hope to evaluate whether bone tracer uptake (BTU) was related to lesion types and visual analogue scale (VAS) pain scores in arthritis patients with or without bony impingement. **Subjects & Methods:** All patients included in this study underwent ankle SPECT/CT. Uptake grade of bone tracer, lesion types by anatomical changes and VAS pain scores before and after surgical intervention were retrospectively collected and prospectively analyzed. **Results:** From November 2015 to January 2018, 50 individuals with arthritis were selected in the current study, including 29 (58.0%) participants with osseous impingement of the ankle and 21 (42.0%) patients without ankle impingement syndrome. Among the 29 patients with bony impingement, 16 (55.2%), 4 (13.8%) and 9 (31.0%) were anterior, posterior or both types of ankle impingement existed in the same patient, separately. Uptake grade on ankle SPECT/CT was significantly related

to lesion types of ankle impingement ($P < 0.001$). The VAS pain score was significantly associated with BTU grade before treatment ($P < 0.001$), however, showed no obvious correlation with lesion types. **Conclusion:** For ankle SPECT/CT in arthritis with or without bony impingement syndrome, bone tracer uptake was related to lesion types and the VAS pain scores showed strong association with BTU grade. Ankle SPECT/CT can provide better visualization of bone metabolism on impingement lesions and may help to make treatment decision.

E-PW033

Clinical study on the hybrid SPECT/CT imaging for patients with chronic pain on the foot and ankle

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Purpose: To investigate the characteristics and potential clinical applications of hybrid SPECT/CT imaging for patients complained of chronic foot and ankle pain. **Subjects & Methods:** This study retrospectively collected 161 cases with chronic foot and ankle pain and analyzed the imaging features of 99mTc-MDP hybrid SPECT/CT scans, including type of bone tracer uptake, locations and CT manifestations of lesions. **Results:** All 161 patients had chronic foot and ankle pain. Among them, 159 cases showed positive hybrid SPECT/CT findings and 158 cases (98.1%) had positive 99mTc-MDP uptakes. Four of the 6 cases with negative or indeterminate CT scans had positive 99mTc-MDP uptake, while 1 out of the 3 cases with negative 99mTc-MDP uptake cases presented positive changes by CT. Among the 158 patients with 99mTc-MDP positive uptake, the most common lesion sites with increased bone tracer uptake was unilateral lesion at single foot (65.8%), mostly located in the upper (81/158; 51.3%) and subtalar joints (56/158; 35.4%). CT findings of those SPECT-positive lesions showed articular sclerosis (107/158; 67.7%) and increased bone density (76/158; 48.1%). **Conclusion:** Hybrid SPECT/CT image can effectively evaluate the characteristics of patients with chronic foot and ankle pain. Using bone tracer uptake (hotspots) to locate the specific site (pain sites) in foot and ankle, thus guide clinical precision treatment. SPECT/CT tomographic imaging has potential clinical application prospects and promotion value.

E-PW034

Usefulness of ^{18}F -FDG PET/CT in the follow-up of musculoskeletal inflammation in patients with polymyalgia rheumatica

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Purpose: Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disease predominantly affecting older people

and characterized by pain and stiffness of the neck, shoulder and pelvic girdles. Our aim was to evaluate the usefulness of ^{18}F -FDG PET/CT in the study of severity and extent of musculoskeletal inflammation and also in the follow-up of patients with PMR. **Materials and Methods:** This retrospective study included 34 consecutive patients (25 women, mean age: 66.4 ± 9.9 y.) with a diagnosis of PMR. ^{18}F -FDG PET/CT was requested for atypical symptoms, persistently increased C-reactive protein and erythrocyte sedimentation rate, no treatment response or relapse after treatment reduction or withdrawal. An initial and follow-up ^{18}F -FDG PET/CT at 3-23 months were performed in all patients. Twenty-four (70.6%) of them were on immunosuppressive treatment at the time of the initial PET/CT. A visual analysis (from 0 to 3) of initial and follow-up ^{18}F -FDG uptake was performed in seven musculoskeletal regions: shoulders, sternoclavicular joints, interspinous bursae, hips, knees, ischial tuberosities and subtrochanteric bursae. Based on this analysis, an overall score from 0 to 21 was assigned to each ^{18}F -FDG PET/CT scan. **Results:** Initial PET/CT showed ^{18}F -FDG uptake in 45.7% (113/238) of the musculoskeletal regions evaluated, with a mean $\pm$ SD of 3.3 ± 2.0 involved regions per patient. Follow-up PET/CT showed ^{18}F -FDG uptake in 39.9% (95/238) of the regions, with 2.8 ± 2.1 involved regions per patient. The mean $\pm$ SD overall score decreased from 6.4 ± 5.2 at the initial PET/CT to 4.4 ± 4.1 at the follow-up ($p = 0.0965$). The score also decreased in all the regions evaluated except for the ischial tuberosities, although the differences were not statistically significant. The more frequently and intensely involved region was the shoulders (79.4% of the patients at the initial PET/CT and 61.8% at the follow-up). Twenty-five patients experienced clinical improvement at follow-up. In these patients, the percentage of regions with ^{18}F -FDG uptake decreased from 50.8% (89/115) to 40% (70/115) ($p = 0.0058$). The mean $\pm$ SD overall score also decreased from 6.9 ± 5.6 to 4.2 ± 3.9 ($p = 0.0428$). In the other 9 patients with no clinical improvement the percentage of regions with ^{18}F -FDG uptake increased from 38.1% (24/63) to 39.7% (25/63) and the mean $\pm$ SD overall score increased from 4.9 ± 3.9 to 5.1 ± 4.6 , although the differences were not statistically significant. **Conclusion:** ^{18}F -FDG PET/CT was a good marker of musculoskeletal inflammation in patients with PMR, both initially and in the follow-up, in correlation with the clinical outcome.

E-PW035

Differences of articular and extraarticular involvement in polymyalgia rheumatica: comparison by whole-body ^{18}F -FDG-PET/CT

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Aims: This retrospective study sought to clarify differences of articular and extraarticular involvement in patients with polymyalgia rheumatic (PMR) using ^{18}F -fluorodeoxyglucose posi-

tron emission tomography/computed tomography (FDG-PET/CT). **Material and Methods:** Eighteen newly diagnosed PMR patients (mean age 72 years) were enrolled in this study and underwent FDG-PET/CT scanning. Eleven patients also underwent lower-extremity scanning in addition to conventional scanning. We visually and semi-quantitatively analyzed the FDG-PET/CT images, and compared the incidences of abnormal FDG accumulation, visual scoring (accumulation score, AS: 0–4), and SUVmax among proximal joints (shoulder, hip, and sternoclavicular joints), distal joints (upper and lower extremities), and extraarticular synovial structures (ESS: greater trochanter, ischial tuberosity, praepubic region, and spinous process). AS and SUVmax of periarticular bursas and articular capsules were also compared in shoulder and hip joints. **Results:** The incidences of FDG accumulation were extremely high in proximal joints (95.4%) and ESS (96.0%), with both values being significantly higher than those in distal joints (32.8%, $p < 0.0001$). However, the knee-accumulation incidence was exceptionally high (95.5%) in the distal joints. Proximal joints (3.14 ± 0.94) and ESS (2.83 ± 0.94) showed high AS values, which were significantly higher than those for the distal joints (1.01 ± 1.51 , $p < 0.0001$), although all three structures tended to show similar SUVmax (3.84 ± 1.23 , 3.39 ± 1.16 , and 3.62 ± 1.52 , respectively). In shoulder and hip joints, AS (3.25 ± 0.81 vs. 2.22 ± 0.59 in shoulder, 3.17 ± 1.03 vs. 1.0 ± 1.10 in hip) and SUVmax (3.84 ± 1.24 vs. 2.37 ± 0.67 in shoulder, 4.33 ± 1.52 vs. 2.33 ± 0.62 in hip) were significantly higher in periarticular bursas than articular capsules ($p < 0.0001$). **Conclusion:** ESS were considered to be the main affected areas in PMR patients, followed by the proximal joints, and bursitis played a major role. Distal joint involvement occurred with low frequency except in the knee joints.

E-PW036

Tc-99m-DPD bone scan quantification: Tibial and Patellar Subchondral Bone Uptake Assessment in Knee Osteoarthritis (OA)

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Purpose: Bone scintigraphy with Tc-99m labeled DPD can identify osteoarthritic bone changes with a high sensitivity especially at the knee level due to osteoblastic reactions. The aim of this study was to investigate the emerging role of Tc-99m DPD uptake quantification with SPECT/CT in normal and osteoarthritic tibial and patellar subchondral bone and to correlate SUV to CT density using Hounsfield units (HU). **Materials and Methods:** We retrospectively assessed 12 patients (mean age 51 ± 15 years) with minimal or no knee OA and 11 patients (mean age 61 ± 12 years) with advanced knee OA and contralateral total knee replacement. Quantitative xSPECT/CT (SYMBIA INTEVO, Siemens Healthineers) was acquired and SUV quantified on post-processed images with measurements of SUVmax, SUVmean (g/mL) in tibial and patellar subchondral bone. HU of the same regions of interest were measured on CT images. **Results:** A total number of 11 osteoarthritic knees were analyzed showing a mean tibial and patellar SUVmax, SUVmean (g/mL) and CT density (HU) of 6.7 ± 2.6 , 4.9 ± 2.3 and 273.7 ± 76.9 and 7.7 ± 3.9 , 4.9 ± 1.8

and 389 ± 288 , respectively. In 12 knees with no or minimal OA mean corresponding SUVmax, SUVmean (g/mL) and CT density (HU) were 3.7 ± 1.2 , 2.3 ± 0.8 and 2669 ± 356 and 3.9 ± 1.9 , 2.4 ± 1 , and 288 ± 57 respectively. Comparison of both SUVmax and SUVmean between the OA and no or minimal OA groups showed a statistically significant difference only for tibial SUVmax and SUV mean, with $p = 0.004$ and $p = 0.032$. We found a positive correlation between SUVmax and SUVmean with CT density (HU) in tibial subchondral bone in the group with no or minimal OA ($\rho = 0.36$, $p = 0.013$ and $\rho = 0.38$, $p = 0.09$), but not in the OA group ($\rho = 0.36$, $p = 0.1$ and $\rho = 0.37$, $p = 0.08$). **Conclusion:** This study showed significant differences in Tc-99m-DPD uptake on bone scan between OA and no or minimal OA in the subchondral tibial bone based on quantitative data analysis. There were significantly higher SUVmax and SUVmean in OA group but no significant difference in CT density (HU). Thus, integrating quantitative analysis of bone scan data in future knee OA study models might be of value.

E-PW037

Hybrid image (SPECT-CT) in the diagnosis of condylar hyperplasia

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Purpose: To study the diagnostic validity of hybrid single photon emission computed tomography (SPECT) integrated with multidetector computed tomography (SPECT/CT) in diagnosis of condylar hyperplasia (CH). **Subjects and Methods:** 55 patients with suspected CH underwent SPECT/CT were studied during the period from January 2011 to December 2014. In all cases, bone scintigraphy with 99mTc-MDP was performed, including static views and SPECT-CT scan of the skull 3 hours post injection. A hybrid double-head gamma camera, Siemens, model Symbia T6 was used. The SPECT images were made on 128×128 matrix, elliptical rotation in step and shoot mode, with a time of 20 sec / image and high resolution collimator. The CT cuts (low intensity, 2.5mAs) were made every 5 mm. The planar, tomographic and fused images were analyzed, recording the detection of asymmetry in tracer uptake in temporomaxillary joints. The results were confirmed with clinical follow-up at least 24 months. **Results:** Increased bone activity was noted in the affected condyles for all CH patients. The relative percentage uptake on the affected side was significantly higher than the uptake on the contralateral side (58.8 ± 3.78 vs 41.2 ± 4.19 %, $P < 0.0001$). Also, the condyle to clivus ratio on the affected side was significantly higher than that on contralateral side (1.05 ± 0.42 vs 0.76 ± 0.32 , $P < 0.001$). The diagnostic performance of SPECT/CT in diagnosis of CH was demonstrated as a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 90%, 92%, 93%, 88%, and 90.9% respectively. **Conclusion:** SPECT/CT had a high diagnostic validity in assessment of CH and can provide a reference for treatment options.

E-PW038

The value of wrist ^{99m}Tc MDP SPECT/CT in identifying the pain generator in both surgical and non-surgical patients.

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Introduction: ^{99m}Tc MDP SPECT/CT is increasingly used in cases of wrist pain to identify potential pain generator in both surgical and non-surgical patients. It provides both functional information regarding blood flow and new bone formation along with anatomical detail to identify the source of pain. In our Trust, hand surgeons use conventional radiological imaging (plain film, MRI and USS) along with ^{99m}Tc MDP SPECT/CT to investigate the cause of patient's symptoms and to plan further management. **Methods:** We did a retrospective analysis of ^{99m}Tc MDP SPECT/CT wrist studies performed between 01/01/2013 and 31/03/18. The scans were performed on Philips Precedence 16 slice SPECT/CT camera. Results were obtained from the departmental database and correlated with the electronic patient records. Data collected included indications for imaging, referral source, previous interventions, additional imaging and SPECT/CT reports. **Results:** 133 studies were performed over five years. The indications included wrist pain following trauma, continued symptoms following intervention or possible osteomyelitis. Localising a pain generator was the leading clinical question asked. Two thirds of the patients were female (66%) and one-third males (34%). The vast majority of referrals was from plastic surgeons (68%) the remaining from orthopaedics, rheumatology and general practitioners. Of these 133 patients 39 % of these patients had undergone previous surgery or other intervention done on the wrist while 61% were non-surgical patients. Of the surgical patients SPECT/CT of the wrist was able to localise the pain generator in 90% of patients while in the non-surgical patients SPECT/CT could localise the source of pain in 74% of patients. Of these total 133 patients, 19% had an MRI scan previously. **Discussion:** ^{99m}Tc MDP SPECT/CT is a valuable hybrid imaging tool used in conjunction with conventional imaging modalities. It is particularly useful in painful wrists where functional information is required to confirm a diagnosis, narrow down the differential diagnosis or localise a specific pain generator site. Clinical assessment and other cross section imaging can be limited in its ability to identify specific pain generators in the wrist especially in post-operative patients due to metal artefact. This is especially challenging while performing MRI and SPECT/CT can circumvent some of these issues. **Conclusion** The SPECT/CT is an effective imaging tool to localise the pain generator in painful wrists, particularly those who have undergone surgical intervention.

E-PW039

Value Of SPECT / CT In Mandibular Condylar Hyperplasia

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Purpose: To assess the usefulness of SPECT / CT in patients with Mandibular Condyle Hyperplasia (MCH). **Materials and Methods:** A retrospective study was carried out through the review of medical records. 60 patients from the Maxillofacial Surgery Service were included in the period between January 2016 and April 2018 with clinical suspicion of HCM. 71 SPECT / CT were processed, taking areas of interest in the temporomandibular joints in the axial plane and the findings were interpreted quantitatively by calculating the condyle index. **Results:** In 15 of the 60 patients studied, a condylar index (CI) $\geq 55\%$ was found, with values between 55.1% and 66.6%, with the right condyle affected in 62.5% of the cases. The female sex represented 86.7% and the average age at diagnosis was 23 years. Follow-up with SPECT / CT was performed in 18.33% of patients, at 3 and 24 months in 9.1% each, at 6 months in 27.2%; at 7, 12 and 17 months in 18.2% each case. There was evidence of normality persistence in 54.5%, normalization and persistent hypercaptation presented a value of 9.1%, and conversion to a pathological CI in 27.3%. In terms of management, high condylectomy of the affected side was scheduled to 53.4%, while expectant management was decided in 33.3% (representing 6.7% of a false positive case that corresponded to NMR with hypoplasia), the remaining 13.3% is waiting for appointment with maxillofacial. **Conclusions:** The importance of the use of SPECT in MCH is evidenced, since it allows to assess the osteoblastic activity of the condyles, as well as their quantification. SPECT / CT allows a better anatomical correlation of the joint, increasing the specificity of the test. Therefore, it provides essential information for the diagnosis of the pathology in active phase, as well as for its follow-up and constitutes a determining factor in the surgical decision.

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Monday, October 15, 2018, 08:00 - 09:00, Hall A

e-Poster Walk 5 - Do.MoRe: Instrumentation & Data Analysis

E-PW040

Investigating the Quality of 3D Printed Tungsten Collimators for Nuclear Medicine Imaging

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Introduction: Tungsten collimators can now be 3D-printed using a technique called Selective Laser Melting (SLM). SLM is an additive, layer-wise manufacturing technology that utilises a high-energy-density laser to fuse multiple layers of tungsten powder into complex compact structures. This process can be used to build high resolution or complex collimators for nuclear medicine imaging applications at lower costs and in less time compared with traditional milling and turning production. However, intrinsic properties of tungsten - such as its high thermal conductivity, high affinity for oxygen, and low ductility at room

temperature - complicate the SLM process and can result in porous sections within the structure and rough profiles across surfaces. **Aim & Methods:** Three parallel-hole tungsten collimators built using SLM were investigated - one with 7 x 7 2mm square holes, one with 5 x 5 1mm diameter circular holes and a more complex design with 42 x 48 1mm hexagonal holes. These collimators were produced by two different companies, 3T RPD and M&I Materials. A lead collimator that has been conventionally manufactured at the University of Leicester was also investigated for comparison. Scanning electron microscope (SEM) images and fluorescence emission spectra were taken for each collimator. The variability of the thickness along septa was measured to ascertain the quality and consistency of the collimator holes. The fluorescence emission spectra were used to obtain information on the elemental composition of the collimator material. **Results and Conclusion:** Cracks and small porous regions of up to 100µm in diameter can be observed across the surfaces of the tungsten collimators. The formation of spherical droplets (known as the balling phenomenon), a consequence of tungsten's high thermal conductivity and high surface tension, was visible on surfaces. The consistency of the hexagonal holes for the more complex tungsten collimator degrades at the edges of the collimator. A tungsten purity ranging from 80-90% was observed and the intra- and inter- septal thicknesses were largely consistent. Further tests are needed to accurately measure the collimator purity given that SEM electrons could only penetrate a few µm beyond the surface. Despite the visible imperfections across surfaces, SLM is a promising manufacturing technology for more easily producing tungsten collimator designs tailored to specific energy and resolution needs.

E-PW041

Quantitative SPECT/CT Imaging of Lutetium-177 (¹⁷⁷Lu): a comparison of methods

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Background & Aims: In previous work, seven European hospitals participated in a quantitative imaging comparison exercise of Lu-177, with free choice of calibration, acquisition, reconstruction and segmentation methods. The participants were provided with a comparison phantom of a shell-source of unknown activity, consisting of an active inner sphere and a less active outer shell, placed within an elliptical Jaszczak phantom with body contour rings and a lung-spine insert, and asked to report activities for each active compartment. The participants reported results for the activity in each compartment ranged from -34 to +83% of the true values. In order to determine whether the range in reported values can be solely explained by the use of different calibration methods, we have now extended this work to replicate each of the calibration methods used on a single SPECT/CT camera. This also allowed us to assess the impact of each variable. **Materials and Methods:** Eleven different quantitative SPECT/CT camera calibration methods were performed. The calibration data and comparison exercise data were each reconstructed in eight different ways and then

three different segmentation methods were applied. A counts per second (cps)/MBq factor calculated from the calibration data was applied to the cps data for the comparison exercise data. The difference between the true and calculated activities in the comparison phantom were assessed. **Results:** The use of a calibration source similar in size and geometry to the area of assessment in the comparison phantom gave the most accurate results. Petri-dish calibration sources gave the most accurate results for calibration sources dissimilar to the comparison phantom. The use of dispersed calibration sources yielded the most accurate results for low activity areas adjacent to higher activity areas. Using the 113keV photopeak in conjunction with the 208keV photopeak reduced the accuracy of the calibration in comparison to the 208keV photopeak alone. Resolution recovery improved the accuracy of the results, whilst the use of post-reconstruction filtering either improved or did not alter the accuracy in these results. Segmenting on the CT volume and adding an additional margin resulted in the most accurate results for active regions, whilst the use of autocontouring algorithms was most accurate for low activity regions. **Conclusion:** This work presents an assessment of the impact of each calibration method and variable used by seven hospitals in an intercomparison exercise. Recommendations for improved accuracy of quantitative imaging of ¹⁷⁷Lu are offered, and limitations of these recommendations discussed.

E-PW042

Software Guided PET Uptake Recognition in Patients with Lymphoma and Lung Cancer

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The interpretation of 18F-Fluorodeoxyglucose (FDG) PET/CT images is challenging given the sources of variability such as data acquisition, reconstruction methods and physiological tracer distribution. Recent advances in machine learning have enabled multi-parametric image classification with unprecedented accuracy. In this work, a convolutional neural network (CNN) was trained on PET/CT data to classify the malignancy of regions with increased uptake. PET/CT images of 628 patients with known lung cancer or lymphoma were analyzed by two experienced nuclear physicians: each uptake region was annotated in anatomical location and physiological characterization (e.g. benign, malignant) and served as ground truth for the CNN. The algorithm incorporated image features such as multi-planar PET and CT reconstructions focused around each region of uptake to describe the region and its local context. A non-rigid registration of a maximum intensity projection (MIP) PET image to an anatomical atlas was used to characterize the anatomical location. The network comprised a series of alternating convolutional and pooling layers to extract imaging features while fully connected layers integrated the non-imaging features into a single network. The available data were divided into training (60%), validation (20%) and testing (20%) subsets. A total of 12,959 PET regions of uptake were manually annotated from 302 lung

cancer and 326 lymphoma cases resulting in 4,677 malignant lesions and 7,276 regions of physiological uptake. Characterization into benign or malignant classes using the CNN was shown to have an area under the ROC curve of 0.96 on the test subset demonstrating a good ability at discriminating benign versus malignant FDG uptake in this patient cohort. Furthermore, the MIP PET image proved to be useful to discriminate brown fat uptake and left-right symmetrical physiological uptake. In this study we have demonstrated that the characterization of lesions in patients with lung cancer or lymphoma can be successfully performed using a convolutional neural network. While further image data and refinement of algorithms will be required for the application of such technology in clinical decision making, there are several potential use cases using the presented technology: reading workflow could potentially be simplified by pre-processing PET/CT to more efficiently derive clinically relevant parameters such as automatic parametric lesion description (e.g., total lesion glycolysis or total metabolic tumor burden), lesion differential diagnosis and pre-population of appropriate reporting fields. Finally, the same technique could be expanded onto other PET indications.

E-PW043

18F-FDG PET/CT texture analysis in patients with head and neck cancer

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Aim: To evaluate the role of ¹⁸F-FDG-PET/CT texture analysis in the staging and prediction of outcome of patients with head and neck cancer. **Materials and Methods:** Twenty-two patients with head and neck cancer (15 male; mean age 61 ± 11 years) were included in this study. All patients underwent whole-body ¹⁸F-FDG PET/CT at diagnosis and their records were retrospectively evaluated. PET images were processed to calculate, for each primary lesion, parameters such as SUV_{max} , SUV_{mean} , Metabolic Tumor Volume (MTV), Total Lesion Glycolysis (TLG), and a total of 17 texture indices. An in-house software written in IDL (Exelis Visual Information Solutions, Inc.) was used to calculate MTV with a 40% SUV_{max} threshold and 5 texture indices derived from the intensity-histogram of the lesion volume: **Standard deviation, Skewness, Kurtosis, Coefficient of variation, Area under cumulative SUV-volume histogram curve (AUC-SHC)**. Moreover, the Matlab (The MathWorks, Inc.) cooc3D.m function was used to calculate the other 12 texture indices derived from the three-dimensional grey level co-occurrence matrix: **Uniformity, Entropy, Correlation, Contrast, Homogeneity, Variance, Sum mean, Dissimilarity, Cluster shade, Cluster tendency, Max probability, Inverse variance**. Texture features were normalized as Z-scores and four distinctive groups were identified using hierarchical clustering approach with Euclidean distance. Results were represented

in the form of a heat map. Four indices were selected, each to be representative of a group: **Skewness, Homogeneity, AUC-SHC, and Dissimilarity**. After ¹⁸F-FDG PET/CT examination, patients were treated with radiotherapy alone or combined with chemotherapy, and 15 of them underwent a mean follow-up period of 30 months. **Results:** The role of conventional PET parameters such as SUV_{max} , SUV_{mean} , MTV, and TLG, and the selected representative textural indices were evaluated in relation to clinical parameters using the ANOVA test. MTV, Homogeneity and Dissimilarity showed a statistically significant difference in terms of mean values with respect to stage ($p < 0.05$), while TLG and Skewness showed a statistically significant difference in terms of mean values with respect to tumor grade ($p < 0.05$). At multivariate analysis, only TLG and MTV were retained in the model for prediction of overall survival. By Kaplan-Meier analysis and log-rank testing, overall survival was significantly better in patients with an MTV < 9.27 mL. **Conclusion:** The results of this study suggest that conventional PET parameters and textural indices can be useful in the evaluation and prediction of outcome in head and neck cancer patients.

E-PW044

Gender independence of a novel simple equation for accurate glomerular filtration rate (GFR) determination by ⁵¹Cr-EDTA plasma clearance with only two blood samples

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Purpose/Introduction: We have recently developed and validated a novel, simple, accurate, power equation (NE) of the form $GFR-NE = 1.5 \cdot GFR^{0.9}$ for predicting glomerular filtration rate calculated by multiple blood samples (GFR-MS) from GFR values derived by the “slope-intercept” technique with only 2 time blood samples during the late phase of the tracer disappearance (GFR2). However, as sex is a major modifier of many GFR determinants like body size, metabolism and extracellular fluid volume, the performance of any new relevant formula should be tested for gender differences. The purpose of the present study is to explore potential sex differences in the predictive performance of the above-mentioned NE. **Patients and Methods:** A total of 605 Caucasian patients with a wide range of age (12–88 years), body size and renal function (2–168 mL/min/1.73 m²) referred for routine GFR measurement, consisting the validation group of the NE, were included. Ten blood samples were obtained between 5 min and 240 min after bolus i.v. injection of ⁵¹Cr-EDTA. GFR (mL/min) was determined by a) tracer elimination approximation by two-compartmental exponential modelling (GFR10) and b) by the “slope-intercept” method using blood samples at 2 and 4 hours (GFR2) and scaled to 1.73 m² of BSA calculated by the Haycock formula (SGFR, mL/min/1.73 m²). Patients were divided in male (M) and female (F) groups. For both groups, the correlation of GFR-NE with GFR-MS values and their difference were assessed for both the

non- (GFR) and BSA-scaled (SGFR) values. **Results:** 35.5% of the patients were females. For both M and F sex groups, the linear GFR2-GFR-MS and SGFR2-SGFR-MS regression was excellent, with regression line slopes non significantly different than or very close to unity (R^2 ; M, 0.973 and 0.972; F, 0.982 and 0.980, respectively; p less than 0.0001 for all; Slope; M, 1.02 and 1.00; F, 0.98 and 0.97, respectively, p less than 0.0001 for all). Also for both M and F sex groups, the differences GFR-NE - GFR-MS and SGFR-NE - SGFR-MS were non-significant and less than ± 1.5 ml/min or ml/min/1.73 m² for all. **Conclusions:** The excellent accuracy of our novel power equation for predicting GFR-MS from GFR2 values, is clearly sex-independent.

E-PW045

Supine/prone patient position significantly affects primary breast cancer quantification on FDG PET/CT acquisition

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Aim: In standard clinical routine PET/CT study is performed in supine position with hands raised over the head. However, for breast imaging basic anatomical study - MRI is executed in prone position. Acquisition in the same position during the PET/CT scan will provide the studies comparison and metabolic characterisation of lesion visible in MRI. In this study we have compared both PET/CT scans in prone and supine position, to verify if the metabolic characterization of lesion change significantly regarding to position of the patient. **Materials and Methods:** Thirty three patients with lesions in breast were selected and double PET/CT series were performed in two positions: standard supine and additional prone. Mean age of analysed women was 52 years $\pm$ 12 (with range of 30 to 74 years). Prone position was achieved using a homemade special pad, with the shape of breast coil in MRI. Regions of interest including lesions have been drawn on Philips IntelliSpace station using three segmentation methods: adaptive contouring, 41% maximum value and 2.5 SUV. The following metabolic parameters was considered: SUVmin, SUVmax, SUVmean, SUVstd, metabolic tumour volume, SULpeak, TLG. Data analysis was performed using Statistica v.13 StatSoft to compare above mentioned parameters. Statistical significance was determined using Wilcoxon matched-pairs signed rank test. A p -value less than 0.05 was considered significant. **Results:** Each tested contouring method present significant differences in tumour quantification for parameters: SUVmax (for each method $p=0.0049$), SUVstd (adaptive: $p=0.0003$; 41%max: $p=0.0028$ SUV2.5: $p=0.0018$), SULpeak (adaptive: $p=0.0038$; 41%max: $p=0.0123$; SUV2.5: $p=0.0217$) and TLG (adaptive: $p=0.0060$; 41%max: $p=0.0005$, SUV2.5: $p=0.0005$). For SUVmean significant differences were observed in 41%max ($p=0.0031$) and SUV2.5 ($p=0.0009$). Metabolic tumour volume was different only for SUV2.5 method ($p=0.0008$). **Conclusions:** Statistical significant differences were observed in metabolic tumour parameters

like SUVmax, SUVstd and TLG independently of the contouring method. This shows that the position of the patient during the PET/CT study in breast cancer imaging is fundamental and can influence the analysis of the image regarding the most often used metabolic parameters. **Acknowledgment:** Grant No. STRATEGMED2/267398/4/NCBR/2015.

E-PW046

A new device (COTI) for thyroid uptake measurement and prospective dosimetry oriented therapy

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Aim: COTI device has been newly invented as innovative technology for providing more information about the actual effective half-life of the radioactivity which lead to more accurate quantification and dose estimation during radioiodine therapy.

Methodology: COTI device is equipped with 2 CsI LoHi detectors which is sensitive to activity ranges from 0.02 - 30 MBq, and attached to 4 SiPMs. Wireless communication system operates the device where the detectors are inserted inside special designed collars to match the size of the thyroid lobes. COTI's sensitivity was found to be 5-6 folds superior than the conventional thyroid probes. COTI can continuously measure the photons emitted from thyroid gland and exclude non-thyroidal contribution up to days. The feasibility and affordability of this device for routine implementations was tested through 88 patients (72 pts thyroid cancer and 16 pts hyperthyroidism) up to 24 hours, 10 patients among them were monitored for ≥ 96 h. The uptake values of COTI device was compared to those generated by the conventional Probe (reference line) after administration of 0.44- 2 MBq ¹³¹I. The major statistical analysis was made via SPSS software. **Results:** The average deviation between COTI and the reference line was %11 and -26% at 2 and 24 h respectively. The correlation between both devices were $R_2=0.7$ and 0.9 for 2 and 24 hours' uptake. Mann-Whitney U test showed no significant difference between the reference line and COTI device in both 2 and 24 hours' uptake values. % 85 of the patients had 24th hour's uptake with COTI less than the reference line which reflects the effect of non-thyroidal tissue uptake on the measures obtained from the traditional probe. The average deviation between the two measures after 96 h was -18 %. For patients with hyperthyroidism ($n=16$), the obtained results exhibited deviation of -29% compared to the reference line. **Conclusion:** CoTI device is portrayed by high sensitivity which can reasonably quantify the thyroid gland or residues as a function of time and uptake curves might be generated to calculate the radiation dose with less effect to the non -thyroidal compartments. CoTI is able to provide records of uptake before and after radioiodine therapy with compatible detectors that would be considered valuable and relevant for simple dosimetry oriented therapy.

E-PW047

Performance evaluation of Cerenkov Luminescence Imaging versus Autoradiography

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Purpose: Cerenkov Luminescence Imaging (CLI) is an emerging technology involving optical imaging of Cerenkov photons. CLI has potential for intraoperative tumour margin assessment, which has been proven in breast cancer surgery using ¹⁸Fluorine-fluorodeoxyglucose (¹⁸F-FDG). CLI of ⁶⁸Gallium prostate-specific membrane antigen (⁶⁸Ga-PSMA) could enable margin assessment in prostate cancer surgery. Autoradiography is an alternative strategy to improve light yield by conversion of β^+ -particles into light photons using scintillation. The aim of this study was to investigate performance of ⁶⁸Ga and ¹⁸F with CLI and autoradiography. **Methods:** CLI images were acquired using the LightPath system (Lightpoint Medical). Exposure times of 60s and 300s were used, with 2x2 and 8x8 binning respectively. A 60mm diameter petri dish, filled with 40kBq/mL ¹⁸F or ⁶⁸Ga, was imaged in all experiments. First, imaged without scintillation sheets. Thereafter, 6 μ m flexible and 1mm rigid scintillation sheets were accordingly added. Lastly, the effect of 550nm and 800nm short-pass filters was evaluated, with and without scintillators. The detectable activity level was determined as SNR=2. **Results:** The detectable activity with 60s exposure of ¹⁸F and ⁶⁸Ga was 29.38kBq/mL and 1.57kBq/mL, 2.49kBq/mL and 0.73kBq/mL, 0.24kBq/mL and 0.04kBq/mL for CLI, flexible and rigid scintillator, respectively. Flexible scintillation improved the signal compared to CLI 11x and 2x and rigid 131x and 44x for ¹⁸F and ⁶⁸Ga, respectively. The detectable level with 300s exposure of ¹⁸F was 3.83kBq/mL and 0.18kBq/mL for ⁶⁸Ga. The flexible scintillator resulted in a ¹⁸F detectable level of 0.25kBq/mL. Filtering reduced the CLI signal intensity to 65% with 550nm filter and 92% with 800nm. The addition of a flexible scintillator led to signal reduction to 49% and 95%, respectively. With the rigid the signal was 95% for both filters. **Conclusion:** ⁶⁸Ga is superior over ¹⁸F in terms of detectable level, with and without additional scintillators. The relative signal increase with scintillators was less explicit for ⁶⁸Ga compared to ¹⁸F, yet the detectable level for both isotopes decreased. Optical filters reduce the signal more using flexible scintillator than ridged ones, resulting from their emission spectrum. Clinically, injected activity can be reduced when applying scintillators, improving radiation safety and using a practical exposure of 60s. This research suggests to use rigid scintillators, however, there are significant advantages of flexible scintillators for intraoperative margin assessment during prostate surgery using ⁶⁸Ga-PSMA. **Research Support:** This research is supported by KWF Kankerbestrijding and Technology Foundation STW, as part of their joint strategic research programme 'Technology for Oncology'.

E-PW048

Evaluation of a novel hybrid intensity and gradient-based method for PET tumor segmentation using a Monte Carlo simulated NSCLC phantom

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Purpose: Accurate and consistent PET segmentation continues to be a challenge for prognosis, therapy response assessment, and treatment planning. Reducing variability is essential to make the quantitative metrics consistent between clinicians. The goal of this study is to examine how a hybrid intensity and gradient based PET segmentation algorithm (hybrid method) compares to a previously studied gradient-only based segmentation algorithm (gradient-only method) with respect to accuracy and variability. Previously, the gradient-only method was found to be the most accurate when compared to thresholding and manual methods (Werner-Wasik 2012). **Methods:** 24 Monte Carlo simulated PET scans of the thorax with 27 clinically realistic lung tumors were used for evaluating segmentation accuracy and variability. The mean tumor volume was 95ml (range 7-264ml). Tumor locations were within the lung, adjacent to the mediastinum or chest wall. 6 observers (4 radiation oncologists and 2 PET-trained nuclear radiologists) used the gradient-only method to contour each tumor. The hybrid method was initialized at 6 different locations corresponding to the centroids of 6 different axial slices equally spaced from the second top-most to the second bottom-most slice of the ground truth contour. Both the gradient-only and the hybrid method contours were compared to the ground truth contours. In order to examine the variability between the observers with each method, an Intraclass Correlation (ICC) test was done. **Results:** The hybrid method had a significantly higher median Dice coefficient of 0.934 compared to 0.915 for the gradient-only method ($p < 0.001$). The hybrid method had a significantly lower average absolute percent error in volume with 8.1% (7.4% SD) for the hybrid method versus 9.3% (9.8% SD) for the gradient-only method when compared to the ground truth volume ($p < 0.05$). The ICC value for the hybrid method was 1.00, compared to 0.998 for the gradient-only method ($p < 0.01$). This suggests that the hybrid method had less inter-user variability. **Discussion:** While the previously studied gradient-only method had low inter-user variability, it still required the user to provide both a central point and a diameter estimate in order to initiate segmentation. This new hybrid method is even less user-dependent in that it only requires the user to locate to a point within the tumor. This hybrid method provides a consistent and accurate semi-automatic PET segmentation technique that improves upon the gradient-only predecessor in accuracy and variability throughout this preliminary study. Future studies with more varied test data are planned.

E-PW049

Regularized Reconstruction of ⁶⁸Ga-PSMA Whole-Body Examinations Acquired on a Digital Time-of-Flight PET/CT Scanner

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Introduction: Prostate-specific membrane antigen (PSMA) PET has shown to enable unique discrimination of whole body tumor burden in prostate cancer (PCa) patients. To further optimize target to background expression levels we sought to in-

investigate the image quality and quantitative outcome measures of regularized reconstruction by block-sequential regularized expectation maximization (BSREM). The aim was to evaluate image quality in relation to reconstruction regularization parameter (β -value) and acquisition duration. **Materials and Methods:** The study encompassed retrospective reconstruction and analysis of 16 digital time-of-flight PET/CT examinations acquired 60 min post injection of 2 MBq/kg of ^{68}Ga -PSMA in patients with PCa biochemical relapse after primary treatment. Reconstruction by ordered-subsets expectation maximization (OSEM; 3 iterations, 16 subsets, 5-mm gaussian post-processing filter) and BSREM (β -values of 100–1600) were used, both including time-of-flight and point spread function modelling. Lesion standardized uptake values (SUVs) were obtained by applying a 41% threshold of the maximum voxel value. Background variability (BV) was measured by placing a spherical volume of interest in the right liver lobe in the axial plane and defined as standard deviation divided by the mean SUV. The image quality was evaluated in terms of lesion to noise and lesion to background ratios. **Results:** OSEM reconstruction produced images with a BV of 15%, whereas BSREM with a β -value above 400 resulted in lower BVs than OSEM. Decreasing the acquisition duration from 2 to 1 and 0.5 min per bed position increased BV for both reconstruction methods, although BSREM with a β -value of 800 and 1200 and above, respectively, kept the BV below 15%. In comparison of BSREM with OSEM, the mean lesion SUV_{peak} to BV ratio improved by 5 to 77% with an increasing β -value of 300–1300 (from 71.7 to 73.6–126.4), whereas the mean lesion SUV_{peak} to background SUV_{mean} ratio decreased with an increasing β -value ranging from 0 to 18% (from 2.8 to 2.9–3.4) with a β -value of 100–1100. Decreased acquisition duration resulted in β -values 800 to 1200 and 1200 to 1400—for 1 and 0.5 min per bed position, respectively—producing improved image quality outcome measures compared with OSEM at a full acquisition duration of 2 min per bed position. **Conclusion:** Accurate localization of the recurrent disease is critical especially if the intent is curative radiotherapy. BSREM reconstruction with β -value 500–1100 resulted in lower background variability and higher lesion to background ratio images in comparison with OSEM.

911 Monday, October 15, 2018, 14:30 - 16:00, Hall A

e-Poster Walk 6 - Cardiovascular: Different Aspects of Cardiovascular Imaging I

E-PW050

Comparison between 72hours- specific diet and no-diet in evaluation of endocarditis with PET/CT

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Aim: 18Fluorine-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography 18F-FDG-PET/CT) has been proposed as an important imaging modality for detecting Infective Endocarditis (EI). However, intense dishomogeneous physiologic

ical myocardial 18F-FDG uptake may mask pathological uptake in valve lesion. The aim of this study is to retrospectively analyse the impact of a low carbohydrate, high protein, high fat (LCHPHF) diet starting 72 hours before the examination with a classic overnight fasting in reducing physiologic myocardial 18F-FDG uptake and helping the diagnostic accuracy in the detection of IE. **Materials and Methods:** We included 53 patients (38 male; 15 female; mean age 63) who underwent 18F-FDG-PET/CT scan for suspicious of EI. Nine diabetic patients with insulin-therapy were excluded. Twenty-two patients with LCHPHF diet were compared to twenty-two patients with an overnight fast preparation only. PET/CT images were analysed qualitatively by assigning a visual score (0= clearly and reportable examination ; 1= doubtful examination and 2= not reportable examination) and semiquantitatively by measuring maximum and mean standardized Uptake Value (SUVmax and SUVmean) of the suspected lesion, of the blood-pool, of the liver at the VIII hepatic segment and of the right atrium. Moreover, an ellipsoid volume of interest (VOI) was designed to include the whole left ventricular myocardium activity. **Results:** In LCHPHF-diet group, at visual analysis 21 patients (95%) had score 0, and 1 patient score 1; while in the control group, 13 patients (59%) achieved score 2.4 (18%) score 0 and 5 (22%) score 1. Comparing PET/CT report and clinical final diagnosis, LCHPHF-diet group had higher diagnostic accuracy than the second group with a Sensitivity of 91%, Specificity of 100% Negative Predictive Value of 92%, Positive Predictive Value of 100% and of Accuracy 95% compared to Sensitivity of 20%, Specificity of 75%, Negative Predictive Value of 43%, Positive Predictive Value of 50% and Accuracy 44% respectively. Semiquantitative analysis showed that left ventricle SUVmax's mean in diet group was 2.87 vs 6.58 in controls ($p < 0.001$); lesion to myocardium SUVmax ratio was significantly higher in diet group 1.10 vs 0.28 ($p < 0.07$). There were no significant differences in the other semiquantitative parameters between two groups. **Conclusion:** Our preliminary study showed that LCHPHF-diet started 72h before the exam suppresses cardiac glucose metabolism significantly better than prolonged fasting protocol, leading to a significant improvement in the interpretability and diagnostic accuracy of 18F-FDG PET scans for detection of IE.

E-PW051

Myocardial ^{18}F -FDG Suppression In Patients With Suspected Endocarditis Comparing Two Preparation Strategies

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Introduction: ^{18}F -FDG-PET/CTA has high sensitivity in detecting infection, with increasing relevance in the diagnosis of prosthetic valve endocarditis (PVE). For correct cardiac assessment it's necessary to obtain the minimum myocardial FDG uptake (myocardial suppression), which can be achieved with prolonged fasting associated with Heparin IV and/or a high-fat/low-carbohydrate diet. **Objective:** To evaluate the efficacy of myocardial suppression by using Fasting+Heparin vs Fasting+Heparin+Diet.

To assess possible correlation between different clinical variables (cholesterol, triglycerides, LDL, ejection fraction) and the degree of suppression achieved. **Methods:** We analyzed 63 patients who underwent a PET/CTA due to suspected PVE (52 prosthetic valves, 11 valved tubes). All of them underwent fasting (≥ 18 hours) plus Heparin (50 IU/Kg EV) 15 minutes before FDG injection; 41 patients also conducted a diet. The degree of myocardial suppression was assessed qualitatively (5-degree visual scale) and semi-quantitatively by measuring left myocardial SUVmean. The reference uptake was measured at the liver (SUVmeanL). Adequate suppression was considered when SUVratio Heart/Liver (H/L) was ≤ 1 . **Results:** The visual assessment showed adequate myocardial suppression in 45 patients (71%), 13/22 with Heparin (59%) and 32/41 with Heparin+Diet (78%). There are significant differences in the myocardial SUVmean values ($p=0.036$) and SUVratioH/L ($p=0.03$) between the Heparin groups (SUV 2.48 ± 1.21 ; H/L 1.1 ± 0.59) and diet (SUVmean 1.91 ± 0.88 ; SUVratioH/L 0.84 ± 0.37). Patients with adequate visual suppression showed a SUVratioH/L ≤ 1 in 44/45 while 15/18 patients without suppression had SUVratioH/L > 1 . There is good correlation ($r=0.8$) between SUVratioH/L and visual assessment. No correlation was found between the clinical variables assessed and the degree of suppression, although suppressed patients had higher cholesterol levels (155.5 ± 47 vs 145.2 ± 50 mg/dL) and triglycerides (161.7 ± 179.7 vs 130.2 ± 60.2 mg/dL) compared with not suppressed. **Conclusion:** A 78% of patients with Fasting+Heparin+Diet achieved a good suppression vs only 59% of Fasting+Heparin, with good correlation between visual and semi-quantitative assessment.

E-PW052

Improving image quality of ^{18}F FDG myocardial viability PET images in diabetics: A prospective cohort based kappa analysis

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Introduction: Obtaining good quality myocardial FDG PET viability images with oral glucose load has always been cumbersome in diabetics[1]. Established guidelines (SNMI/ASNC/SCCT) recommend delayed/repeat imaging or “hyperinsulinemic -euglycemic” clamp for better quality images. These methods are inconvenient, cumbersome, time consuming, risk laden and costly. **Subject and Methods:** A pilot study done in our institute which included 24 patients (15 were diabetic) - a new protocol, had revealed better quality images. Herein, 50 diabetic patients (26 males and 24 females), who were referred to the tertiary health care center were recruited into the study with prior consent. Patients were randomly assigned to group A or group B. Each cohort consisted of 25 patients each. Patients in group A were imaged according to the ASNC/SNMI/SCCT protocol. Group B were imaged with the new protocol - simultaneous administration of oral glucose and IV regular insulin (sliding scale - based on fasting plasma glucose levels). Images were ob-

tained after 45-90 minutes of ^{18}F -FDG injection. Image sets were blinded for clinical details, randomized and were assigned to three qualified nuclear medicine physicians for visual interpretation. Image quality was graded into - excellent, good, average, poor, based on visual analysis (parameters included- blood pool uptake and background). A quantitative parameter called M/B ratio was devised- ROI (2X2 pixel width) placed over the most intense part of myocardium and the blood pool (myocardial cavity) and ratio of counts was calculated. **Results:** Results revealed that degree of agreement among clinicians (image quality) was good in patients assigned to group B (weighted kappa- 0.693, moderate agreement), than in group A (weighted kappa- 0.593, weak agreement). The M/B ratio was higher in group B (7.4 ± 1.7) versus group A (5.8 ± 1.5). The correlation between M/B ratio and quality of images on visual assessment was significant (p value=0.03), yielding various ranges for each category. **Conclusion:** In conclusion, the new protocol yielded better quality of myocardial PET images with higher M/B ratio especially in diabetics and was non-inferior to the established ASNC protocol. Further delayed and repeat imaging was sought in three patients assigned to group A (ASNC protocol) to get good quality images. However, further research and studies comparing it with established gold standard, i.e., “euglycemic -hyperinsulinemic clamp” are required to establish the same.

E-PW053

Clinical Significance Of Quantitative Assessment Of Glucose Utilization In Patients With Ischemic Cardiomyopathy

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Purpose: FDG PET is widely used to evaluate myocardial viability. However, the kinetics of glucose metabolism in viable and non-viable myocardium using dynamic FDG PET have not been extensively explored. The aim of this study was to prospectively quantify the rate of myocardial glucose uptake (MRGlu) in myocardium with different perfusion-metabolism patterns and determine its prognostic value in patients with ischemic cardiomyopathy. **Subjects & Methods:** Patients with coronary artery disease and heart failure with reduced ejection fraction ($\leq 45\%$) were prospectively enrolled for FDG PET between November 2012 and June 2017, and were then followed for at least 6 months after PET. Dynamic glucose-loaded insulin-stimulated FDG PET with list mode was performed. Perfusion-metabolism patterns were determined based on visual score analysis of ^{201}Tl SPECT and FDG PET. Segmental MRGlu ($\mu\text{mol}/\text{min}/100$ g) was

analyzed using the Patlak kinetic model. The primary endpoint was cardiovascular mortality. Differences in MRGlu between different patterns and their relationships with the clinical characteristics were compared. Associations among MRGlu and patient outcomes were analyzed using Kaplan-Meier survival analysis. **Results:** A total of 79 patients (mean age 62.8 ± 12.5 years, male 86.0%, ejection fraction $37.2 \pm 15.8\%$) with 710 myocardial segments were included. A significantly higher MRGlu was observed in mismatch and reverse mismatch (RM) compared with the transmural and non-transmural match patterns ($P = 0.03$). Negative correlations were found between MRGlu in transmural match and a history of hyperlipidemia, statin usage and triglyceride levels (all $P < 0.05$). Patients with diabetes receiving dipeptidyl peptidase-4 inhibitors (DPP4is) had a significantly lower MRGlu in transmural match, mismatch and RM, irrespective of glucose levels at FDG injection or the dose of insulin given. Patients with MRGlu in transmural match ≥ 23.40 (log-rank = 6.55, $P = 0.01$) or RM ≥ 36.90 (log-rank = 4.47, $P = 0.03$) had a worse outcome with a median follow-up time of 27.20 ± 17.57 months. **Conclusion:** Myocardial glucose utilization was influenced by substrates and medications, including statins and DPP4is. MRGlu could discriminate between viable and non-viable myocardium, and MRGlu in transmural match and RM may be prognostic predictors of cardiovascular death in patients with ischemic cardiomyopathy.

E-PW054

[18F]-Sodium fluoride PET/CT and [18F]-FDG PET/CT in investigation of the mechanisms of aortic stenosis formation

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Purpose: was to investigate the relationship between aortic stenosis (AS) severity and intensity of [18F]-Sodium fluoride ([18F]-NaF) and [18F]-FDG uptake in the aortic valve structures. **Materials and Methods:** 58 patients (60.83 ± 7.44 years, m: f 1: 1.15) with degenerative origin of AS were included in the study. Maximal flow rate on the aortic valve (Vmax) was considered as a marker of AS severity and this parameter was evaluated by the standard protocol of transthoracic echocardiography (Vivid 7; GE). All patients underwent PET/CT of the aortic valve (Discovery 710; GE). Measurement of the aortic valve calcification was performed by [18F]-NaF PET/CT. Aortic valve inflammation was assessed by PET/CT with [18F]-FDG. For assessment the severity of calcification and inflammation target-to-background ratio (TBR) were calculated using SUV max in aortic valve region and SUVmax in blood pool. Calcium scoring was measured in Agatston units using traditional CT protocol. **Results:** The average value of Vmax was 3.01 ± 0.62 m/s and the average aortic valve calcium index was 1548.23 ± 1396.7 . We observed that TBR mean value for [18F]-NaF was higher in comparison with TBR mean value for [18F]-FDG (1.63 ± 0.42 vs 1.1 ± 0.14 , $p < 0.001$). There was no correlation revealed between [18F]-FDG uptake and Vmax ($r = 0.018$, $p = 0.909$). At the same time, a close relationship was found between Vmax and [18F]-NaF uptake ($r =$

0.546 , $p < 0.001$) and the calcium score ($r = 0.622$, $p < 0.001$). In addition, a positive correlation was found between the calcium score and the [18F]-NaF uptake ($r = 0.702$, $p < 0.001$). There was not observed correlation between the [18F]-FDG and [18F]-NaF accumulation ($r = 0.064$, $p = 0.68$). **Conclusion:** Calcification is the prevalent pathological process in the AS formation. Contribution of the inflammation seems to be not significant. Further investigations are required in a larger cohort of patients.

E-PW055

[18F]-Sodium Fluoride PET and [18F]-FDG PET/CT in prediction of aortic stenosis progression

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The aim of this study was to assess the diagnostic abilities of PET/CT with [18F]-sodium fluoride ([18F]-NaF) and [18F]-fluorodeoxyglucose ([18F]-FDG) to predict of aortic stenosis (AS) progression. **Methods:** 34 patients (60 ± 8.05 years) with asymptomatic AS were included in the study. There weren't included patients with infective endocarditis and rheumatic heart disease. Severity of AS was assessed by values of the aortic jet velocity (Vmax). At the baseline all patients underwent 2-dimensional echocardiography (ECHO) (Vivid 7, GE) and hybrid PET/CT (Discovery 710, GE) with [18F]-NaF and [18F]-FDG. Follow-up ECHO was performed in 6-12 months. PET/CT with [18F]-NaF and [18F]-FDG both was performed in 60 minutes after intravenous administration of tracers in different days. Spherical VOI (3.52 cm^3) was drawn around aortic valve. SUVmax and SUVmean for [18F]-NaF and [18F]-FDG both were calculated within VOI. Blood pool in left atrium was selected as a background, where also SUVmax and SUVmean for [18F]-NaF and [18F]-FDG were measured. Using values of SUVmax and SUVmean within VOI in aortic valves and background the target-to-background ratios (TBR) were calculated (TBRmax-to-max, TBRmean-to-mean, TBRmax-to-mean) to assess severity of calcification and inflammation in aortic valve. CT calcium scoring was performed using SmartScore 4.0 software and recorded in Agatston units. **Results:** Vmax values were in the range from 2.3 to 5.0 m/s. Average Vmax was 3.24 ± 0.76 m/s. We found the correlation between Vmax and calcium scoring ($r = 0.648$; $p < 0.001$). Additionally there were obtained correlations between Vmax and TBRmax-to-max, TBRmean-to-mean, TBRmax-to-mean for PET/CT with [18F]-NaF ($r = 0.446$; $r = 0.502$; $r = 0.411$ respectively; $p < 0.05$). There were not any correlation between Vmax and the TBRmax-to-max, TBRmean-to-mean, TBRmax-to-mean for PET/CT with [18F]-FDG. Follow-up ECHO revealed the progression of AS as the Vmax increase in 24 patients. No changes of Vmax values were observed in 10 patients. ROC-analysis revealed the accuracy PET/CT with [18F]-NaF as 70.8% ($p = 0.038$) for prediction of AS progression. It was established that the most accurate predictive criterion was TBRmean-to-mean for PET/CT with [18F]-NaF with the cut-off TBRmean-to-mean was more than 1.29. There were no significant relations for PET/CT with [18F]-FDG. **Conclusion:** PET/CT with [18F]-NaF can predict AS progression based on the cut-off value of TBRmean-to-mean more

than 1.29. Inflammatory process, which was assessed by PET/CT with [18F]-FDG, did not have any substantial significance in prediction of AS progression.

E-PW056

Myocardial ¹⁸F-Sodium Fluoride PET/MRI Imaging in Patients With Suspected Cardiac Amyloidosis

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Purpose: To evaluate the diagnostic performance of myocardial ¹⁸F-sodium fluoride (¹⁸F-NaF) PET/MRI in patients with suspected cardiac amyloidosis (CA). **Methods:** Between June 2017 and April 2018, 19 consecutive patients with suspected CA underwent cardiac PET/MRI imaging 1 h after injection of 4 MBq/kg ¹⁸F-NaF (according to Trivieri, JACC 2016) on a Biograph mMR (Siemens, Erlangen, Germany). Simultaneous MRI sequences included cardiac-gated and respiratory-motion corrected cine MRI in 2, 3 and 4 cavities, T1 and T2 mapping, first-pass and late Gd enhancement. NaF uptake was measured by 2 independent observers visually and quantitatively by drawing a left myocardial ROI on the 4-cavity MR image, and myocardium-to-blood pool ratio (M/B) were calculated. CA was confirmed by endomyocardial biopsy or cardiac MRI+peripheral tissue biopsy. Early-phase ^{99m}Tc-HMDP SPECT/CT was also performed in 15 patients (according to Galat, JACC Imaging 2017). **Results:** Transthyretin (TTR) CA was diagnosed in 14 patients, systemic light-chain (AL) CA in 3 patients and no CA in 2 patients. Visual interpretation of the PET images revealed significant myocardial NaF uptake in only 2 patients with TTR CA and decreased myocardial uptake (below intraventricular blood pool) in 6 patients (2 without CA, 2 AL and 2 TTR). M/B ratio were slightly higher in TTR patients (median 1.04; extremes 0.83–1.21) than in patients with AL CA or no CA (median 0.83, extremes 0.71–0.86, Mann-Whitney P=0.002). The optimal cut-off by ROC analysis to distinguish TTR from AL/no CA was >0.86 (area under the ROC curve, AUC=0.971) and was >0.81 to distinguish CA from no CA (AUC=1.000). Performances of NaF M/B ratio, HMDP uptake and MRI parameters to classify patients between TTR and AL/no CA was P=0.0005, P=0.0007 and P=0.01, respectively (Fisher's exact test). **Conclusion:** Myocardial ¹⁸F-NaF uptake is very low in patients with TTR CA 1 h after injection. Visual interpretation cannot reliably distinguish TTR from AL/no CA while quantification of M/B ratio shows promising results but with very faint differences. In 2 TTR patients, a dynamic PET acquisition was performed immediately after NaF injection and showed higher myocardial uptake early after injection than at 1 h, suggesting fast wash-out by opposition to HMDP.

E-PW057

Relationships Between Myocardial Perfusion Abnormalities And Integrated Indices Of Atherosclerotic Burden In Patients With Intermediate Pre-test Probability Of Coronary Artery Disease

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Purpose: To assess myocardial perfusion in stable CAD patients with different degrees of coronary artery stenosis. **Methods:** We selected 94 patients (58 men; mean age of 62.9±7.3 years) with intermediate pre-test probability of CAD. All patients underwent coronary CT angiography (CCTA) and stress-rest MPI using GE Discovery NM/CT 570C. Coronary plaques were considered significant, intermediate, and non-significant when associating with a luminal narrowing ≥70%, 40% to 69%, and <40%, respectively. The Segment Involvement Score was calculated as the total number of coronary artery segments with atherosclerotic plaques. The Segment Stenosis Score was computed by grading each coronary segment with a 5-point scoring system (0 = no plaque; 1 = 1–24% stenosis; 2 = 25–49% stenosis; 3 = 50–69% stenosis; and 4 = ≥70% stenosis). The summed rest score (SRS), stress score (SSS), and difference score (SDS) were derived from MPI images. **Results:** The median Segment Involvement Score and Segment Stenosis Score were 4.0 (interquartile range 2.0–5.0) and 7.5 (interquartile range 3.0; 13.0), respectively. Normal MPI images were observed in 38 patients, abnormal in 56. The frequencies of normal and abnormal MPI in patients with <40% (normal MPI 53%; abnormal MPI 47%) and 40% to 69% (normal MPI 44%; abnormal MPI 56%) coronary artery stenosis did not significantly differ (p=0.40 and p=0.22, respectively). In patients with ≥70% coronary artery stenosis, abnormal MPI was observed significantly more often (normal MPI 29%; abnormal MPI 71%) than normal MPI (p=0.001). In the overall population, both Segment Involvement Score and Segment Stenosis Score had weak correlations with SSS (r=0.3 and r=0.34, respectively; P<0.01 for both), SRS (r=0.27 and r=0.35, respectively; P<0.01 for both), and SDS (r=0.3 and r=0.36, respectively; P<0.01 for both). In patients with <40% stenosis neither CT scores correlated with MPI parameters, while SDS correlated moderately with Segment Involvement Score (r=0.45; p=0.03) and Segment Stenosis Score (r=0.53; p=0.01) in those with 40% to 69% stenosis. In patients with ≥70% stenosis, the Segment Stenosis Score had moderate correlations with SSS (r=0.50; p=0.005) and SDS (r=0.43; p=0.02). **Conclusion:** Myocardial ischemia may frequently develop even in the absence of critical coronary artery lesions, presenting in a consistent proportion of patients with either intermediate or even non-significant coronary stenosis. In those patients, the extent of regional myocardial perfusion defects correlates more with measures of global CAD burden than with focal stenosis severity, as a sign of the significant inter-relation between diffuse coronary atherosclerosis and myocardial ischemia.

E-PW058

Comparison of Fimasartan versus Amlodipine Therapy on Carotid Atherosclerotic Plaque Inflammation

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Objectives: We investigated the effects of fimasartan and amlodipine therapy on carotid atherosclerotic plaque inflammation using ^{18}F -fluorodeoxyglucose (^{18}F FDG) positron emission tomography (PET) imaging. **Background:** The renin-angiotensin system plays an important role in promoting atherosclerotic plaque inflammation, which may be inhibited by angiotension-II receptor blockers. **Methods:** Fifty patients with acute coronary syndrome and at least one lesion with ^{18}F FDG uptake in the carotid artery (target-to-background ratio [TBR] ≥ 1.6) were randomly assigned to receive either fimasartan (60mg once a day) or amlodipine (5mg once a day). ^{18}F FDG PET examinations were performed in all patients at baseline and at 6 months. The primary endpoint was the percent change in the TBR of the index vessel at the most diseased segment (MDS). **Results:** The two groups were similar in baseline characteristics. At the 6-month follow-up, the MDS TBR of the index vessel and aorta significantly decreased in both groups. However, the percent change in the MDS TBR of the index vessel was similar between the two groups ($-9.33 \pm 14.2\%$ vs. $-7.73 \pm 19.1\%$, respectively, $p=0.9$). No difference was also found for the percent change in the whole vessel TBR of the index vessel between the two groups. Similar findings were found for changes in the MDS TBR or whole vessel TBR of the aorta. Total cholesterol, LDL cholesterol levels and blood pressure improved to a similar degree in both groups. **Conclusions:** Fimasartan and amlodipine similarly reduces carotid atherosclerotic plaque inflammation in patients with acute coronary syndrome, offering the same level of effectiveness.

E-PW059

Left Ventricular Dyssynchrony Parameters Measured by Phase Analysis of Stress and Resting Gated ^{13}N -NH3 PET/CT Myocardial Perfusion Imaging

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Aim: The relationship between perfusion pattern and stress-induced changes in left ventricular mechanical dyssynchrony (LVMD) has been previously described with controversial results on stress-rest perfusion imaging studies. Using regadenoson, as a stress inducer, causes maximum vasodilation and hyperemia immediately, unlike other vasodilatory agents. The aim of the study is to assess the relationship of perfusion pattern with stress-induced changes in LVMD on stress-rest ^{13}N -ammonia positron emission tomography/computed tomography (^{13}N -NH3 PET/CT). **Materials and Methods:** In this retrospective study we enrolled 49 patients (average age 65; male 26 and female 23) who underwent stress-rest ^{13}N -NH PET/CT. We divided our population in two groups considering imaging result: patients with reversible myocardial perfusion defect at stress (Ischemic group, $n=16$) and patients without myocardial reversible perfusion defects (Non-ischemic groups, $n=33$). We evaluated epidemiological/clinical characteristics (age, sex, cardiovascular risk factors), main imaging features (summed stress score, summed rest score, summed difference score, LV ejection fraction) and LVMD parameters: phase standard de-

viation (PSD) and phase histogram bandwidth (PHB), both assessed during-stress and at rest. ΔPSD (during-stress PSD - rest PSD) and ΔPHB (during stress PHB - rest PHB) were calculated to measure stress-induced changes in LVMD. **Results:** Considering the epidemiological/clinical features, no significant difference was present between the two groups, except for sex, history of diabetes and previous revascularization that were higher in ischemic-group (p value 0.03; p value 0.017; p value 0.081, respectively). There were no significant differences in the LV dyssynchrony parameters (PSD during stress, PSD at rest, PHB during stress, PHB at rest) between during stress and at rest in both groups. Mean stress-LVMD parameters were significantly higher in ischemic group than non-ischemic (PSD 7.19 ± 5.05 vs 4.1 ± 1.45 , p value 0.002; PHB 29.93 ± 23.7 vs 17.21 ± 6.47 , p value 0.005); also the same variables at rest were significantly higher in the ischemic cohort in comparison to non-ischemic (PSD 5.96 ± 4 vs 4.44 ± 1.6 , p value 0.043; PHB 23.9 ± 17.9 vs 16.3 ± 4.79 , p value 0.020). Both ΔPSD and ΔPHB were significantly higher in ischemic patients (1.22 ± 2.48 vs -0.14 ± 1.3 and 4.93 ± 19.96 vs 0.90 ± 5.5 respectively) **Conclusion:** In conclusion, all LVMD parameters were significantly higher in the ischemic patients compared to non-ischemic, while there was no significant difference in each cohort between stress and rest evaluation. Unlike technetium radiotracers, ammonia-PET/CT were performed immediately during regadenoson stress induction and may explain our evidences partially in contrast with other studies.

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Monday, October 15, 2018, 16:30 - 18:00, Hall A

e-Poster Walk 7 - Inflammation & Infection: Infection & Inflammation

E-PW060

Diagnostic and therapeutic impact of ^{18}F -FDG PET/CT and CTA in suspected TAVI endocarditis

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Introduction: In transcatheter aortic valve implantation (TAVI), a stented valve is inserted inside the native aortic valve to treat severe aortic valve stenosis. TAVI endocarditis is a devastating complication that is difficult to diagnose and relies on the Duke criteria comprising echocardiography and blood cultures. We assessed the additional diagnostic value of ^{18}F -fluorodeoxyglucose (^{18}F -FDG) positron-emission/computed tomography (PET/CT) and cardiac computed tomography angiography (CTA) in suspected TAVI endocarditis on top of echocardiography and blood cultures. **Subjects & Methods:** From our institutional endocarditis database, all patients suspected of TAVI endocarditis were selected who underwent ^{18}F -FDG PET/CT and/or cardiac CTA. PET/CT and CTA images were assessed in clinical practice by a nuclear medicine physician and cardiovascular radiologist respectively, while additional quantitative PET/CT analyses were

performed by a nuclear medicine physician blinded to all clinical data. The maximum standardized uptake value (SUV_{max}) was measured in an automated VOI with a 40% isocontour around the valve on EARL-accredited reconstructions (where available), while the SUV_{ratio} was calculated as the ratio of the SUV_{max} and the mean SUV in the blood pool of the descending aorta. The final diagnosis of TAVI endocarditis was determined by our Endocarditis Team based on European Society of Cardiology guideline recommendations. **Results:** Fourteen patients (age 76 ± 13 years; 6 males, median time since implantation 106.5 days [IQR 74–495]) were identified, including 10 with a final diagnosis of TAVI endocarditis. PET/CT was performed in 13/14 patients and CTA in 11/14. Overall, 8/10 patients (80%) with a final diagnosis of TAVI endocarditis had signs of endocarditis on either the PET/CT ($n=6$) and/or CTA scans ($n=5$). Four patients were newly diagnosed based on visually abnormal uptake around the valve on PET/CT ($n=3$) and/or a vegetation on CTA ($n=2$), as echocardiography was only positive for signs of TAVI endocarditis in 4/10 (40%) patients. In 3/4 patients (75%) with an alternative diagnosis (central/peripheral line infections or pneumonia), the diagnosis of TAVI endocarditis was rejected based on the PET/CT. The average EARL SUV_{max} and SUV_{ratio} in the patients with endocarditis were 4.22 ± 1.82 (range 2.66–8.00) and 2.20 ± 0.81 (range 1.52–3.94), respectively. In patients without endocarditis, these averages were 3.52 ± 0.43 (range 3.27–4.01; $p=0.54$) and 1.73 ± 0.41 (range 1.31–2.13; $p=0.36$), respectively. **Conclusion:** The combined use of 18F-FDG PET/CT and cardiac CTA resulted in the diagnosis of TAVI endocarditis in a substantial number of patients in whom echocardiography was negative, while also allowing the ruling out of endocarditis by providing an alternative focus for infection.

E-PW061

Imaging of Skull Base Osteomyelitis with FDG PET CT - How Critical is it?

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Background and Purpose: Skull base osteomyelitis (SBO) is a life-threatening clinical condition usually seen in uncontrolled diabetics. Its presentation as non-specific symptoms and absence of signs of severe infection make it challenging to diagnose. There is a vital role for imaging in SBO diagnosing the extent of disease, monitoring treatment response and relapse rate. Computed Tomography and Magnetic Resonance Imaging (MRI) give excellent anatomical details, whereas nuclear medicine techniques help in identification of functional process. Fluorodeoxyglucose Positron Emission Tomography (FDG PET-CT) combines the strength of anatomical and functional biomarkers. In this study, we evaluated the diagnostic performance of FDG PET-CT in skull base osteomyelitis and compared with MRI whenever available. **Materials and Methods:** Institutional review board approval was taken for this retrospective analysis. We retrieved the hospital records of 55 patients (male: female =39:16; mean age, 65.6 ± 12.5 years; range, 50–92 years) with clinically suspected SBO between January 2015 to December 2017. All patients had undergone technically adequate FDG

PET-CT. FDG PET-CT images were analyzed in dedicated workstations for presence, intensity (Maximum Standardized Uptake Value- SUV_{max}), and localization of increased FDG uptake. The final diagnosis was based on histopathology, culture of the surgical samples and clinical or imaging follow-up. We also tried to compare the findings of FDG PET-CT with MRI whenever available. **Results:** The 54/55 patients had uncontrolled type-2 diabetes mellitus. The 25 (45%) patients presented with ear discharge and cranial nerve palsy, 17 (30%) with only ear pain and discharge, 4 (7.3%) with a fever of unknown origin, 8 (14.5%) with sinonasal symptoms and 1 patient (1.8%) with a parotid abscess. The median C-reactive protein (CRP) at presentation was 15.2 mg/L (range: 3.2–25 mg/L) and erythrocyte sedimentation rate (ESR) was 67 mm/hr (range: 10.2–108 mm/hr). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of FDG PET-CT for diagnosing SBO were 97.9%, 87.5%, 97.8%, 87.6% and 96.4% respectively. The average SUV_{max} of the lesions was 6.3 ± 3.0 . The 18/55 patients had undergone both FDG-PET CT and MRI. The findings were concordant in 14/18 (77.8%) and discordant in 4/18 (33.2%) patients. FDG-PET CT was positive in 3 MRI negative patients and FDG PET was negative in one MRI positive patient. **Conclusion:** FDG-PET CT allows for accurate detection of site and disease activity in SBO with high performance indices. Hence it can be used as a modality of choice for primary diagnosis as well as for follow-up imaging.

E-PW062

Inflammation focus search with 18F-FDG-PET/MRI: comparative or additive value of PET and MRI

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Purpose: To evaluate the comparative or additive value of 18F-FDG PET and MRI for identifying the etiology of inflammation of unknown origin. **Methods:** A total of 24 patients (13 m, 11 w, age 42 ± 23 [8–82] y) with suspicion of an inflammation focus due to laboratory inflammation markers (increased CRP, leukocytes) or fever and up to now non-leading conventional imaging underwent a whole-body PET/MRI. Image analyses included the detection and localization of pathologically (focal) increased tracer uptake in PET including determination of SUV_{max} using VOI technique and evaluation of the contrast enhancement and diffusion restriction (ADC values) of abnormal lesions in MRI. Descriptive analysis included mean values, standard deviation and range. PET/CT, clinical, and radiological follow-up as well as histopathology served as standards of reference. **Results:** In 17/24 patients the PET/MRI contributed to the diagnosis of a (focal) pathological etiology of the inflammatory disease (vasculitis $n=5$, inflammatory bowel disease $n=4$, pneumonia $n=1$, infected vascular prosthesis $n=2$, (active) retroperitoneal fibrosis $n=1$, peritonitis and cholecystitis $n=1$, synovitis $n=1$, mycotic infection (hepatic candidosis) $n=1$, bone marrow activation $n=1$). In PET all pathological foci showed a moderately to significantly increased FDG uptake (SUV_{max} 5.3 ± 3.5 , range 1.4–14.2). The MRI satisfactorily allows the localization of the findings, but only

in 12/17 a corresponding contrast-enhancement and in 13/17 a corresponding diffusion restriction could be found. 3/17 patients showed neither a contrast-enhancement nor a diffusion restriction, but only an increased FDG uptake. **Conclusions:** Integrated ^{18}F -FDG-PET/MRI shows high potential in identifying the etiology of inflammation of unknown origin. The MRI satisfactorily allows the localization of the findings, but a significant higher detection rate could be found in PET compared to MRI. Considering the significantly lower dose of ionizing radiation, PET/MRI may serve as a powerful alternative to PET/CT.

E-PW063

C-reactive protein levels predict positive findings on ^{18}F -FDG PET/CT imaging and are associated with spleen and muscle ^{18}F -FDG uptake in patients with bacteremia

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Purpose: Bacteremia portends high rates of morbidity and mortality. Although ^{18}F -fluorodeoxyglucose positron emission tomography and computed tomography (^{18}F -FDG PET/CT) imaging has clinical value in patients with fever of unknown origin, its usefulness in bacteremia has not been entirely elucidated. We therefore designed the current single-center retrospective study to investigate the associations between clinical and laboratory data of patients with bacteremia and their ^{18}F -FDG PET/CT findings. **Subjects and Methods:** We examined 102 patients with bacteremia who had undergone ^{18}F -FDG PET/CT imaging. Clinical and laboratory data were reviewed and analyzed in relation to ^{18}F -FDG PET/CT findings. Patients with positive results underwent quantitative measurements of ^{18}F -FDG uptake. **Results:** Positive ^{18}F -FDG PET/CT findings were identified in 72 (70.6%) patients. We found significant associations between positive results on ^{18}F -FDG PET/CT and both a higher white blood cell (WBC) count and C-reactive protein (CRP) levels ($p = 0.012$ and < 0.001 , respectively). CRP level is associated with spleen and muscle ^{18}F -FDG uptake. Notably, CRP levels accurately predicted (area under curve = 0.752; $p < 0.001$) positive ^{18}F -FDG PET/CT findings (optimal cut-off point: 54.025 mg/L). **Conclusion:** Leukocytosis and increased CRP levels are significantly associated with positive ^{18}F -FDG PET/CT findings in patients with bacteremia. A CRP level > 54.025 mg/L was an accurate predictor of positive ^{18}F -FDG PET/CT results.

E-PW064

Clinical usefulness of Tc99m-HMPAO labeled leucocyte scan in the diagnosis of infection on Charcot foot

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Background-Aim: Diagnosing infection on Charcot foot remains challenging despite multimodality imaging. The study

is aiming to explore the role of $^{99\text{m}}\text{Tc}$ -HMPAO labeled leucocyte scan (LS), alone or combined with SPECT/CT scan and $^{99\text{m}}\text{Tc}$ -nanocolloid bone marrow scan (BMS) in diagnosing infection on Charcot foot. **Methods:** Eighty Charcot feet, in 72 patients, with clinical suspicion of diabetic foot osteomyelitis (DFO) were investigated by planar LS. Fifty Charcot feet had concomitant plantar ulcers. Thirty one Charcot feet were further investigated by SPECT/CT scan. In 18 Charcot feet BMS was also performed to interpret abnormal leucocyte bone uptake. LS images were interpreted alone and in conjunction with SPECT/CT scans and were compatible with DFO when persistent increased leucocyte bone uptake was observed. Increased leucocyte bone uptake without corresponding BMS uptake confirmed the diagnosis of DFO. Final diagnosis was based on clinical and radiological/scintigraphic follow-up or surgical results. **Results:** Among the 80 Charcot feet investigated, final diagnosis was DFO in 21, acute Charcot arthropathy (CA) in 20, soft tissue infection in 24 and no infection in 15. LS showed focally intense bone uptake in 18/21 and focally mild bone uptake in 3/21 cases of DFO. Conversely, LS showed mild diffuse or no leucocyte bone uptake in 16/20 cases of acute CA and in all uninfected Charcot feet, a pattern clearly distinguishable from that of DFO. Sensitivity, specificity, accuracy, positive (PPV) and negative predictive value (NPV) of planar LS for DFO on Charcot foot were 90.5%, 86.4%, 87.5%, 70.4% and 96.2% respectively. SPECT/CT enabled exact assessment of the extent of infection, especially in cases with concomitant ulcers. SPECT/CT addition highly improved sensitivity and NPV to 100%, but only slightly specificity from 86.4% to 88.5% and accuracy from 87.5% to 90.3%. BMS addition further improved specificity and accuracy of LS (to 91.7% and 94.4%, respectively) by reducing false positive LS results caused by leukocyte accumulation at sites of active bone marrow. **Conclusion:** LS is a reliable imaging modality for diagnosing infection on Charcot foot. SPECT/CT addition improved the diagnostic performance of LS for DFO especially in cases with concomitant ulcers. With a NPV of 100%, LS-SPECT/CT is a valuable method to exclude bone infection on Charcot foot, and it could serve as a screening test in cases with clinical suspicion of infection on Charcot foot. In cases of increased leucocyte uptake on Charcot foot, BMS addition is helpful in discriminating DFO from acute CA.

E-PW065

Long-term chronic suppressive antibiotic therapy (CSAT) in chronic joint infection evaluated by (99m)Tc-HMPAO radiolabeled leucocytes scintigraphy (LS)

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Purpose: The management of prosthetic joint infections (JI) and fixation devices-related infections (FDI) remains a clinical challenge. $^{99\text{m}}\text{Tc}$ -HMPAO radiolabeled leucocytes scintigraphy (LS) is an important tool for diagnosis and follow-up. No single-treatment procedure is considered appropriate for all patients but long-term chronic suppressive antibiotic therapy (CSAT) can be considered as palliative approach, especially in case of failure of

curative treatment. Aim of this study was to evaluate the clinical effectiveness of CSAT and the role of LS in clinical decision-making associated to monitoring of inflammatory index. **Subjects and methods:** 23 patients (11 male, 12 female) that presented JI (72%) or FDI (23%) underwent CSAT due to contraindication to surgery or to persistence/relapse after curative therapy. CSAT results were evaluated by LS and periodical clinical examination. LS was performed after 2–6 months in all patients and was repeated according to clinical features. Therapeutic goals were stability or regression of disease: absence of pathological LS; stability/reduction of pathological LS associated to clinical improvement. **Results:** In 8 patients, after CSAT(2–6 months) LS resulted normal and results were confirmed by a long period of clinical stability (1,5 y). One subject underwent surgery for aseptic PJI mobilization. In these patients CSAT achieved therapeutic goals, even if in 2 patients CRP was increased despite an improvement of clinical features. In 14 patients, initial LS showed persistence of infection and CSAT was continued (0,26–0,86y; mean 0,5y); control LS demonstrated a total regression (12 subjects) or a stability (2 subjects) of scintigraphic features, achieving a therapeutic goal. Clinical findings and CPR values assessed an improvement of clinical condition in most of cases, even though in one of these patients CRP value remained significantly higher despite clinical improvement. In one patient LS showed persistence of osteomyelitis after about 7 months of CSAT, with a partial regression of osteomyelitis in a second LS performed after 1,65 y. In this subject an alternative use of multiple series of CSAT followed by periods of stop was proposed, leading to stability of clinical features even if persistence of osteomyelitis was described. **Conclusions:** CSAT achieved therapeutic goal in most of patients confirmed by LS, which was in agreement with clinical and laboratory signs of disease in most of cases. LS resulted an important tool in personalized evaluation of efficiency and monitoring of CSAT.

E-PW066

¹⁸F-FDG PET/CT in the follow-up of large vessel vasculitis associated to polymyalgia rheumatica. Correlation with clinical and biochemical data

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Aim: Polymyalgia rheumatica (PMR) and large vessel vasculitis (LVV) are two closely related inflammatory entities that frequently occur simultaneously. Patients with PMR and associated LVV frequently had poor treatment response and require higher doses of steroids or other immunosuppressive drugs. Our aim was to analyze the contribution of ¹⁸F-FDG PET/CT in monitoring large vessel inflammation in patients with PMR in correlation with clinical and biochemical data. **Materials and methods:** This retrospective study included 30 patients (23 women,

65.7±9.6 years) with PMR and positive ¹⁸F-FDG PET/CT for LVV. PET/CT was requested for suspicion of LVV (atypical symptoms, persistent increase of acute-phase reactants, relapse or no treatment response). Follow-up PET/CT was performed 3–23 months after the initial scan. Twenty-one (70%) of the patients were on immunosuppressive treatment. ¹⁸F-FDG uptake was visually analyzed in five vascular regions: supraaortic trunks (ST), thoracic aorta (TA), abdominal aorta (AA), iliac arteries (IA) and lower limbs arteries (LLA). The intensity of ¹⁸F-FDG uptake in each region was graded from 0 to 3 in comparison to liver uptake and a total vascular score from 0 to 15 was assigned to each PET/CT scan. PET/CT findings were compared with clinical and biochemical outcome. **Results:** Twenty-three out of 30 patients experienced clinical improvement at follow-up or remained asymptomatic. In these patients, initial PET/CT showed uptake in 65/115 (56.5%) vascular regions evaluated and follow-up PET/CT in 50/115 (43.5%) ($p = 0.0460$). The mean±SD total vascular score decreased significantly from 5.3±2.8 at the initial PET/CT scan to 3.9±2.9 at the follow-up ($p = 0.0399$). Seven out of 30 patients showed no clinical improvement. Initial PET/CT showed uptake in 18/35 (51.4%) vascular regions and follow-up PET/CT in 20/35 (57.1%) ($p = 0.6308$). The mean±SD total score was 4.9±2.9 at the initial PET/CT scan and 4.0±1.4 at the follow-up ($p = 0.7015$). The total vascular score decreased in 17 patients. In these patients, C-reactive protein decreased from 3.7±6.6 to 1.6±1.9 ($p = \text{ns}$) and erythrocyte sedimentation rate decreased significantly from 49.3±35.5 to 24.6±20.4 ($p = 0.0409$). The total score remained unchanged or increased in 13 patients. C-reactive protein declined from 1.5±2.1 to 0.8±0.7 and erythrocyte sedimentation rate from 35.4±28.0 to 20.8±15.6, although the differences were not significant. **Conclusion:** ¹⁸F-FDG PET/CT findings had good correlation with clinical outcome in the follow-up of vascular inflammation in patients with PMR but not with biochemical data.

E-PW067

Contribution Of ¹⁸F-FDG-PET/CT Detecting Hidden Metastatic Focus In Invasive Fungal Infections

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Haematological dissemination in invasive fungemia is an independent factor of mortality, reaching values of up to 75% and being essential an optimal initial staging to achieve the ideal treatment. **Objective:** To evaluate the role of ¹⁸F-FDG-PET/CT detecting metastatic foci in invasive fungal infection patients. To compare the outcome with the evidence of symptomatology and findings in conventional imaging. **Material and Method:** It is a retrospective review of 21 patients, who underwent a PET/CT study for the assessment of invasive fungal infection and at least presented one risk factor for dissemination. The involved microorganisms were analysed. The extension of the fungemia was evaluated and a description, by patient and by lesion, of the metastatic findings was made. Finally we correlated with its symptomatology if present, and with possible results in other

diagnostic tools (CT, MRI and echocardiogram). **Results:** We found a male predominance (85%) with an average age of 60 years and CCI of 4.5. 33.3% of the patients were immunosuppressed, 42.8% had solid tumours and 14.3% haematological ones. The 81% of the patients were candidemias [*C.albicans* (45%), *C.tropicalis* (20%), *C.glabrata* (15%), *C. parapsilosis* (10%)], and 19% Aspergillus. 33 metastatic foci were detected in 13 out of 21 patients (62%); located in soft tissues 8 (61.5%), bone 6 (46%), spleen 4 (30.7%), endovascular 3 (23%), lung 3 (23%), liver 2 (15.3%), intra-abdominal collections 2 (15.3%), endocarditis 1 (5.7%) and other 4 (30.7%). 7 out of 13 metastatic patients (53.8%) and 79% of the metastasis lesions did not present associated symptomatology. 5/13p (38.5%) and 19/33 lesions (57.5%) were not diagnosed by other imaging technics. PET/CT was singularly sensitive detecting abdominal viscera, soft tissues, bone and endovascular metastatic lesions. Among metastatic patients, we found an increase on the proportion of patients who demonstrate positive blood cultures > 48h and fever > 72h. **Conclusions:** PET/CT is a useful tool for the initial staging of invasive fungemia, being able to find a high proportion of metastatic disease that often does not present symptoms or is not identified by other diagnostic techniques. It is mainly profitable in locating septic foci in abdominal viscera, soft tissues, bone and endovascular. The evidence of positive blood culture > 48h and fever > 72h should suggest an invasive dissemination to other locations.

E-PW068

A novel application of ^{99m}Tc-UBI-29-41 scintigraphy in knee joint prosthesis infection diagnosis

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Introduction: The use of Total knee arthroplasty (TKA) has had a steady growth in recent years and it is considered a safe and cost-effective orthopedic procedure for the alleviation of chronic pain and treatment of progressive osteoarthritis. This procedure, like any other surgical procedures, may have some complications including prosthetic infection as the most serious one and aseptic loosening as the most common one. Differentiating between these two entities is important because each has a different therapeutic approach. This study was conducted to investigate the ability of ^{99m}Tc-UBI scan, which is a novel imaging technique for diagnosis of musculoskeletal infection, to distinguish septic from aseptic loosening in a painful knee prosthesis. **Method:** 34 patients aged 18 to 75 years who had painful knee prosthesis were included. The ^{99m}Tc-UBI scan was performed immediately after IV administration of 20mCi (740 MBq) of ^{99m}Tc-UBI in an early dynamic and 30-minute static images. Time-activity curve was drawn for all patients and target to the non-target ratio (T/NT) was calculated on 30-minute images. The final diagnosis was confirmed by surgical findings, microbiologic culture results or active clinical follow up of the patient. **Results:** Using time activity curve analysis, 24 ^{99m}Tc-UBI scans were considered negative and 10 were positive for an infectious process. Sensitivity, specificity, and negative and positive predic-

tive values were 56%, 80%, 83% and 50%, respectively. T/NT ratio analysis on 30-minute static images demonstrated 9 positives and 25 negative patterns, with a cut off value of 1.83 for the T/NT ratio. The sensitivity, specificity, negative and positive predictive values and accuracy of this testing modality were all 100%. The ^{99m}Tc-UBI scintigraphy was able to differentiate between infected and non-infected knee prostheses with excellent precision. **Conclusion:** Our findings showed ^{99m}Tc-UBI scintigraphy is an excellent clinical diagnostic test for differentiating infectious from the mechanical loosening of the knee prostheses with perfect sensitivity and specificity. Highly accurate results were obtained only 30 minutes after injection

E-PW069

Malignant Colo-Rectal Findings In ¹⁸F-FDG PET-CT Of Infectious Endocarditis Patients Caused By Enterophilic Microorganisms

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Objective: To determine the frequency of benign, premalignant and malignant colo-rectal pathology in ¹⁸F-FDG PET studies that were performed to patients with infective endocarditis and bacteraemia caused by enterophilic microorganisms. **Material and Method:** Retrospective analysis of ¹⁸F-FDG PET study of 61 patients that were done to evaluate de extension of infectious endocarditis or persistent bacteraemia by streptococci, enterococci or enterobacteria, typified by blood culture. The uptake at endocarditis focus and presence of septic metastasis was evaluated, as well as exhaustive search of focal uptake along the colon or rectum. The metabolic and tomographic appearance of the lesions and the implicated microorganism was correlated with histopathology obtained by colonoscopic biopsy. **Results:** Average age of 59 years, 56.6% men, mean CCI: 4.1. The involved microorganisms were; *S.bovis* (8/60), *S.viridans* (20/60), other streptococci (8/60), *E.faecalis* (11/60), *E.faecium* (3/60), other enterococci (1/60), *E. coli* (7/60), *Proteus* (1/60) and other enterobacteria (4/60). PET-CT was able to detect active endocarditis in 34.5% of the patients and found colonic lesions in 29.5% of them corresponding to 19patients. Histopathological confirmation was performed in all cases. According to the image we saw a diffuse uptake in 4/19 and focal in 15/19, single foci were found in 16/19 and multiple in 3/19, the mean SUV_{max} was 6.2. When analyzing the histology we found; benign lesions in 14% of the patients, premalignant in 19% and malignant lesions in up to 21%. No pathological finding was observed in 46% considering them as false positive results. Most frequently involved microorganisms in malignant pathology were *S. bovis* (37.5%), *S. viridans* (36.5%) and *E.faecalis* (18.2%). Enterococci and enterobacteria showed higher association with pre-malignant disease. **Conclusion:** There is a high prevalence of colorectal carcinoma and premalignant lesions in infective endocarditis caused by enterophilic microorganisms, mainly *E.faecalis* and *S.viridans*, in addition to *S.bovis* (whose association is already well described). It is essential to perform an exhaustive search of colonic lesions

due to the relevance of their early detection for the therapeutic management and prognosis.

1111 Tuesday, October 16, 2018, 08:00 - 09:00, Hall A

e-Poster Walk 8 - Paediatrics / Other Clinical Studies:
Joint Paediatrics / Other Clinical Studies

E-PW070

DMSA SPECT/CT for complex renal calculi imaging in children

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Introduction: Complex renal calculi in children, including stag-horn calculi and calculi causing obstruction to urine flow, require detailed radiological imaging to delineate the calculus, the anatomy of the collecting system, and to identify possible renal scarring. We explore the clinical value of a new diagnostic algorithm with unenhanced kidney, ureters and bladder CT scan (CT KUB) and Tc-99m-DMSA with SPECT/CT as a one-stop-shop.

Subjects and Methods: 31 consecutive children (15 males, 16 females, mean age 8 years, range 3-16 years) with complex renal calculi underwent a DMSA SPECT/CT prior to a therapeutic surgical procedure (Percutaneous Nephro-Lithotomy - PCNL - or Extracorporeal Shock Wave Lithotripsy - ESWL). Patients were scanned on a Siemens Symbia T2 SPECT/CT, with a low-dose CT protocol (kVp 80-110, mAs 26-50). The stone density in Hounsfield Units (HU) was evaluated on CT. All patients had a previous renal ultrasonography. 15 patients presented with recurrent urinary tract infections (UTI), 6 with hydronephrosis, 5 with abdominal pain, 5 with residual calculi following a previous surgical procedure. 4 patients had an underlying genetic or metabolic predisposition (hypercalciuria, cystinuria, hyperoxaluria). **Results:** In total 21/31 (61%) patients had an abnormal DMSA scan. The DMSA scan showed focal renal scars in 11/15 patients presenting with UTIs and in 4/5 patients with previous PCNL. DMSA showed globally reduced parenchymal function in 5/6 patients presenting with hydronephrosis. A further patient with hyperoxaluria had stones filling all calyces and globally reduced renal parenchymal function. The CT KUB demonstrated the anatomical location of the calculi in all cases. In 21 patients with dense stones (HU >1000) CT allowed planning of the optimal surgical approach with PCNL. 5 patients with low density stones (HU <700) were treated with ESWL. Calculi within the infundibulum obstructing the related calyces were identified in 3 patients. One of them had been treated with 7 previous PCNLs for recurrent stones due to cystinuria; in him the calculus was locked in situ by an infundibular stenosis, with no residual cortical function in the adjacent parenchyma on DMSA; this was therefore not treated by a further PCNL tract. The mean effective dose equivalent from the CT component was 0.35 mSv (range 0.21-0.75 mSv). **Conclusion:** In the work up of paediatric complex renal calculi a diagnostic approach involving DMSA with

SPECT/CT is proving clinically helpful, providing simultaneous anatomical and functional information and thus allowing a planned personalised operative management, at a low radiation burden.

E-PW071

1-year Predictive Value Of Baseline Pediatric Renal Transplant Scintigraphy

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Purpose: Quantitative indices of renal transplant scintigraphies (RTS) performed within 2 days after transplantation in pediatric patients were analyzed for prediction of 1-year graft function after transplantation. **Subjects & Methods:** All pediatric patients (N=51; 27 male, 24 female; mean age: 12.4±4.2; 28 deceased, 23 lived donor transplants) to whom kidney transplantation was performed between January 2012 and March 2017 were retrospectively analyzed. Seven patients (3 photopenic kidneys due to vascular thrombosis, 2 en-bloc transplants and 2 with improper bolus of injection) were excluded from the study. The indices of Hilson's perfusion index (HI), graft index (GI), time between peak perfusion and peak iliac artery (ΔP) and the ratios of peak perfusion to plateau (P:PI), peak perfusion to peak iliac artery (P:A) and peak perfusion to peak uptake (P:U) counts were obtained. 1-year eGFR values were calculated with the "Bedside Schwartz" formula. 1-year eGFR value of <60 ml/min was accepted as graft dysfunction. In addition, age of the donors and the ratio of donor-age to recipient-age (age-D/R) were recorded. Spearman's correlation coefficient and Mann-Whitney U tests were used for statistical analysis. Receiver Operating Characteristic (ROC) curve analysis was applied for significant parameters. Accuracy was measured by the area under the curve (AUC). **Results:** Fourteen of 44 patients had graft dysfunction (eGFR <60ml/min) at 1-year after transplantation. When comparing with normal group, mean values of HI, GI and ΔP were significantly high and mean value of P:A was significantly low in the group of 1-year graft dysfunction ($p < 0.05$). Differences of the mean values of the indices of P:PI and P:U were nonsignificant. The ROC curve analysis was used to assess the ability of the significant indices in predicting 1-year graft dysfunction. AUC of P:A, HI, GI and ΔP were 0.79, 0.79, 0.75 and 0.72 respectively. The indices of P:PI and P:U were significantly correlated with age-D/R ($p < 0.05$). However, correlation between age-D/R and the other indices, which were significant in predicting 1-year graft function, were nonsignificant ($p > 0.05$). **Conclusion:** This study underlined the importance of baseline RTS of pediatric patients in predicting 1-year graft function. It can be considered that the indices of P:A, HI, GI and ΔP , which are not affected by age-D/R ratio, are useful in predicting 1-year graft function. However, the indices of P:PI and P:U are nonsignificant, probably because they are affected by age-D/R ratio.

E-PW072

The role of Future Remnant Liver Function in children with liver tumors

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Introduction: Liver resection remains the most important method of treatment of liver tumors. Postoperative outcomes mainly depend on function of remnant liver, which is directly related to quality of its parenchyma. Post-resection hepatic failure remains the main problem, which requires precise methods of preoperative evaluation of future remnant liver function (FRL-F). It has been shown in adults that the threshold value of FRL-F more than 2.7 %/min/m² allows avoiding liver failure after resection, but in our knowledge there is no study for evaluation of FRL-F in children. **Aim:** Finding the value of preoperative FRL-F assessment in children with liver malignancy. **Materials and Methods:** 11 patients with hepatoblastoma (4 boys, 7 girls, aged 4 months to 13 years) who underwent partial or extended hemihepatectomy between May-2017 and March-2018 were included in this study. Hepatobiliary scintigraphy with ^{99m}Tc-mebrofenin was performed in all patients before surgery. Visualization was carried out immediately after the intravenous injection of ^{99m}Tc-mebrofenin (dose was calculated with the help of EANM pediatric dose calculator) following standard protocol: first dynamic phase, a fast SPECT/CT of the liver and the second dynamic phase. For more accurate segmentation of the liver, the venous phase of CECT was used. The boundary of future remnant liver was manually drawn on CT images. **Results:** FRL-F was evaluated in all 11 patients. The average value of FRL-F was 13.8%/min/m² varies from 2.8 to 29.5 %/min/m². 4 patients underwent right side extended hemihepatectomy including segment 4, the FRL-F was evaluated in S2, S3 segments and ranges from 3.08 to 11.74 %/min/m² (mean 7.6%/min/m²). 3 patients underwent right hemihepatectomy, the FRL-F was evaluated in S2, S3, S4 segments and ranges from 2.8 to 13.41%/min/m² (mean 8.15%/min/m²). 3 patients underwent left hemihepatectomy, the FRL-F was evaluated in S5, S6, S7, S8 segments and ranges from 27.1 to 29.5%/min/m² (mean 28.5%/min/m²). 1 patient underwent atypical resection of S4, S5 and S8 segments; the FRL-F value was evaluated in S2, S3, S6 and S7 segments. The result was 12%/min/m². No one has developed post-resection hepatic failure following one month after liver resection. **Conclusions:** Our results demonstrated that the value of FRL-F for all patients were more than 2.7%/min/m², which can be explained by lack parenchymal diseases such as steatosis and cirrhosis in children. The methodology of FRL-F evaluation in adult can also work in children. To obtain reliable data it is necessary to continue the study with further recruitment and analysis.

E-PW073

Role of intestinal transit scintigraphy in management of severe bowel motility disorders

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Purpose: gastrointestinal motility disorders (GIMD) are common in pediatric age and can range from relatively benign conditions (such as functional constipation) to more serious disorders (such as Hirschsprung disease, HD, and chronic intestinal pseudoobstruction, POIC). Management of recurrent episodes of intestinal subocclusion mimicking a mechanical obstruction is a critical aspect in severe GIMD. The correct level of decompressive stoma or segmentary resection is crucial to relief obstruction. Conventional radiographic studies and histology are not always contributive to evidence the correct level where it could be realized. Intestinal transit scintigraphy (ITS) is a non-invasive method for the quantitative evaluation of overall and regional intestinal transit to localize any sites of obstruction. The aim of our work was to evaluate the usefulness of ITS as complementary tool to standard radiology and surgery, to improve the bowel function outcomes in motility intestinal disorders. **Subject&Methods:** we included in a multidisciplinary work-up pediatric patients affected by POIC/HD with persistent/recurrent obstructive symptoms after conventional surgical treatment stoma or bowel resection. The small-bowel and colon ITS studies begin from a gastric-emptying study after administration of a ⁶⁷Ga-citrate radiolabeled meal followed by static images up to 144 h after meal ingestion. Due to bowel anatomy variability in our population, ITS evaluation consisted in a multidisciplinary visual analysis with total transit time calculation. A resolution of obstruction with a correct stoma output or normalization of fecal excretion, and increase in enteral autonomy were considered the end-point to evaluate the efficacy of scintigraphy in the improvement of GIMD management. **Results:** we evaluated 17 patients with severe GIMD (7 POIC; 10 HD (7 total colonic, 3 extended)), 13M-5F, median age 3.1 years, range 0.05-22yrs. No adverse reactions after radiolabeled meal administration were observed. The calculated effective dose was 0.2-0.6 mSv in normal vs slow intestinal transit (1/15 and 1/5 of effective dose compared to barium radiography). The median transit time was 59 hours (range 24-143 h). Of the 17 patients, 59% (10/17) had abnormal transit and in 80% of these (8/10) there was a change in surgical management (3 botox injection, 2 stoma revision, 1 ileal resection, 1 jejunostomy closure) with clinical improvement in all. **Conclusion:** our preliminary experience suggests the clinical value of scintigraphy in the management of severe GIMD. In our cases scintigraphy findings combined with others diagnostic tools helped to guide the correct stoma placement, intestinal resection or Botulin Toxin injection, improving bowel function and patient outcome.

E-PW074

Brown Fat Detection at 18F-FDG PET/CT: Differences between Adult and Pediatric Population in a 12 Years Experience

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Purpose: Brown adipose tissue (BAT) activation is a phenomenon frequently detected by fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG

PET/CT) that may interfere with images interpretation reducing the diagnostic performance. Aim of our study was to describe the epidemiological (age, sex) and anthropometric (BMI, glycaemia, examination's season, season of birth) features of patients with BAT activation and analyze a possible role of these parameters in the prediction of BAT detection in PET. **Materials and Methods:** Between 2005 and 2017, 818 18F-FDG PET/CT in 611 patients positive for BAT detection were retrospectively included; among them, 567 were adults, 51 pediatrics and 7 underwent scans in both age groups; patients were considered as adults from 18 years old. Seventy hundred and forty-two PET/CT were performed in adult population (Male 154, Female 588), with a mean age of 44.17 years, mean glycaemia of 93.62 mg/dL and mean BMI of 22.75 Kg/m²; 76 PET/CT were performed in pediatric population (Male 30, Female 46), with mean age of 14.34 years, mean glycaemia of 89.67 mg/dL and mean BMI of 20 Kg/m². A Chi-squared test was performed to compare features distribution between adult and pediatric population. **Results:** Comparing adult and pediatric population, adults showed a higher BAT activation detected at PET/CT in female sex (79% vs 61%, $p < 0.001$) and within the impaired glucose tolerance range (>100 mg/DL) (24 % vs 16%, $p = 0.02$), while no significant difference was present considering the overweight BMI range (>25 Kg/m², overweight cut-off corrected for age and sex according to Cole tables in pediatric patients) (22% vs 20%, $p = 0.55$). Considering female group only, adults showed a higher rate of BAT detection within the impaired glucose tolerance range (83% vs 42%, $p < 0.001$) and the overweight BMI range (80% vs 67%, $p = 0.005$). Moreover, in both populations BAT activation happened more frequently in cold seasons (winter and autumn) compared to hot (summer and spring); there was no significant distribution difference between the two population considering birth's season ($p = 0.2$), excluding from the analysis PET studies performed in patients known to be not born in four seasons temperate climate zones. **Conclusions:** Sex, glucose blood levels and BMI play a major role in BAT activation, with significant differences between adults and pediatrics. Cold exposure is confirmed to be important in predicting BAT activation, while birth's season is not significant.

E-PW075

99mTechnetium-macroaggregated albumin perfusion lung scan versus contrast enhanced echocardiography in the identification of the hepatopulmonary syndrome in liver cirrhosis

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Background: The hepatopulmonary syndrome (HPS) is a triad of liver cirrhosis (LD), arterial hypoxemia and intrapulmonary arteriovenous shunting in the absence of a primary cardiopulmonary disease. The aim of this project was to diagnose the prevalence of the HPS in LD because of different etiologies. We also assessed to evaluate the role of 99mTechnetium labeled macroaggregated albumin (99mTc-MAA) perfusion lung scan versus contrast enhanced echocardiography (CEE) with intravenous

injection of agitated saline in the measurement of intrapulmonary shunts and their association with important clinical and laboratory data. **Materials and methods:** In total, 27 patients (18 males, 9 females) with 52.37 ± 17.28 yrs were investigated. All had proved cirrhosis. The two modalities 99mTc-MAA perfusion lung scan and contrast enhanced echocardiography (CEE) were carried out in all participants. The some clinical and paraclinical tests were done. **Results:** 99mTc-MAA perfusion lung scan diagnosed shunts in 14 patients while CEE in 5 patients (p value=0.03). The Model for End-Stage Liver Disease (MELD) score was 13.19 ± 7.25 . In comparison of patients with and without shunting on perfusion lung scan, there was only a significant difference in duration of disease and other parameters did not showed significant difference. **Conclusion:** 99mTc-MAA perfusion lung scan was more sensitive than CEE in detection of intrapulmonary shunts in liver cirrhosis.

E-PW076

The clinical utility of lymphoscintigraphy in diagnosis of lymphedema

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Aim: Lymphoscintigraphy is a robust, easily applied and well-tolerated objective imaging method to diagnose upper and lower extremity lymphedema. The purpose of this study was to evaluate patients with lymphedema underwent lymphoscintigraphy scan in our clinic. **Methods:** Between January 2015-March 2018, we intradermally injected Technetium-99m-labeled nanocolloid in the first web spaces of both feet in 345 patients, the second interdigital space of both hands in 64 patients and both feet-hands in 17 patients who had clinical evidence of extremity swelling with suspicion of lymphedema and were referred for routine lymphoscintigraphy (M-F:202-224, mean age 46.4 years, range 3-87 years). A total of 886 extremities were examined. Lymphoscintigraphy scan was started as dynamic viewing followed by static whole body imaging at 10 minute, 1 hour and 4 hours after injection. The scans were analyzed and staged (I to IV) for visualization of lymph vessels and lymph nodes, dilatation of lymphatic vessels, existence of collateral vessels and dermal back flow. **Results:** The diagnosis of lymphedema was established in 502 of 886 extremities (56.7%), including lymphangiectasia, lymphatic obstruction, and lymphatic leakage. The majority of patients (41.4%) had primary lymphedema and the remaining ones had secondary lymphedema (15.3%) caused by malignancy-malignancy surgery, trauma, tuberculosis lymphadenitis etc. The most common scintigraphic patterns were decreased flow, collateral vessels, dermal back flow and decreased lymph node uptake. Based on lymphoscintigraphic staging (L-stage), 194 cases (38.7%) had Stage I, 152 cases (30.3%) had Stage II, 88 cases (17.5%) had Stage III and the remaining 68 (13.5%) cases had Stage IV lymphedema. **Conclusion:** Lymphoscintigraphy allows the characterization of lymphatic morphology. Effective use of this imaging technique is necessary to find out understanding of the pathophysiology of lymphedema and to plan treatment.

E-PW077

Role Of Isotopic Renogram Performed 24 Hours Post-Transplantation in long-Term Follow Up And Clinical Evolution Of Patients

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Aim: To evaluate the contribution of isotopic renogram performed 24 hours post-transplantation on the long-term evolution and follow up. **Materials and Methods:** We included 225 patients who underwent renal cadaver transplantation from January 2011 to December 2015 (145 males, 80 females; mean age: 59 ± 14.95 years old). 24 hours after transplantation we performed a 30 minutes renogram study focusing on the abdomen in anterior projection after the administration of 370 MBq of ^{99m}Tc -DTPA, followed by planar images at 30 and 180 minutes. **Results:** Of the 225 reviewed patients, 189 (84%) presented good clinical evolution 2 years after the transplantation, 34 (16%) developed renal failure (12 vascular thrombosis, 10 chronic kidney disease - stages II to V-, 5 obstructive uropathy, 3 membrane proliferative nephropathy, 3 acute rejection, 2 multiple infections, 1 nephrotoxicity and 1 Burkitt lymphoma). Of the 189 patients with good evolution, 125 (66.1%) presented acute tubular necrosis (ATN) in the scintigraphy study (80 (64%) mild, 37 (29.6%) moderate and 8 (6.4%) severe), and 15 patients (7.9%) other alterations were observed in the renogram (8 urinary leakage, 5 renal pelvis dilatation/ectasia and 2 infarct). In the 34 patients with renal failure during the follow up, the renogram showed ATN in 18 patients ((1 (5.5%) mild, 13 (72.2%) moderate and 6 (33.3%) severe) and renal pelvis dilatation/ectasia in 1 case. In 11/12 patients diagnosed with vascular thrombosis in the renogram, transplantectomy was performed in the following days. **Conclusions:** Our experience demonstrates the great utility of post-transplantation renogram to evaluate kidney perfusion as well as early transplant complications. This study indicates that 24 hours post-transplantation renogram may have a role in the evaluation of clinical evolution, follow-up and evaluation of moderate to severe ATN, allowing to prognosticate future complications of the implant.

E-PW078

Determining true plasma MAG3 - A New Approach to the Rutland-Patlak Processing Method

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Introduction: Background correction and 'blood' curves are fundamental for Rutland-Patlak analysis of MAG3 studies to get renal function (from the first few minutes) and Renal Output Efficiency (ROE) excretion values (final frames). Appropriate regions of interest (ROI) are vital, as is an understanding of their components. **Method:** A previous study has shown that the 'Spleen' ROI was the best match for the renal ROIs in relation to 'blood pool' data. However both spleen and renal ROIs also contain tissue and extravascular background components. For

Rutland-Patlak analysis the component relating to "integrated blood" ideally needs the values for the MAG3 plasma content only. We used the MAG3 physiological two-exponential model to derive a fractional correction curve with time, $f(t)$, that represents plasma only in a ROI i.e. $f(t) \times \text{Spleen ROI}(t)$. This 'plasma-only' MAG3 data is used for the "integrated blood" and the 'Spleen' ROI used for background subtraction within the Rutland-Patlak analysis; $\text{Kidney ROI}(t) / \text{Spleen ROI}(t) = A \times [\Sigma(f(t) \times \text{Spleen ROI}(t)) / \text{Spleen ROI}(t)] + B$ A = relative kidney function, B = background subtraction. **Results:** We compared the Rutland-Patlak analysis using the above and also using 'Spleen' ROI; a standard 'T-shaped' ROI (placed between kidneys); and the Manchester 'MANREN' analysis, which uses an initial normalised area tissue subtraction. We examined the error of the gradient of the Rutland-Patlak plots for $n=98$ kidneys. Gradient errors with our new technique were significantly smaller ($p < 0.001$), with average error increases of $\times 2.3$ (spleen only); $\times 2.1$ ('T-shape'); and $\times 2.8$ (MANREN). The 'Rutland-time' points for the straight-line gradient are easier to define with this plasma analysis. In addition, the error of the Rutland-Patlak gradient can be used to automatically determine the best points for the analysis. By iteration through the data points in the initial 5 minutes, the minimum gradient value can automatically identify the best data points to use. In addition, the new integrated plasma curve gives a more physiologically correct zero excretion curve for defining kidney excretion. Curves based only on the Spleen ROI also include other components and so can overestimate the excretion calculated values. For ROE values of $< 85\%$ ($n=40$), the new plasma/spleen model gave ROE values 15.3% lower than using the spleen only. **Conclusion:** A new analysis based on MAG3 physiology gives improved Rutland-Patlak analysis and also better excretion data.

E-PW079

A new method for obtaining highly concentrated viable platelet-rich plasma for ^{111}In Oxinate labeling

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Introduction: Labeled platelets (PLT) are used in Nuclear medicine for identifying the main site of destruction in patients with thrombocytopenia and for imaging of platelet-activating endo-arterial plaques. Nevertheless platelet labeling with ^{111}In -oxinate and the efficiency of platelet separation methods and their influence on platelet function preservation were never well standardized. We studied and verified a new fast and effective procedure for platelet separation and labeling with ^{111}In -Oxinate, for getting standardized platelet quantitative parameters (**DEPER:** Dose of injected platelet, **Enrichment** of PLT concentration, **Purity** of labeled PLT, labeling **Efficiency**, PLT **Recovery**). We then checked labeled PLT biologic parameters (**AV:** Activation of PLT, **Viability** of PLT). **Subjects and Methods:** We took 30 ml of whole blood mixed with 6 ml ACD from 20 healthy volunteers. We then processed the blood using a commercial kit for white blood cell separation (WBC marker kit, Celltech, Turin, Italy) using a double centrifugation technique (440

g and 2200g, 10-min. each) for obtaining the PLT concentrate in a small volume (0.5 ml) of plasma. After labeling, we evaluate DEPER parameters using Hemocitometry and AV parameters using cytofluorimetry, P-selectin membrane expression and trypan blue vital dyeing. The whole process was then replied as a Mediafill analysis and small amount of the final sample were thereafter tested for apyrogenicity and sterility. **Results:** The mean $\pm$ DS results in the 20 samples by DEPER classification are: **Dose** of injected platelet $4650 \pm 1358 \times 10^6$, **Enrichment** factor of PLT 16.7 ± 2.2 , **Purity** of labeled PLT as % of WBC_{NEUTR} and RBC residual factor, respectively $6 \pm 3.3\%$ and $3.6 \pm 2.9\%$, labeling **Efficiency** 70%, PLT **Recovery** 58 %. All functional tests showed normal platelet function, in particular AV classification demonstrates a vital PLT percentage at rest >99%. All apyrogenicity and sterility tests showed normal results. **Conclusions:** our method seems to be fast, safe and efficient. The increase in labeled platelet absolute number allows to draw a smaller amount of blood volume in patient with thrombocytopenia, an higher labeling efficiency and consequently better quality images. The use of a commercial kit makes it easy and easily reproducible preserving biological function of platelet for war-ranting reliable and high quality exams.

1311 **Tuesday, October 16, 2018, 11:30 - 13:00, Hall A**
e-Poster Walk 9 - Neuroimaging: Neuroimaging

E-PW081

In vivo Imaging of Microglial Activation in Patients with Clinical Suspected Progressive Supranuclear Palsy: A 18F-GE180 PET study

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Introduction: Progressive supranuclear palsy (PSP) is a 4R-tauopathy with a severe clinical course. The pathophysiological processes are not sufficiently understood and a causal therapy for this life limiting disease is still missing. The neuro-pathological hallmark of PSP are accumulated tau protein fibrils that were claimed to be responsible for following neurodegeneration. Microglial activation has been shown to occur in PSP as another hallmark of the disease. Therefore, we aimed to establish in vivo imaging of microglial activity by 18kDa translocator protein (TSPO) PET. **Methods:** Seven patients with probable PSP according to current diagnosis criteria underwent 18F-GE180 TSPO PET. All images were scaled by the global mean and standardized uptake value ratios (SUVr) were generated in brain regions typically affected in PSP. Voxel-wise differences were calculated using seven healthy individuals (HC) serving as controls. Furthermore, we compared patterns of microglial ac-

tivity with 18F-THK5351 PET (tau/MAO-B ligand) deriving from previously imaged patients with PSP, matched for age and disease severity. **Results:** Significantly increased 18F-GE180 binding in PSP versus HC was found in the anterior cingulate gyrus (+22%, $p < 0.001$), globus pallidus (+14%, $p < 0.005$), and nucleus dentatus (+24%, $p = 0.001$). Voxel-wise microglial activation matched known regions of disease affection in PSP except for the midbrain. Contrary 18F-THK5351-PET showed increased binding predominantly in the midbrain (+19%, $p < 0.001$) and binding was also significantly elevated in brain regions with increased TSPO activity. **Conclusion:** TSPO-PET imaging in PSP patients is feasible and patterns of microglial activation correlated topologically with most brain regions known to be affected in PSP. The particularly low microglial activation in the midbrain compared to highest binding of tau/MAO-B ligands needs further investigation by specific ligands for tau and astrocytosis.

E-PW082

Changes In Metabolism And Related Connectivity In Patients With Acrophobia Treated By Virtual Reality Therapy: A 18F-FDG PET Study Sensitized By Virtual Reality Exposure

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Purpose: Research into the underlying causes and treatment of acrophobia is of particular interest owing to its high prevalence, chronicity and cumulative social impact. Virtual reality exposure therapy (VRET) has shown its effectiveness in the treatment of this disease. The aim of this PET study was to characterize brain metabolism of patients with acrophobia, and investigate the impact of VRET on metabolic rate of glucose and related connectivity. **Methods:** Before VRET, 18 patients with acrophobia performed a brain 18F-FDG-PET sensitized by VR exposure during the radiopharmaceutical administration. Among them, 9 patients were tested again with PET during VR exposure after VRET. Clinical response to VRET was evaluated by subjective unit of discomfort (SUD) and behavioural avoidance test (BAT). Statistical Parametric Mapping-T-scores-maps were applied for comparison between patients and 18 age- and gender-matched healthy control subjects ($p < 0.05$, corrected for family wise error comparison), and for comparison between patients before and after VRET ($p < 0.005$, corrected for cluster volume). Metabolic connectivity was evaluated through inter-regional correlation analysis. **Results:** SUD and BAT were significantly improved in patients after VRET ($p \leq 0.02$). Before therapy, patients with acrophobia showed a decreased of metabolism in bilateral medial temporal areas in comparison with controls. After VRET, patients presented an increased metabolism in left frontal superior gyri and left precentral gyrus, and an increase of metabolic connectivity between this region and occipital areas (respective coefficient of correlation before and after treatment

between left precentral gyrus and occipital areas of 0.24, $p=0.34$ and 0.73, $p=0.03$). **Conclusion:** These findings provide insight of the limbic involvement in acrophobia mental disorder, and the connectivity increase of visual-motor control system induced by VRET.

E-PW083

Striatal Dopamine D₂ Receptors Changes in Patients off First-Episode Major Depressive Disorder and Correlation Analysis of Clinical Features

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Purpose: To study a group of patients with first-episode major depressive disorder (MDD) with the 11C-Raclopride PET/CT, to observe striatal dopamine D₂ receptors non-displaceable binding potential (BPND) changes of MDD and analyze the relationship between BPND and Hamilton depression rating scales (HAMD). **Subjects & Methods:** From December 2014 to December 2015, MDD patients and healthy controls who matched with MDD patients in age and gender underwent brain MRI and 11C-Raclopride PET/CT to make a prospective study. BPND of bilateral striatal dopamine D₂ receptors (SDDR) were calculated by molecular imaging and kinetic analysis toolbox (MIAKAT). BPND changes of bilateral SDDR and their relationship with HAMD were analyzed. Chi-squared test, paired-t test, two-sample t test and Pearson correlation analysis were used.

Results: A total of 20 MDD patients (8 males, 12 females, age: 32.80 ± 9.76) years) and 20 healthy controls (9 males, 11 females, age: 29.25 ± 6.93) years) were enrolled in this study. The brain tissues intake of 11C-Raclopride of the MDD group and control group were mainly distributed in bilateral striatum, and very few 11C-Raclopride was distributed in bilateral cerebral cortex and cerebellum. In MDD group, the BPND level of bilateral SDDR had no statistical differences ($t=0.69$, 0.35 , both $P>0.05$). In control group, the BPND level of bilateral SDDR had no statistical differences ($t=0.28$, 0.24 , both $P>0.05$). Compared with the control group, the BPND levels of bilateral SDDR of the MDD group were all reduced ($t=3.13$ – 4.41 , all $P<0.05$). The BPND of bilateral caudate nucleus and/or putamen D₂ receptors had correlation with HAMD total scores, anxiety/somatization factor scores, cognitive impairment factor scores, retardation factor scores and sleep disturbance factor scores ($r=-0.688$ – -0.453 , all $P<0.05$). **Conclusions:** The binding potential of SDDR of MDD is declined, and the BPND levels of SDDR are correlated with symptoms of depression. The abnormality of SDDR may be one of the important molecular mechanisms of the abnormality of midbrain-striatal dopamine reward circuits of MDD.

E-PW084

The metabolic basis of psychosis in bipolar disorder

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Psychotic symptoms are a common feature in Bipolar Disorder (BD), especially during manic phases, and are associated

with a more severe course of illness. However, not all bipolar subject experience psychosis during the course of their illness, and this difference often guide assessment and pharmacological treatment. In this context, the aim of the present study is to elucidate, for the first time, the metabolic dysfunctions associated with psychosis in a group of bipolar patients with and without psychotic symptoms, using FDG-PET. Fifty bipolar patients with psychosis, 40 bipolar without psychosis, and 27 healthy controls were recruited and underwent an FDG-PET session. The statistical analyses were performed using Statistical Parametric Mapping (SPM12). The T1-series MR images were segmented according to GM, white matter and CSF probability maps to generate the normalization deformation field into the MNI space to be applied to the co-registered FDG-PET scan. Inference on brain glucose metabolism differences between groups was made using double-sided t-tests ($p<0.01$, cluster Family-Wise Error [cFWE] corrected with an extended threshold of at least 50 contiguous voxels). Compared to healthy controls, BD subjects showed decreased metabolism in several brain areas, including insula, middle and inferior temporal gyrus as well as middle and inferior occipital gyrus. Moreover, in the direct comparison between the two patient groups, we found that patients with psychosis had decreased metabolism in the right fusiform gyrus compared to patients without psychosis (all $p<0.01$ cFWE corrected). Overall, our results suggest that metabolic alterations in brain regions involved in emotion regulation are a key feature of BD, regardless the presence of psychosis. Finally, we demonstrated that the metabolic reduction in fusiform gyrus is associated with that the presence of psychotic symptoms in BD, ultimately leading towards the idea that the fusiform gyrus might be considered a putative biomarker of psychosis.

E-PW085

Molecular Mapping of Serotonergic and Dopaminergic Projections from Brainstem to Striatal Areas in Early Parkinson's disease Patients

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Introduction: Dopaminergic and serotonergic systems are involved in the pathophysiology of motor and non motor impairments in Parkinson's disease (PD) patients. The potential to evaluate serotonergic and dopaminergic targets in the brainstem (i.e substantia nigra and raphe nuclei) has so far been challenged by methodological limitations. The aim of this study with high-resolution PET imaging and a dedicated methodology was to examine the relative loss of the serotonin (SERT) and the dopamine transporter (DAT) in the axonal terminals (striatum) as compared with cell bodies (substantia nigra) in early PD patients and control subjects. **Materials & Methods:** Twenty

non depressed early PD patients (15M/5F, 62 ± 8 y, range 47–74y, disease duration 2.8 ± 2.6 y; UPDRS-m: 21.1 ± 5.9) and 20 age and gender matched control subjects were included in the study (15M/5F, 62 ± 7 y, range 50–72y). They underwent PET measurements with the SERT radioligand [^{11}C]MADAM and the DAT radioligand [^{18}F]FE-PE2I using the HRRT PET-system and 3T MRI. Binding potential (BP_{ND}) images were generated with wavelet-aided parametric imaging software and reference based modelling methods. For each biochemical target a dedicated anatomical and molecular template was generated to define specific volumes of interest for the brainstem and striatal VOIs. A series of independent-samples t-tests with BP_{ND} values of [^{11}C]MADAM and [^{18}F]FEPE2I were conducted, comparing PD and controls for each outcome measures in the four regions of interest using Bonferroni's correction with an alpha threshold of 5%. **Results:** SERT availability in the dorsal and median raphe were 4% and 1.8 % lower (non significant) in early PD patients vs. controls. On the other hand, DAT availability in the substantia nigra was 30% lower in PD patients compared with controls ($p < 0.001$). In PD patients, SERT availability in caudate and putamen was 25% lower than in controls. For the putamen, the difference was significant after Bonferroni correction ($p < 0.01$). Putamen and caudate DAT availability in PD patients were 70% and 40% lower than in controls ($p < 0.001$). **Conclusions:** The findings of this study suggest that in non-depressed PD patients, at an early stage of the disease, there is a more pronounced loss of dopaminergic projections compared with serotonergic projections. At the level of the cell bodies, the DAT in the substantia nigra is relatively more preserved as compared with the striatum, whereas in the raphe nuclei of PD patients the SERT availability is apparently not impaired. Overall, this study suggest that the serotonin system is less impaired than the dopaminergic system in early PD.

E-PW086

First-in-man Study in Parkinson Syndromes with the New CZT SPECT Camera (VERITON®) and ^{123}I -FP-CIT

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Introduction: Based upon the breakthrough of cardiac CZT cameras, there is now an interest to apply this same technology to other SPECT imaging targets. Recently, an organ specific CZT-SPECT scanner (VERITON® Spectrum Dynamics, Caesarea, Israel) that utilizes a focused body/organ and contouring detector technology has been introduced, interesting for neuro-nuclear medicine. In this study, we compare dopamine transporter SPECT imaging between a conventional and the VERITON® cameras. **Subjects and Methods:** With the approval of the ethical committee, on patients undergoing the routine clinical procedures as part of their clinically referred care, dopamine transporter SPECT imaging have been acquired with a conventional gamma camera and the VERITON® camera, with no additional injection of radiopharmaceutical to patients. ^{123}I -FP-CIT brain

SPECT data was acquired for 15 to 18min in body contouring mode using 12 CZT detectors and 180 projections per detector. The images were reconstructed using OSEM iterative algorithm with resolution recovery, 2.46mm voxel size, 8 iterations, 8 subsets, Chang attenuation correction. **Results:** To date, dopamine transporter SPECT imaging have been acquired in 8 patients (age 66 ± 7) injected with 145.2 (± 8.1) MBq of ^{123}I -FP-CIT. Initial experience with the CZT-SPECT system has shown that it is possible to acquire a dopamine transporter SPECT image in approximately 15 minutes, half the time required by a conventional SPECT system (~ 30 minutes), and with a better resolution. Diagnosis of Parkinson disease was done in 2 patients out of 8 in both modalities. **Conclusions:** CZT technology has the potential to provide high resolution SPECT images with potentially lower time acquisition and/or radiation dose to the patient than when using conventional gamma camera technology. Further investigation is necessary, not only with ^{123}I -FP-CIT but also SPECT perfusion tracers, to demonstrate the benefits of applying this new CZT technology to SPECT neuro-nuclear Imaging.

E-PW087

Detection of triple-pathology disease windows by means of multimodal imaging in patients with Alzheimer's disease and mild cognitive impairment with probable Alzheimer's disease

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Purpose/Introduction: We identified regions affected by multiple versus single neurodegenerative pathologies in Alzheimer's disease (AD) and mild cognitive impairment (MCI) with probable AD, thus describing specific regional susceptibility to neurodegenerative pathologies and detecting regions best suited for biomarker disease staging. Multimodal pathology was assessed by MRI, ^{18}F -FDG-PET and ^{11}C -PIB-PET in different clinical disease stages. **Subjects/Methods:** We included 79 patients (32 AD, 47 MCI) and 15 age-matched healthy controls (HC). All subjects underwent neuropsychological tests, including Clinical-Dementia-Rating (CDR). Patients were divided into subgroups with very mild dementia (VMD, $n=54$) and mild dementia (MD, $n=23$) by their CDR-SOB-score. All subjects underwent structural T1-weighted-MRI, ^{18}F -FDG-PET and ^{11}C -PIB-PET imaging. Pre-processing was done using SPM8 and VBM8. For each modality and patient group data was compared to HC by voxelwise two-sample t-test in SPM8 (FWE $p < 0.05$, cluster size > 20) correcting for age, gender and APOE-status. The resulting abnormality T-maps were saved as binary-ROIs and used to calculate the intersections of all modalities, reflecting brain regions affected by all three neuropathologies (referred to as tripath-ROIs). Individual image data was extracted within the tripath-ROIs for each modality in all patients and correlated with CDR-SOB. **Results:** Despite mild symptomatic stages, VMD and MD groups showed a very widespread significantly increased PIB-uptake sparing only few cortical regions. MD

showed a more widespread pattern of reduced FDG-uptake than VMD, including large parietal, temporal and frontal parts. Opposed to VMD, MD also showed an increased atrophy pattern involving the parietal, temporal and frontal lobe with a temporal focus. The atrophy pattern was the least extended of all three modalities. The VMD-tripath-ROI mainly involved regions of the left temporal lobe. The MD-tripath-ROI spread in the temporal lobes of both hemispheres and extended to the left parietal lobe partially including the posterior cingulate and precuneus. CDR-SOB and PIB-values in the tripath-ROIs did not correlate significantly. FDG- and VBM-values correlated significantly with cognitive performance in the tripath-ROIs.

Discussion/Conclusion: We identified specific regions affected by overlapping neurodegenerative pathologies in different stages of disease and regions struck by single pathologies, particularly amyloid-burden. Our findings support a pathophysiological disease model defined by widespread deposition of amyloid-pathology and more circumscribed and topographically related neurodegenerative pathology (hypometabolism followed by atrophy). Clinical decline and extent of neurodegenerative pathology correlated significantly in regions struck by all three pathologies in early disease stages. These regions might qualify as universal “disease windows” suited for standardized disease monitoring even when applied to different imaging modalities.

E-PW088

¹⁸F-DG-PET and morphometric brain analysis in retired soccer players exposed to long-term mild traumatic brain injuries.

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Purpose/Introduction: Chronic traumatic encephalopathy (CTE) can result from exposure to minor traumatic brain injuries, leading to cognitive decline and being presumably related to a progressive tauopathy or a disturbance on TDP-43. This condition is mostly described in boxers and NFL football players. Although soccer players are exposed to minor head traumas (mild traumatic brain injury - mTBI), the prevalence and effects of CTE on these athletes remains elusive. We aimed to evaluate cortical thickness and regional brain metabolism of retired soccer players' brains compared to age-matched healthy controls. **Subjects & Methods:** We included eighteen retired professional soccer players and eighteen age-matched healthy controls. Brain [¹⁸F]FDG-PET and magnetic resonance imaging (MRI) with volumetric T1 (3DT1) sequences were performed in our 3T PET/MR scanner (SIGNA, GE Healthcare). [¹⁸F]FDG-PET and 3DT1 images were processed and analyzed with Statistical Parametric Mapping software (SPM8) and FreeSurfer for assessment of regional brain glucose metabolism and cortical thickness, respectively. **Results:** Surface-based morphometry revealed clusters of reduced cortical thickness several areas (left inferior frontal gyrus, left superior parietal lobule, right inferior supramarginal gyrus and superior parietal lobules, right lingual gyrus and right medial orbitofrontal gyrus) of soccer

players. These results, however, did not remain significant after correction for multiple comparisons (FDR). [¹⁸F]FDG-PET analysis revealed three clusters of reduced glucose metabolism in soccer players compared to controls bilaterally in posterior and inferior temporal regions reaching statistical significance after correction for multiple comparisons (FWE and FDR $p < 0.05$): left middle temporal gyrus, left inferior temporal gyrus and right middle temporal gyrus. **Discussion/conclusion:** Soccer players are exposed to minor head traumas for extended periods, and the effects of mTBI on these athletes remain unclear. The results of cortical thickness presented here are partially in accordance with reported data on the impact of mTBI in NFL football players, fighters or subjects exposed to isolated mTBI event. [¹⁸F]FDG-PET scan findings of reduced glucose metabolism in temporal lobes are in accordance with previous reports. It's noteworthy that most studies in the literature performed voxel-based morphometry instead of surface-based morphometry and only a minority of papers of brain morphometry and none exploring brain metabolism approached soccer players. To our knowledge, this is the first study analyzing long-term effects of mTBI in soccer players using surface-based morphometry and brain [¹⁸F]FDG-PET. This is an ongoing study, and we presented here its first partial results.

E-PW089

Amyloid PET as a marker of Normal-Appearing White Matter early damage in Multiple Sclerosis: correlation with CSF β -Amyloid levels and brain volumes

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Purpose: The disease course of multiple sclerosis (MS) is still unpredictable and there is an urgent need to identify reliable prognostic biomarkers. PET with β -amyloid (A β) tracers is a promising tool to evaluate white matter (WM) damage and repair, and cerebrospinal fluid (CSF) A β levels has recently been suggested as a predictive biomarker of disease progression. Aim of this study was to investigate amyloid PET uptake in WM of MS patients, and to evaluate possible correlations between CSF A β levels, amyloid tracer uptake and brain volumes. **Subjects & Methods:** Twelve MS patients were divided according to their disease activity into active and non-active groups. All participants underwent neurological examination, neuropsychological testing, lumbar puncture, brain MRI, and ¹⁸F-florbetapir PET. A β levels were determined in CSF samples from all patients. Using SPM12, MRI and PET images were co-registered and WM mean standardized uptake values (WM-SUV) were calculated for each patient. Using LST toolbox, we used T2-weighted scans to quantify WM lesion load, and voxel-based morphometry to measure brain volumes. **Results:** We found a lower WM-SUV in damaged WM (DWM) compared to normal appearing WM (NAWM) ($p = 0.0005$) in all patients. A decreased NAWM-SUV in active compared to non-active group was observed ($p = 0.028$). Considering only active patients, NAWM volume correlated with NAWM-SUV ($p = 0.01$). Interest-

ingly, CSF A β concentration was a predictor of both NAWM-SUV ($r=0.79$; $p=0.01$) and NAWM volume ($r=0.81$, $p=0.007$).

Conclusions: This study provides evidence on the role of amyloid PET in the assessment of MS, particularly in relation to disease activity and early prognosis. The correlation between CSF A β levels and WM-SUV suggests that the predictive role of A β may be linked to myelin early damage and may reflect the disease activity and the clinical progression.

E-PW090

[¹⁸F]DPA-714 PET-MRI imaging in (auto-)immune limbic encephalitis

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Introduction: (Auto-)immune limbic encephalitis (LE) usually presents with mesial temporal lobe epilepsy and cognitive changes and is thought to be mediated by adaptive neural immunity. Targeting the translocator protein (TSPO) with a second generation PET-Tracer (F-18-DPA-714) permits visualisation of TSPO overexpression in activated microglia and other innate immune cells. The aim of this study is to investigate the feasibility of a combined F-18-DPA-714 PET-MRI protocol for visualisation of innate inflammation in seropositive and seronegative LE patients. **Methods:** Five LE patients underwent combined F-18-DPA-714-PET-MRI between 9/2017 and 2/2018. Dynamic images were acquired 0–60 min p.i. on a Siemens PET-MRI system (mMR). T1w, T2w and Flair MR-images were effected for correlation purposes. Inclusion criteria were recent diagnosis of limbic encephalitis (2 x seronegative; 1 x anti-GAD65 antibodies, 2 x anti-LGI1 antibodies) and naivety to immunotherapies. Inflammation to background ratios ($SUV_{max} \text{ tumor} / SUV_{mean} \text{ reference region}$) measured in 30–60 min p.i. summation images were standardized to a cortical reference region including grey and white matter on the less-affected brain hemisphere. Time activity curves were implemented for the hippocampus in both hemispheres and the cortical reference region. **Results:** This study provides first insights into microglia activation in LE as assessed by DPA-714-PET-MRI. All LE patients showed increased uptake in the mesial temporal lobe (amygdala, hippocampus) on the affected side compared to the contralateral hemisphere and the reference region. TSPO expression correlated with signal alterations in T2 and FLAIR images. Time activity curves showed high activity in LE over time compared to the contralateral reference region. **Conclusion:** We demonstrate the feasibility of [¹⁸F] DPA-714-PET-MRI to visualize the innate immunity in LE. [¹⁸F] DPA-714-PET-MRI may be a promising future tool for the assessment of individual inflammation patterns in LE independent of the absence or presence and targets of an underlying adaptive immune response.

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Tuesday, October 16, 2018, 14:30 - 16:00, Hall A

e-Poster Walk 10 - M2M: Quality Control & Radiopharmaceutical Aspects

E-PW091

⁶⁸Ga-radiotracer production: Reliable HEPES quantification and investigation of synergistic effects

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Aims: Successful ⁶⁸Ga-radiolabeling is strongly linked with an adequate pH range. Therefore, a suitable and non-toxic buffering system is required which additionally provides a safe application of the radiopharmaceutical to patients. Most commonly used buffers for ⁶⁸Ga-complexation are sodium acetate (NaOAc) and 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES). Although low toxicity of HEPES was demonstrated in rats (2000 mg/kg; data taken from safety sheets of commercial suppliers) the European Pharmacopoeia (Eur. Ph.) states a considerably low limit of 200 $\mu\text{g/V}$ for the latter one. As a result, the Eur. Ph. describes an assay for HEPES quantification by TLC and iodine staining. However, this method is neither reliable nor reproducible. Therefore, aim of this study was the development of an improved TLC assay for HEPES quantification and examination of HEPES' toxicity *in vitro*. Additionally, potential synergistic effects of HEPES and [⁶⁸Ga]Ga-PSMA-11 will be investigated *in vitro*. **Materials and Methods:** Gallium-68 was obtained from a ⁶⁸Ge/⁶⁸Ga-generator (IRE elit, Gallieo, 1850 MBq). HEPES was purchased from Sigma Aldrich. For improving the TLC assay different parameters as mobile phase, spotting method, solvent for the HEPES reference and heating of the TLC chamber were evaluated. Furthermore, quantification was performed using ImageJ software. Potential toxicity of HEPES on PC3 and PC3-PSMA cells was examined by means of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Effects on radiotracer accumulation will be evaluated by treating PC3-PSMA cells with [⁶⁸Ga]Ga-PSMA-11 simultaneously with different concentrations of HEPES. **Results:** An improved TLC assay was developed by using the same composition of the product solution and the reference solution. Mobile phase optimization lead to acetonitrile/EtOH/H₂O (10/15/65) as the best method. Iodine staining by heating the iodine chamber resulted in a better reproducibility and comparability. Quantification using ImageJ gave a high reproducibility and linearity ($R^2=0.9956$) throughout the tested range. Evaluation of HEPES toxicity showed an IC_{50} value in the micromolar range for both cell lines. HEPES in high concentrations significantly effects the pH and osmolality of the applied solution to the cells, subsequently potential toxic effects due to acidic pH and high osmolality cannot be ruled out. **Conclusion:** Improving the TLC assay of the Eur. Ph. is necessary to obtain comparable and reliable results. The parameters found in this study are providing a visual and software based quantification of HEPES. Additionally, a relatively low toxicity was obtained

in both cell lines and further experiments will demonstrate the influence of HEPES on [^{68}Ga]Ga-PSMA-11 accumulation in PC3-PSMA cells.

E-PW092

Sources and Impact of Metal Impurities on Radiochemical Yield of ^{68}Ga -DOTA-TATE in a GMP Facility

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Introduction: We produce ^{68}Ga -PSMA and ^{68}Ga -DOTA-TATE in 78–83% radiochemical yield and >98% purity. Over 4 months, ^{68}Ga -DOTA-TATE yield gradually decreased by 70%; there was no effect on ^{68}Ga -PSMA yield. We confirmed the buffer pH and integrity of DOTA-TATE precursor and increased the precursor quantity from 20 to 40 μg showing partial recovery in yield to above 60%, suggesting saturation with competing metal ions. Our aim was to investigate the cause of the reduction in yield.

Materials & Methods: Both ligands were prepared by the cationic pre-purification method on a Scintomics-GRP module using 10 μg of PSMA and 20 μg DOTA-TATE precursors in sodium acetate buffer (1.5M, pH 4.5). Initially, the buffer was prepared in advance, by dissolving sodium acetate in Ultrapure Water (UP-W) or Water for Injection (WFI); pH was adjusted to 4.5 using acetic acid and it was stored in sterile, glass vials with rubber septa. All reagents used in the preparation of sodium acetate buffer were of ultrapure or analytical grade with Certificates of Analysis confirming low metal ion concentrations. We then prepared new sodium acetate buffer and stored it for 3 months in the following sterile conditions: i) glass vials capped with rubber septa, ii) glass vials without rubber septa, iii) glass vials with rubber septa stored upside down, iv) plastic vials, v) glass vials with plastic lids and vi) plastic syringes. The sodium acetate buffer (1.5 M) solutions were analysed by ICP-MS. All buffer solutions were stored at 4°C. **Results:** ICP-MS analyses showed metal ions were low except for zinc. There were high concentrations of zinc in: a) glass vials with rubber septa; b) vials stored upside down. Zinc concentrations were higher when compared to vials that were upright and higher than in vials with septa removed. Low zinc concentrations were found in buffer stored in plastic vials, glass vials with plastic tops or plastic syringes. There was a minimal difference between WFI and UP-W. The source of zinc was attributed to leaching from rubber septa reflecting the reported rubber manufacturing process. Yield from all subsequent ^{68}Ga -DOTA-TATE preparations using buffer stored in plastic was >80%. **Conclusion:** Our findings indicate that long term storage of sodium acetate buffer in vials capped with rubber septa, results in contamination by zinc ions that then saturate the DOTA-macrocycle and reduce yields through Ga/Zn ion competition. We suggest that sodium acetate buffer, for ^{68}Ga -DOTA-TATE, is prepared and stored in plasticware.

E-PW093

Purification of ^{67}Ga Gallium for (pre)clinical applications as surrogate for ^{68}Ga Gallium

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Purpose/Introduction: ^{68}Ga is a PET radionuclide which is often used in daily clinical practice. Several ^{68}Ga -labeled radiopharmaceuticals, such as ^{68}Ga -DOTA-TATE/TOC and ^{68}Ga -HBED-PSMA, are widely applied all over Europe. However, for preclinical research ^{68}Ga is not always ideal due to its short half-life and poor resolution images in small rodents. Therefore, we investigated if ^{67}Ga could be used as surrogate of ^{68}Ga for (pre)clinical studies. ^{67}Ga , which is chemically identical, can be used to image small animals at later time point and with a higher resolution. Unfortunately, ^{67}Ga is usually offered with poor chemical purity, since it often contains relative high amounts of Zn, Fe and Cu. Therefore, our aim was to develop a purification method resulting in highly concentrated ^{67}Ga with minor trace metal impurities to label biomolecules with high molar activities. **Subject & Methods:** Our purification process was initially optimized by using ^{68}Ga . A low volume semi-automated peek system, containing a LN-resin-B column (35–70 mg, Triskem), was assembled. Gallium was absorbed using different concentrations of HCl (from low range of 0.025–0.1 M to high range 4–7 M). To demonstrate the efficiency of our purification method, gallium was spiked with large amounts of Zn (250 and 2500 nmoles). Then, desorption was performed by eluting gallium with 1M HCl. Concentrations of trace metals were quantified by using a previously described UPLC-technique (Breeman et al 2014). **Results:** Approximately 80 % purification yields of gallium were obtained by using 0.1 M and 5 M HCl and gallium was desorbed in a 3 mL 1 M HCl final solution. For 0.1 M HCl $67 \pm 1\%$ could be desorbed in only 500 μL of 1M HCl. Purified gallium was used to label DOTA-TATE and after decay, metals were quantified by UPLC. After purification of the Zn-spiked ^{68}Ga -eluates the 1 M HCl solution contained Zn concentrations of 5.3 ± 1.4 and 4.2 ± 1.4 nmoles/mL, respectively. Thus, efficiency of purification technique is >98%. This will theoretically result in similar molar activities as previously reported with ^{111}In labelling (Breeman et al 2003) **Discussion/Conclusion:** We demonstrated that gallium can be well separated from Zn with our purification technique. It is therefore anticipated that high molar activity ^{67}Ga -labeled biomolecules could be obtained for (pre)clinical applications. Application of our purification method to ^{67}Ga is currently underway.

E-PW094

Determination of Unbound ^{68}Ga in Radiopharmaceuticals: is HPLC Satisfactory?

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Aim: Determination of radiochemical purity (RCP) of radiopharmaceuticals (RPs) based on ^{68}Ga -BCA-conjugates (e.g. ^{68}Ga -DOTA-TOC/TATE, ^{68}Ga -PSMA) is an extremely important part of QC in routine clinical practice. Knowing exact value of content of every radiochemical impurity is very important during R&D as well. Normally combination of TLC and HPLC is used. But do TLC results always match HPLC results, especially for unbound ^{68}Ga content? The aim of this study is to evaluate the correlation between results obtained with TLC and HPLC methods. **Materials and Methods:** $^{68}\text{Ge}/^{68}\text{Ga}$ generator (Cyclotron Ltd, Russia) was

used. All chemicals and solvents were of high-purity or pharmaceutical grade and were purchased from Sigma-Aldrich or Panreac. Radiopharmaceutical precursors were purchased from ABX. iTLC-SG strips by Pall/Varian/Thermo were used. PET-MiniGita radio-TLC scanner was used. For HPLC analysis Knauer Smartline chromatograph with radiodetection system fLumo (Berthold) was used. Mobile phase for HPLC consists of 0.1% TFA solutions in water and acetonitrile in different ratios in accordance with 9th Ph.Eur. recommendations. Different HPLC C₁₈-columns were used (Merck/Phenomenex/ACE). **Results:** Cross-validation of TLC and HPLC methods was carried out for radiopharmaceutical preparations with ⁶⁸Ga-labelled peptides with radiochemical purity in the range of 10–100%. The same was done for mixtures of ⁶⁸Ga-eluate and acetate/HEPES buffer solutions. The influence of pH and buffer concentration on unbound ⁶⁸Ga recovery from HPLC column was studied. It was found that in pH range from 3 to 6, apart from colloidal ⁶⁸Ga, there is a significant capture of the ⁶⁸Ga ionic forms on the reversed phase of the HPLC column (e.g. 60% capture with pH 4.6). The value of the capture also depends on concentration of buffer agent in the preparation. The detailed analysis of the effect will be presented. **Conclusion:** It was found that in the number of cases HPLC results do not reflect the real unbound ⁶⁸Ga content in radiopharmaceutical preparations. Thus, HPLC cannot be a method of choice, and it definitely should not be the only one method when analyzing ⁶⁸Ga-RPs. Since TLC method gives an idea of the content of all radiochemical forms of ⁶⁸Ga in radiopharmaceutical preparations, it is preferable. With all the advantages of the HPLC method, every radiochemist and radiopharmacist should take into account the fact that in the case of ⁶⁸Ga-RPs, and possibly other metal-based RPs (such ¹¹¹In, ¹⁷⁷Lu, etc.), this method can lead to an inadequate assessment of the content of ionic forms of the radionuclide in RP preparations. 1

E-PW095

Performance evaluation and radionuclidic purity tests of a new ⁶⁸Ga generator

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Introduction: A new ⁶⁸Ga generator was recently installed at our institution. Here we report on the performance and radionuclidic purity tests for the first three months of use. **Materials and Methods:** The generator is a Galli Eo generator (IRE Elit, 1850 MBq). The chromatographic column is lead-shielded, and the eluent is entirely contained inside the generator box. Manual elution is performed by connecting an evacuated vial to the generator outlet; it lasts three minutes for a total eluted volume of about 1.1 ml. Elution profile was performed the first time, while the generator yield and radionuclidic purity was evaluated on a regular basis for the first months of use. A total of 15 full elutions were collected during this time. Radionuclidic purity was evaluated by means of a gamma spectrometry sys-

tem equipped with a HPGe detector, suitably calibrated with a multipeak standard source. Amount of ⁶⁸Ge was evaluated by measuring the amount of ⁶⁸Ga after a proper waiting time from the end of the elution (at least 48h) in order to reach secular equilibrium. **Results:** After the first elution yielding 67%, we obtained a stable elution yield throughout the test period: on average 61.8%, coefficient of variation (CV) 1%. Amount of ⁶⁸Ge breakthrough was 380±15 Bq (4.17·10⁻⁵% of eluted activity) that means a radionuclidic purity of 99.99996% on average. No other radionuclides were detected in any sample (minimum detectable activity 10 Bq). **Conclusion:** Performance of this generator appeared stable for the first three months of use. Radionuclidic purity was at least two order of magnitude less than the requirements of the European Pharmacopoeia making it suitable for clinical use.

E-PW096

New Ways to Test the Impurity ²⁰¹Tl(III)Cl₃ in Thallous(²⁰¹Tl) chloride Injection

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Introduction: ²⁰¹Tl is produced in a cyclotron as ²⁰¹Tl(III)Cl₃. To form ²⁰¹Tl(I)Cl for injection the cyclotron product must be reduced. Therefore, ²⁰¹Tl(I)Cl for injection may contain ²⁰¹Tl(III)Cl₃ as a radiochemical impurity. The test of ²⁰¹Tl(III)Cl₃ according to Ph. Eur. is carried out by the obsolete method of zone electrophoresis. We aimed to investigate alternative testing methods by TLC(1) and HPLC(2). **Material and Methods:** ²⁰¹Tl(I)Cl was purchased from CIS. The ²⁰¹Tl(III)Cl₃ reference was prepared by ozone oxidation. To 3ml ²⁰¹Tl(I)Cl solution (53 MBq) 40μl 6M HCl was added and placed into a reactor of a Scintomics GRP synthesiser. A stream of air/ozone (approx. 75ml/min), produced by a generator (Guanglei Electronic, China), was bubbled through (5min). In following, the reaction mixture was heated (10min). TLC: Samples were tested on silica gel (iTLC-SG, Agilent) with MEK as the mobile phase. HPLC: 200μl sample solution was mixed with 200μl 0.02M sodium DTPA solution. The mixture was injected into the HPLC using an SCX column (Nucleosil 100-5-SA 4.6x260) and 0.1M sodium acetate pH4.6 as eluent. **Results:** The preparation of the reference ²⁰¹Tl(III)Cl₃ by ozone oxidation was quantitative. Traces of ²⁰¹Tl(I)Cl were detected neither by TLC nor by HPLC. In acid condition, the ²⁰¹Tl(III)Cl₃ solution remains stable several days. TLC: With the described conditions ²⁰¹Tl(I)Cl remains near the start (Rf=0.1). ²⁰¹Tl(III)Cl₃ migrates near to the front (Rf=0.85). The use of MEK instead of acetone gives a much sharper peak form, resulting in a real baseline separation. HPLC: This method based, that only ²⁰¹Tl(III)Cl₃ can form a DTPA complex rapidly at room temperature. ²⁰¹Tl(III)DTPA elutes under these HPLC conditions at about 4min as a sharp peak. Free ²⁰¹Tl as ²⁰¹Tl(III)Cl₃ or ²⁰¹Tl(I)Cl give a tailed signal at about 14min. Therefore, ²⁰¹Tl(III)Cl₃ can be detected as ²⁰¹Tl(III)DTPA well separated in samples of ²⁰¹Tl(I)Cl by HPLC. **Conclusion:** Two analyses methods to test the radiochemical impurity ²⁰¹Tl(III) in solutions of ²⁰¹Tl(I)Cl for injection were successfully investigated, whereby the necessary reference standards ²⁰¹Tl(III)Cl₃ and ²⁰¹Tl(III)DTPA have been radiochemical pre-

pared. Both tested analysis methods, TLC and HPLC, showed a good separation and encouraged results. The methods are worthy of validation and seem suitable as analytical systems to test ^{201}Tl radiopharmaceuticals. (1)NM. Hijnen et al. Nucl Med Biol 2011; 38: 585–592 (2)M. Akhlaghi et al. Appl Radiat Isot 2008; 66: 479–481

E-PW097

Validation of a modified quality control method for testing radiochemical purity of $^{99\text{m}}\text{Tc}$ -tetrofosmin

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Aim: In our Department, we perform myocardial scintigraphies using $^{99\text{m}}\text{Tc}$ -tetrofosmin according to a single day stress/rest protocol. The standard Quality Control (QC) for testing radiochemical purity (RP) described in the insert package is not satisfying, namely the separation of the three principal components ($^{99\text{m}}\text{Tc}$ -tetrofosmin, $^{99\text{m}}\text{TcO}_2$, and $^{99\text{m}}\text{TcO}_4^-$). We believe that the Retention factor (R_f) variance for the separation of the radiopharmaceutical fraction and the $^{99\text{m}}\text{TcO}_2$ appears too small for an unequivocal visualization of the $^{99\text{m}}\text{Tc}$ -tetrofosmin conjugate from the $^{99\text{m}}\text{TcO}_2$ counterpart. The aim of this study was to validate an alternative method of quality control. **Materials and Methods:** The standard QC method recommends the use of one TLC-SA strip (2x20 cm) as stationary phase and 65:35(%v/v) acetone:dichloromethane mixture as mobile phase. The alternative method consists of ITLC-SG strip (2x20 cm) as stationary phase and 35:65(%v/v) acetone:dichloromethane mixture as mobile phase. In both system, free $^{99\text{m}}\text{TcO}_4^-$ migrates to the top of the strip ($0.8 > R_f > 1.0$), $^{99\text{m}}\text{Tc}$ -tetrofosmin migrates to the center of the strip ($0.4 > R_f > 0.6$) and $^{99\text{m}}\text{TcO}_2$ remains in the origin of the strip. Ten tests for each method were performed. For both procedures, the strips were analysed by autoradiochromatography (Cyclone Plus®, Perkin Elmer). A 10 to 20 µl drop of radiopharmaceutical was applied at the origin line using an insulin syringe. We verified that the strips did not adhere to the walls of the cylinder of chromatography chamber. We evaluated the final %RP and the R_f of $^{99\text{m}}\text{Tc}$ -tetrofosmin and of two impurities. The Wilcoxon test was employed to compare the quality control results of the proposed method with the standard one. **Results:** The following values of %RP were obtained using the standard QC and the alternative QC: %RP = $97.0\% \pm 1.24$ vs %RP = $96.6\% \pm 1.15$, respectively, $p=0.42$. The % $^{99\text{m}}\text{TcO}_2$ was $2.83\% \pm 1.70$ vs 3.3 ± 1.79 ($p=0.38$) and the % $^{99\text{m}}\text{TcO}_4^-$ was 0.12 ± 0.11 and 0.03 ± 0.06 ($p=0.03$), respectively. $^{99\text{m}}\text{Tc}$ -tetrofosmin separation from $^{99\text{m}}\text{TcO}_2$ was incomplete with the standard method, indeed a highly significant difference was found when considering the (R_f): the R_f of $^{99\text{m}}\text{Tc}$ -tetrofosmin with standard QC was 0.30 ± 0.11 vs 0.57 ± 0.11 (alternative QC), $p=0.00003$. **Conclusions:** We introduced an alternative QC method for the assessment of $^{99\text{m}}\text{Tc}$ -tetrofosmin purity. The proposed method is more accurate allowing an appropriate migration of radiopharmaceutical, with a complete separation between $^{99\text{m}}\text{Tc}$ -tetrofosmin and the two impurities (especially from $^{99\text{m}}\text{TcO}_2$).

E-PW098

Have you checked for “stranger things” in your automated dispensing system for PET radiopharmaceuticals ?

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Many nuclear medicine departments are now equipped with automated dispensing systems for PET radiopharmaceuticals. Initial microbiological qualification is classically carried out by the manufacturer or the distributor once the equipment is installed, but the periodic qualification falls to the radiopharmacist. According to ISO14698-1 and ICH-Q7-GMP, this study aimed at setting up an initial and periodic qualification plan of the microbiological safety of Trasis® Unidose, whose monodose-filling, the critical step, implies an open system under ISO4.8. **Materials and Methods:** Both the environment and the process were assessed for microbiological contamination at the end of a session, repeated on 3 different days. Environment surfaces were checked on 3 different sites (ISO4.8 carousel, ISO7 gloves and ISO7 reservoir surface), through the application of 25 cm² trypticase-soy (TS) agar, before and after biodecontamination following our internal procedures. Agars were incubated at 37°C under 5% CO₂ for 5 days and colonies were then counted (CFU/25cm²). The whole process sterility was evaluated through an adapted media-fill test, a sterile TS broth vial in place of the radiopharmaceutical, after biodecontamination. The resulting cartridges were aseptically transferred to TS broth tubes and placed for incubation at 37°C under 5% CO₂ for 5 days with daily monitoring of turbidity. Further identification was realized by our Microbiology Department. **Results and Discussion:** As shown on Table 1, after the incubation period, a minor microbiological contamination was found on TS agars sampled from the carousel before biodecontamination and identified as classical hand-borne microflora (*Micrococcus luteus* and *Staphylococcus sp.*). After biodecontamination, all the agars were found sterile. Most importantly, the media-fill test resulted in clear, sterile cartridges, validating the process sterility. Investigating for the biocontamination origin, the cap reused daily for filter sealing tests was found contaminated (13 CFU/25cm²). We consequently adapted our biodecontamination procedure to include this instrument, and decided to brief our operators once a month on microbiological control results, hygiene and good practices. Our latest results show these corrective actions solved the biocontamination issue. **Conclusion:** The automation of PET monodose conditioning process still implies human intervention for material preparation and manual biodecontamination, and needs initial and periodic qualification of the environment and the conditioning process, to meet the specifications. We therefore recommend a monthly microbiological control of surfaces and instruments and a half-yearly media-fill test. Regular training and information should also be dispensed to the operators, regarding the importance of properly carrying out the biodecontamination of surfaces and instruments.

E-PW099

Production and quality control of microsphere labeled by Scandium 46 and its biological distribution

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Radioembolization therapy is primarily used to treat liver tumors and metastases. This method has been studied with microspheres Zn-65, Au-198, P-32 and Y-90 glass microspheres in different types of tumors. The microsphere used in this study is Chelex-100 (Polystyrene divinyl-benzene iminodeacetate) resin. The aim of this experiment is to investigate the application of ⁴⁷Sc ($T_{1/2} = 3.35$ d; $\beta_{\text{ave}} = 162$ keV; $E\gamma = 159$ keV) for radioembolization. Because of the limitation in availability of ⁴⁷Sc isotope, we have performed preliminary studies using instead ⁴⁶Sc. **Methods:** ⁴⁶Scandium was prepared by irradiation of Sc_2O_3 with thermal neutron flux $3.5 \times 10^{13} \text{ n/cm}^2 \text{ s}$ following dissolving in chloride acid then fixing pH = 7 by NaOH. The radionuclidic purity was tested using beta spectroscopy and HPGe spectroscopy for the detection of various interfering beta and gamma emitting radionuclides. The radiochemical purity was checked by ITLC and 10mM DTPA as mobile phase. 0.3 milliliters of this solution with 3 milligrams of microsphere resin (based on calculations performed for the absorption capacity of resin) were combined and placed in a 100°C for 1 hour. SEM were performed with Digital Scanning Electron Microscope. The stability of the compound was investigated with storage at room temperature and pH=7 up to 72 hours after the formation. Stability in human serum was also investigated with a ratio of 1:10 at 37 °C up to 96 hours. Biodistribution after injection locally in tumor site in mice bearing B16F10 melanoma tumor at 2 hours, 3, 7 and 14 days after injection were determined as percent of injected dose per gram of organ (%ID/g). **Results:** SEM shows microsphere particles as uniform spheres. ⁴⁶Sc with a specific activity of about 280 mc / ml and 99% radionuclide purity was obtained. Radiochemical by ITLC system at room temperature and pH = 7 was about 94%. The stability of the compound at room temperature and up to 72 hours after the formation is about 80% and in the human serum is 74% up to 96 hours. The absorption in the tumor is approximately %ID/g=16% within 2 hours after injection and no significant absorption were observed in other organs up to 14d. **Conclusion:** Resin microspheres were labeled with efficiency of 93% with ⁴⁶Sc. This combination showed a stability at human serum approximately 74%. The complex exhibited excellent in-vivo stability and absorption in tumor mice. This promising results indicate that this compound is suitable for application in radioembolization. **Keywords:** Radioembolization, Microspheres, Scandium-47.

E-PW100

Residual Activity in the Delivery Apparatus after Selective Internal Radiotherapy

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Purpose: Object of this study was to determine the residual activity of yttrium-90 (⁹⁰Y) in the delivery apparatus including vial

after selective internal radiotherapy (SIRT). **Material and Methods:** We analysed data of 115 patients (male/female 68/47, age 65.4 ± 11.4 years), who have received at least one SIRT intervention between January 2017 and April 2018. In total, data of patients with hepatocellular carcinoma (n=25), metastatic colorectal cancer (n=30), cholangiocellular carcinoma (n=15), neuroendocrine tumor (n=9), and breast cancer (n=8) was analysed. In total 208 administration sets of ⁹⁰Y resin microspheres (Sirtex Medical Ltd., New South Wales, Australia) have been used during 158 interventions (one set: n=114; two sets: n=39; three sets: n=4; four sets: n=1). Incomplete administration due to irreversible stasis or catheter dislocation occurred four times; respective boxes were excluded from evaluation. After finishing therapy the residual activity in the delivery system (box, three-way tap, and supply pipes) and the vial were measured in a calibrator. These values were tested administration (Pearson's product-moment correlation) against prepared activity value, time between preparation and administration due to possible sedimentation of spheres, and duration of administration per delivery set. **Results:** When adjusting for decay between preparation and administration the activity dose at the time of application was 903 ± 417 [193 - 2352] MBq; the corresponding time-corrected residual activity was 58.4 ± 19.8 [15.3 - 124.5] MBq. Administration time for one box during intervention required 18.8 ± 9.6 [5 - 85] minutes. Correlation analysis revealed dependency of residual activity on duration of administration ($p = 0.0095$). There was no significant dependency on the absolute value of the prepared activity ($p = 0.1973$) or time since preparation to delivery ($p = 0.1439$). **Conclusion:** An average residual activity of approximately 60 MBq per application box was found. Besides decay, this should be kept in mind when preparing the therapeutic activity in the radiochemistry lab. Prolonged administration results in higher residual activity possibly due to sedimentation effects.

1511 Tuesday, October 16, 2018, 16:30 - 18:00, Hall A
e-Poster Walk 11 - Clinical Oncology: Oncology Mixer

E-PW101

SPECT CT Visualization Of Sentinel Lymph Nodes In Women With Cervical Cancer: Is It Important For "Lymph Flow Guided" Radiotherapy

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Concept of "lymph flow guided radiotherapy" represents logical continuation of sentinel lymph nodes (LN) ideology. This concept is based on visualization of individual patterns of lymph flow from the primary tumour and subsequent irradiation of LNs or lymph node regions with accumulation of radiocolloids. **Purpose:** to evaluate topography of sentinel LN and determine individual patterns of lymph flow in women with cervical cancer; to analyze how this scintigraphic information can influence

radiotherapy planning. **Materials and Methods:** The study was performed in a group of 50 women with IB-IIB cervical cancer. In all cases MRI and US examinations of pelvic and para-aortic LNs didn't reveal signs of metastatic LN involvement. SPECT-CT examinations started 120–240 min after peritumoural injections of ^{99m}Tc -radiocolloids (150–300 MBq in 0.4–1 ml). All visualized LNs with uptake of radiocolloids were regarded as sentinel LN. They were assigned to 6 nodal groups according to their anatomic location in relation to blood vessels: obturator, internal, external and common iliac, pre-sacral, para-aortic. Additionally we determined type of lymph flow (mono-, bilateral) and lymph flow patterns (supra-ureteral paracervical, infra-ureteral paracervical and direct lymph flow to para-aortic LNs). All patients underwent radical surgical treatment with standard postoperative radiotherapy. Finally we analyzed how SPECT-CT information can be used for individual optimization of clinical target volumes. **Results:** SPECT-CT successfully visualized 148 sentinel LNs (in average 3.1 sentinel LNs per patient) in 44 (88%) of 50 women. The unilateral pattern of lymph flow was mentioned in 13 (29.5%), bilateral - in 31 (70.5%) observations. Distribution of sentinel LNs according to nodal regions was as follows: external iliac - 70.5%, internal iliac - 52.3%, obturator - 27.2%, common iliac - 40.1%, para-aortic - 25% and presacral - 9.1% cases. In 43 cases we were able to determine patterns of lymph flow from cervical cancer: supraureteral paracervical route was identified in 28, infraureteral paracervical - in 5 and their combination - in other 10 patients. We didn't see any case of direct lymph flow from primary tumour to para-aortic LNs. **Conclusion:** We suggest that in women without lymph flow to pre-sacral LNs these nodes can be excluded from irradiation volume. Efficacy of prophylactic irradiation of para-aortic LNs must be studied in patients with lymph flow to this region.

E-PW102

Ki-67 expression and FDG uptake in Colorectal Adenomas and Adenocarcinoma

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Introduction: Focal uptake in the colon is often an incidental finding in patients referred for FDG PET scan for cancer staging. The clinical significance of colorectal FDG uptake and its relation to types and grade of hyperplasia of polyps is not well understood. Correlation between FDG uptake and Ki-67 has not been studied. In this study we have quantitatively assessed adenomatous polyps and adenocarcinoma with regard to FDG uptake and Ki-67 expression. **Materials and Methods:** This is a retrospective study consisting of consecutive patients referred for FDG PET/CT for staging over 2 years who had focal colorectal FDG uptake and subsequent removal of polyps. 29 study subjects (age: 72.3 ± 9.1 , M:F=18:11) and 61 specimens were included. Quantification of Ki-67 was carried out by two experienced readers blinded to the patients' clinical and FDG PET data. A minimum of 500 cells were counted manually on each slide under a light microscope (Eclipse E-400, Nikon, Japan) at a magnification of X400. The label index was obtained from the ratio between the number of cells with stained nuclei

and total counted nuclei. FDG PET images were acquired on a GE Discovery 710 Scanner (GE Healthcare) and reconstructed with correction for attenuation and scattering and interpreted on HERMES workstation. SUV_{max} were measured and correlated to types of adenomas, degree of hyperplasia, and Ki-67 index with Pearson's correlation coefficient. Data was reported as median $\pm$ inter-quartile range. **Results:** Of the 61 specimens, 11 were villous, 28 tubular, and 15 tubulovillous adenomas. There were 6 hyperplastic polyps and no available data in 1 specimen. 10 adenocarcinomas arising from adenomas were identified. SUV_{max} measured 5.0 ± 6.3 for adenomas and 11.5 ± 10.4 for adenocarcinoma ($p=0.001$). Regarding the degree of hyperplasia, SUV_{max} was 5.3 ± 7.1 , 9.3 ± 6.0 and 9.2 ± 12.3 for low ($n=36$), high ($n=12$) and invasive ($n=7$) adenomas, respectively. The FDG uptake tended to be higher in villous (8.7 ± 8.1 , $p=0.07$) and was significantly higher in tubulovillous (10.2 ± 6.0 , $p<0.001$) than tubular adenomas (4.5 ± 4.2). There was no correlation between FDG uptake and Ki-67 ($p=0.64$). No significant correlation with Ki-67 uptake was identified for adenomas vs. adenocarcinomas ($p=0.5$) or with degree of hyperplasia ($p=0.4$). Ki-67 did not differ between tubular ($46 \pm 20\%$), villous ($55 \pm 38\%$) and villotubulovillous ($50 \pm 24\%$) adenomas ($p>0.4$). **Conclusion:** More intense FDG uptake was identified in villous and tubulovillous adenomas and in high grade hyperplasia. Although there was some overlap, adenocarcinoma had higher FDG uptake than adenoma. There was no correlation between FDG uptake and Ki-67 expression.

E-PW103

Comparison of ^{68}Ga -DOTATATE and ^{177}Lu -DOTATATE kinetics in neuroendocrine tumors

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Objectives: Peptide receptor radionuclide therapy (PRRT) with ^{177}Lu -DOTATATE is a promising treatment for patients with neuroendocrine tumors. Currently, dosimetry during PRRT is performed post-therapy rather than prior-therapy as in external beam radiotherapy. Absorbed dose planning pre-therapy enables maximize absorbed dose to tumor tissue whilst minimizing risk for side-effects in healthy organs. This is not possible in a similar sense during PRRT with ^{177}Lu -DOTATATE, since the absorbed dose not only depends on the amount of given radioactivity but also on the kinetics of the peptide in each individual patient. ^{68}Ga -DOTATATE-PET, which is used for diagnosis of neuroendocrine tumours, could potentially be used to predict the radiation doses during ^{177}Lu -DOTATATE PRRT. The aim of this study was to compare the kinetics of ^{68}Ga -DOTATATE and ^{177}Lu -DOTATATE in tumors by performing dynamic scans with both in the same patients. **Materials and Methods:** Six NET patients underwent a 45 min dynamic PET scan after injection of 100 MBq ^{68}Ga -DOTATATE and serial SPECT scans (30 min, 1 h, 90 min, 2 h, 4 h, 24 h and 96 h) after administration of 500 MBq

^{177}Lu -DOTATATE at similar and high specific activity. VOIs (50% isocontour) were drawn over tumours to obtain time-activity curves. The net influx rate K_i was determined both for ^{177}Lu - and ^{68}Ga -DOTATATE by non-linear regression of two-tissue irreversible compartment-model and by the Patlak method. Input curves were based on blood sampling for ^{177}Lu -DOTATATE and on a VOI including the descending aorta for ^{68}Ga -DOTATATE. Metabolite correction was performed for ^{177}Lu -DOTATATE based on HPLC analysis, but not for ^{68}Ga -DOTATATE, assumed intact during the PET scan. ^{68}Ga - and ^{177}Lu -DOTATATE K_i were compared using correlation and Bland-Altman analysis. **Results:** Net influx rate values, K_i , based on data <90 min p.i. were 0.11 ± 0.04 for ^{68}Ga -DOTATATE and 0.12 ± 0.04 for ^{177}Lu -DOTATATE (mean $\pm$ SD), with a 9.2 % mean difference and a Spearman correlation (R) of 0.83. Using later time intervals for ^{177}Lu -DOTATATE, Patlak analysis resulted in reduced K_i values. Non-linear regression to the compartment model showed that the kinetics of ^{177}Lu -DOTATATE can be described by the same influx rate constants as ^{68}Ga -DOTATATE, but an additional parameter accounting for clearance of ^{177}Lu from the tumor may be necessary to explain ^{177}Lu -DOTATATE kinetics at later time points. **Conclusion:** Good agreement was found between ^{177}Lu - and ^{68}Ga -DOTATATE K_i , showing that tracer kinetics of ^{68}Ga -DOTATATE indicating its potential for predicting radiation doses during PRRT.

E-PW104

^{18}F FMC-PET/MRI as a surrogate marker for thyroid hormone axis in prostate cancer

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Introduction: Epidemiologic studies showed a higher incidence of prostate cancer (PCa) in men with elevated thyroid hormone levels. Interestingly, mRNA levels of μ -Crystalin (CRYM), a thyroid hormone (3,5,3'-triiodo-L-thyronine, T3) sequestering protein, were found to decrease during tumor progression in CWR22 prostate cancer xenografts suggesting CRYM as a prognostic factor. (1) Recent metabolic analysis using NMR showed that CRYM-overexpression correlates with low levels of intracellular choline (unpublished results), thus suggesting radiolabeled choline analogues as surrogate markers for CRYM expression and therefore thyroid hormone status in PCa. **Methods:** To elucidate the role of CRYM expression in PCa on a molecular level, androgen-sensitive LNCaP cells were transfected with CRYM (or empty vector as control) and incu-

bated with ^{125}I T3 (45 kBq/well) or ^{14}C Testosterone (1.5 kBq/well) for different time points (12, 24 and 48 h). To investigate a potential clinically relevant link between CRYM expression, thyroid hormone receptor status (TR β) and choline levels, ^{18}F FMC-PET/MRI was evaluated in 42 PCa patients before radical prostatectomy. CRYM and TR β protein expression was investigated by immunohistochemistry in PCa specimens derived from the same patients. Additionally, follow-up analysis was performed in 87 patients (mean follow-up time: 508 days) investigating biochemical recurrence (BCR), development of metastasis and ^{18}F FMC uptake. **Results:** ^{125}I T3 uptake was significantly elevated in LNCaP cells overexpressing CRYM compared to LNCaP cells expressing endogenous levels of CRYM (10.5% vs. 6.9% after 12 h, 13.6% vs. 7.1% after 24 h and 14.9% vs. 5.8% after 48 h, expressed as percentage applied dose/ well) (n=3 each, p<0.01). This enhanced thyroid hormone uptake may be linked to CRYM's property to bind T3 and preventing thyroid hormone action. ^{14}C Testosterone uptake was negligible and unaffected by CRYM expression ($\leq 0.2\%$ AD/ well), suggesting that there is no direct interaction between CRYM protein and androgens on a molecular level. Therefore, PET imaging strategies using radiolabeled androgens (e.g. ^{18}F FDHT) were not additionally envisaged. ^{18}F FMC uptake was found to be positively correlated to TR β expression levels (p=0.008) and inversely correlated to CRYM expression levels (p=0.041) identified by IHC in the respective tumor specimens. Moreover, follow-up analysis revealed significantly higher ^{18}F FMC uptake in patients with BCR and/or metastases (n=50) compared to patients not suffering from BCR and/or metastases (n=37) (p<0.001). **Conclusion:** These data indicate that ^{18}F FMC-PET may serve as a surrogate marker for thyroid hormone axis in PCa risk assessment and is correlated to BCR and formation of metastases. (1) Mousses S et al. *Cancer Research*. 2002;62(5):1256-60.

E-PW105

Dual-tracer 18F-FDG and 18F-Fluorocholine PET/CT for hepatocellular carcinoma: correlation with pathological features

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Introduction: 18F-Fluorodeoxyglucose (18F-FDG) and/or 18F-Fluorocholine (18F-FCH) PET/CT are frequently performed during pre-therapeutic work-up of patients with hepatocellular carcinoma (HCC) and may allow the assessment of tumors aggressiveness. We aimed in the present study to determine how HCC PET/CT features relate to its pathological characteristics. **Methods:** A series of 70 tumors developed in 62 patients who underwent liver resection for HCC and preoperative dual-tracer PETCT was investigated. PET/CT scans and histological slides

were systematically reviewed. **Results:** 47% of the tumors were positive for 18F-FDG. For 18F-FCH, increased uptake, same uptake and lower uptake compared with the liver background were observed in 39%, 40% and 21% of the tumors, respectively. Positivity for 18F-FDG was associated with a large tumor size ($>50\text{mm}$, $p < 0.001$), the presence of micro and macrovascular invasion ($p < 0.001$), and the macrotrabecular-massive histological subtype ($p = 0.02$). 18F-FCH lower uptake was associated with a large tumor size ($>50\text{mm}$, $p = 0.004$), the presence of satellite nodules ($p = 0.002$) and micro and macrovascular invasion ($p = 0.001$ and $p < 0.001$, respectively), a poor degree of tumor differentiation ($p = 0.002$), and the macrotrabecular-massive histological subtype ($p = 0.01$). Integration of features obtained with the two tracers allowed the identification of a subgroup of tumors with 18F-FDG positivity and 18F-FCH lower uptake characterized by: the presence of satellite nodules ($p = 0.004$) and micro and macrovascular invasion ($p = 0.002$ and $p = 0.009$, respectively), a poor degree of differentiation ($p < 0.001$), and the macrotrabecular-massive subtype ($p = 0.008$). **Conclusion:** 18 F-FDG and 18 F-Fluorocholine PET/CT features are closely associated with HCC pathological characteristics. Combination of the two tracers allowed the identification of a particular subtype of tumors, positive for FDG and with choline lower uptake, characterized by an aggressive phenotype.

E-PW106

The role of PSMA-based ^{18}F -DCFPyL PET/CT imaging in patients with biochemical recurrence prostate cancer after primary local therapy

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Purpose: To investigate the lesion detection rate of ^{18}F -DCFPyL PET/CT, a PSMA targeted PET agent, in patients with biochemical relapse prostate cancer after primary local therapy. **Materials and Methods:** This is a prospective IRB-approved study including 41 patients with documented biochemical recurrence (average PSA of 3.4 ng/mL, range 0.23–13.2 ng/mL) after local therapy, either radical prostatectomy ($n = 19$), post-radiation therapy ($n = 12$) or both ($n = 10$), with negative conventional anatomical imaging. Patients underwent whole-body ^{18}F -DCFPyL-PET/CT at 2 h p.i. (299.9 ± 15.5 MBq), and multiparametric pelvic MRI (mpMRI), 2 weeks apart. PSMA-PET lesion detection rate was correlated with mpMRI findings, and pre-scan PSA levels. The total PSMA tumor burden (sum MTV) and SUVmax was correlated with PSA levels. **Results:** Twenty-nine patients (70.7%) showed at least one highly suspicious positive DCFPyL-avid lesion, identifying a total of 141 lesions: 14 in the prostate bed, 102 lymph nodes, and 25 distant sites; four patients had no PSMA-avid lesions; and eight patients showed indeterminate lesions, which

were considered negative scans. The detection rates were 54.5% ($n = 6/11$), 40% ($n = 2/5$), 83.3% ($n = 5/6$), and 94.7% ($n = 18/19$) for PSA levels of >0.2 to <0.5 , >0.5 to 1.0, >1 to 2.0, and ≥ 2.0 ng/mL, respectively. The ^{18}F -DCFPyL-PET and mpMRI findings were concordant for 15 lesions (10.6%), while ^{18}F -DCFPyL detected additional 126 lesions (89.3%), 42 located outside the mpMRI field of view. The total PSMA tumor-volume burden (sum MTV) better correlated with PSA values compared to maximum SUVmax, with spearman's $r = 0.710$ vs $r = 0.358$ ($p < 0.001$, and $p = 0.056$, respectively). Out of the 29 patients with PSMA-avid suspicious lesions, tumor recurrence was confirmed by either biopsy ($n = 7$), or matched mpMRI ($n = 6$); 1 patient had a negative biopsy (rib fibrous dysplasia); 3 patients refused biopsy; 9 patients had lesions not amenable for biopsy; and 3 patients are pending for clinical decision. Patient accrual is ongoing for this trial and more results will be available at the time of presentation. **Conclusions:** ^{18}F -DCFPyL-PET imaging is helpful in identifying lesion detection in 70.7% of patients with biochemical recurrence prostate cancer; more importantly, it reveals a high number of positive findings in the range of low PSA values (<0.5 ng/mL), which may substantially impact further clinical management.

E-PW107

Impact of PSMA PET on the clinical management of prostate cancer patients with biochemical relapse who were staged as oligo metastatic based on conventional imaging

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Introduction: Oligometastatic state in prostate cancer has gained much attention recently. While previously considered stage 4 and hence incurable, there is emerging evidence suggesting that more aggressive approach may result in better outcomes in patients with oligometastatic prostate cancer. With new advances in functional imaging with PSMA PET, the oligometastatic state is diagnosed more frequently and more accurately. **Objective:** To assess the impact of PSMA PET on the clinical management of prostate cancer patients with biochemical relapse who were diagnosed as oligometastatic based on conventional imaging. **Methods and Materials:** A total of 39 patients with biochemical relapse that were staged as oligometastatic (as defined by three or less lesions, based on conventional imaging) underwent 68 Ga-PSMA PET/CT. Of these patients, 20/39 (51%) had radical prostatectomy in the past. All examinations were interpreted by one or if necessary two experienced nuclear medicine physician. Prior to undertaking PSMA PET imaging, referring medical specialists completed a questionnaire detailing relevant demographic and clinical data as well as their proposed management plan. We followed up these patients subsequently to determine whether the initial management plan had changed. 36 out of 39 (92%) patients underwent a follow up PSMA PET 6 months later to further assess the accuracy of PSMA PET findings. **Results:** Following initial PSMA PET, 46% (18/39) of patients were confirmed as oligometastatic state, 44% (17/39) of patients were upstaged to poly metastatic state and in 4 patients (10%) PSMA PET was negative. The median PSA level at the time of referral was 7.6 ng/ml. Overall, PSMA PET led to

an impact on subsequent clinical management in 35% of patients. The impact was expectedly more dramatic in the group that PSMA was negative. The main changes in clinical management included continuing surveillance, anti-androgen therapy, adding second line hormonal therapy, stereotactic radiotherapy and salvage radiotherapy. In all 36 patients who undertook the 6-monthly follow up PSMA PET, the findings were concordant with the findings on initial scan. **Conclusion:** Our findings indicate PSMA PET, when compared to conventional imaging, can more accurately define oligometastatic state in patients with prostate cancer who have biochemical relapse. And as such can significantly impact the clinical management of these patients. **Keywords:** Prostate cancer, oligometastasis, biochemical recurrence, PSMA PET, management impact

E-PW108

Baseline Total Metabolic Tumoral volumen and Total Lesion Glycolysis as prognostic biomarkers of the response of treatment in patients con Diffuse Large B Cell Lymphoma. Preliminary Results.

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Aim: Quantify total metabolic tumour volume (TMTV) and total lesion glycolysis (TLG) on pretreatment 18F-FDG PET/CT and analyze its prognostic value as predictors of response of treatment in patients diagnosed of diffuse large B-cell lymphoma (DLBCL). **Patients and Method:** We here present the first 24 patients, of a prospective study carried out in newly diagnosed DLBCL patients treated with 6 cycles of R-CHOP, who have completed the treatment and the response to the end of treatment has been evaluated. Eleven men with a median age of 68 years (range, 30–80 years). All patients underwent two PET/CT studies with 18F-FDG, one at diagnosis (baseline) and the other at the end of the treatment (EoT). TMTM and TLG parameters were quantified by three nuclear medicine physician blinded to a patient outcome on the semiautomatic free software “LIFEX” (<http://www.lifexsoft.org>) using an automatic segmentation of the lesions with a SUV > 3 with an adaptive threshold. To determine whether TMTV and TLG values predict the response to treatment univariate Cox regression analysis was performed. Statistical significance was considered at p<0.05. Data were analysed using SPSS software version 20. **Results:** Of the twenty-four patients, 20 patients (79%) were in complete response at the end of the treatment with mean values of TMTV, TLG and SUVmax of 576,36 cm³ (range, 0.8–1943), 5559 cm³ (range, 2–25496) and 24 (range, 3,1–44,1), respectively. The mean values of TMTV, TLG and SUVmax in the four patients who did not reached complete response at the end of treatment were 1532 cm³ (range 28–2805), 15830 cm³ (range, 299–27972) and 33 (range, 18,1–42,6), respectively. There were statistically significant differences between both group of patients with respect to TMTV (p<0.05) and TLG values (p<0.05), showing higher base-

line TMTV and TLG values the patients that did not get complete response at the end of the treatment, but not with respect to SUVmax. **Conclusion:** Although our results are preliminary, they suggest that baseline TMTV and TLG values might predict the response of treatment in patients with DLBCL.

E-PW109

Prognosis prediction using FDG PET/CT parameters and HPV status in cervical squamous cell carcinoma after concurrent chemoradiotherapy

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Purpose: To evaluate the prognostic value for predicting tumor recurrence of metabolic parameters on F-18-FDG PET/CT, status of human papillomavirus (HPV) infection and known prognostic variables in patients with locally advanced cervical cancer treated with concurrent chemoradiotherapy (CCRT). **Subjects & Methods:** A total of 129 patients with cervical squamous cell carcinoma who underwent initial CCRT were eligible for this study. Univariate and multivariate analysis were performed using traditional prognostic factors, metabolic parameters and HPV infection. Classification and regression decision tree (CART) was used to establish new classification. **Results:** Among 129 patients, 29 patients (22.5%) had recurrence after a median follow-up of 60 months (range, 3–125 months). Multivariate analysis revealed that tumor size, paraaortic lymph node metastasis, nodal SUVmax and HPV infection status were independent prognostic factors. CART analysis classified the patients into three groups. First node was nodal SUVmax and HPV status was second node for patients with nodal SUVmax≤7.49 (p<0.001); Group A (nodal SUVmax≤7.49 and HPV positive), group B (nodal SUVmax≤7.49 and HPV negative) and group C (nodal SUVmax>7.49). Log-rank test showed statistical significance among these groups (p<0.001). Cox proportional hazard model calculated hazard ratios (HRs) of group B (HR, 3.56; p=0.006) and group C (HR, 10.13; p<0.001), compared to the group A (HR, 1.00). **Conclusion:** The nodal SUVmax on F-18 FDG PET/CT and HPV infection status before CCRT are powerful independent prognostic factors for the prediction of disease free survival in patients with cervical squamous cell carcinoma who underwent initial CCRT. And we also suggest simple prognosis prediction model using FDG PET/CT and HPV genotyping.

E-PW110

Predictive performance of FDG signature score for chemotherapeutic response and survival in ER-positive breast cancer patients undergoing neoadjuvant chemotherapy - A pooled analysis of individual participants from publicly available gene expression data

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Purpose: ¹⁸F-fluoro-2-deoxyglucose (FDG) signature score is a multigene panel score developed to predict FDG uptake in tumors. In this study, we analyzed performance of the FDG signature score in predicting chemotherapeutic response and survival in estrogen-receptor (ER)-positive breast cancer receiving anthracycline-based neoadjuvant chemotherapy with or without taxane using publicly available gene expression profile data. **Methods:** We calculated FDG signature score for tumors from six Gene Expression Omnibus or ArrayExpress microarray data series, and analyzed its performance using C-statistic for the prediction of pathologic complete response (pCR) (n = 416) and distant metastasis-free survival (n = 300). We also calculated fifteen published prognostic multigene panel scores (including Oncotype Dx and MammaPrint) and PAM50 intrinsic subtypes as well as standard clinicopathologic variables, and compared their performances with that of the FDG signature score. Logistic and Cox regression was used for multivariable analysis. **Results:** High FDG signature score predicted pCR (AUC = 0.680, *P* < 0.001) and poor survival (C-index = 0.627, *P* = 0.002) comparably or superiorly to the majority of the other multigene panel scores and all of the clinicopathologic variables. About one fourth of the ER-positive breast cancer were of non-luminal intrinsic subtype, and the FDG signature score was significantly associated with the subtype (lowest in the luminal A, and highest in the basal-like subtype). The FDG signature score could discriminate basal-like subtype within the ER-positive tumors with high accuracy (AUC = 0.812) and these basal-like tumors showed high pCR rate and poor survival. In the multivariable analysis, the FDG signature score possessed added predictive value over the standard clinicopathologic variables. The FDG signature score remained significant after adjusted for the clinicopathologic variables but rendered insignificant after adjusted for the PAM50 intrinsic subtype. **Conclusions:** The FDG signature score can predict neoadjuvant chemotherapeutic response and survival in ER-positive breast cancer. Its performance was independent of the standard clinicopathologic variables and comparable to other well-known multigene panel scores. The predictive power of the FDG signature score might be attributed to its ability to discriminate between the intrinsic subtypes better than immunohistochemistry.

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Introduction: The aim of the present study was to assess the additional value of systolic wall thickening to myocardial perfusion in diagnosing myocardial stunning induced by dipyridamole infusion. **Methods:** We selected 52 ischemic patients (43 males; mean age 65.5 ± 7.64), with CAD documented by angiography. Ischemia was defined as a summed difference score ≥ 5 . All patients underwent a 2-day gated perfusion SPECT protocol. The patients received a dose of 740 MBq of ^{99m}Tc-tetrofosmin after stress and at rest. **Results:** The post-stress LVEF was significantly lower than rest LVEF ($48.3\% \pm 14.5\%$ vs. $50.7\% \pm 15\%$; *p* = 0.0001). The wall thickening-summed difference score was 3.97 ± 3.84 (*p* = 0.0001). At a multivariate regression analysis, only WT-SDS as independent variable was significantly correlated with myocardial ischemia (SDS) (*p* = 0.001). We divided patients according to SDS in those with mild (SDS < 8) and severe (SDS ≥ 8) ischemia. WT-SDS, but not Δ LVEF, was significantly different between groups. **Conclusions:** WT-SDS showed a better correlation with the degree of ischemia than the depression in the global function of the left ventricle. It allowed to better identify the stunning phenomenon in patients submitted to pharmacological stress. Abbreviations: CAD: coronary artery disease; SPECT: single photon emission computed tomography; LVEF: left ventricular ejection fraction; SSS: summed stress score; SRS: summed rest score; SDS: summed difference score; WT-SSS: wall thickening summed stress score; WT-SRS: wall thickening summed rest score; WT-SDS: wall thickening summed difference score; ESV: end-systolic volume; EDV: end-diastolic volume.

E-PW112

Lower limb tissue muscle 99m-MIBI perfusion scintigraphy in diabetic and non-diabetic patients

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Introduction: Peripheral artery disease in patients with diabetes mellitus (DM) is insufficiently explored. The aim of our study was to correlate the Doppler ultrasonography, pedo-brachial index and CT-angiography with perfusion reserve of lower limbs in diabetic patients (pts). **Materials and Methods:** 60 pts with DM, age 30 to 70 years, average age of 61.8 ± 10.5 years, with a duration of diabetes over 5 years. Doppler ultrasonography and pedo-brachial index (PBI) measurement were performed and afterwards tissue-muscle perfusion scintigraphy with ^{99m}Tc-MIBI. CT-angiography was performed in 20 diabetic pts. **Results:** Significantly lower average value of the perfusion reserve (PR) was registered in diabetic group, where the Doppler finding demonstrated obstruction of aa. tibialis posterior bill. or obstruction of aa. dorsalis pedis. PR of left calf (LC): $33.1 \pm 14.6\%$ vs. $46.93 \pm 11.3\%$, *p* = 0.0001, while for the right calf (RC): $33.62\% \pm 9.5$ vs. $46.0 \pm 9.3\%$, *p* = 0.000004 in pts with obstruction of aa. tibialis post. bill. PR for LC was $31.85\% \pm 16.2$ vs. 47.12 ± 8.7 , *p* = 0.000018, while for the RC: 32.93 ± 9.5 vs. 45.82

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e-Poster Walk 12 - Cardiovascular: Different Aspects of Cardiovascular Imaging II

E-PW111

Better Characterization of dipyridamole induced myocardial stunning by Systolic Wall Thickening. A gated perfusion SPECT study

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± 8.9 , $p = 0.000001$ (pts with obstruction of aa.dorsalis pedis). Lower values of PR was obtained in pts with reduced PBI, as well as Meckenberg sclerosis compared to subjects with normal PBI. CT-angiography positively correlated with perfusion scintigraphy - 71.43% of pts with pathological findings on CTA had lower PR, while perfusion scintigraphy detected microcirculatory changes in 28.57% of pts (showing lower PR) when CTA finding was normal. **Conclusion:** The scintigraphic method can earlier estimate microcirculatory disorders than Doppler ultrasonographic findings and CTA and may help in evaluating the perfusion status in individuals with Meckenberg sclerosis. **Key words:** muscle perfusion, diabetes, perfusion reserve, Doppler, pedo-brachial index, CT-angiography

E-PW113

Metabolic Characteristics of Takotsubo Syndrome by BMIPP imaging

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Objective: Takotsubo syndrome is a heart syndrome with an acute onset defined by chest symptoms, ST segment elevation on electrocardiograms. Patients with Takotsubo syndrome are sometimes misdiagnosed as having acute myocardial infarction. Therefore non-invasive diagnostic method needed to be established for setting up appropriate strategies. The purpose of this study was to detect myocardial metabolic abnormalities and to determine the diagnostic usefulness of ^{123}I -beta-methy-iodophenyl pentadecanoic acid (BMIPP) imaging in patients with Takotsubo syndrome. **Methods and Results:** We examined 16 patients with Takotsubo syndrome and 12 with acute myocardial infarction in the left anterior descending artery lesion. All patients were studied with resting ^{123}I -BMIPP imaging. Total defect score (TDS) of ^{123}I -BMIPP and perfusion were semi-quantitatively determined with SPECT imaging using a 17-segment 5-point model. TDS of ^{123}I -BMIPP were 4.8 ± 2.7 in patients with Takotsubo syndrome and 22.4 ± 10.7 in AMI. The ratio of summed BMIPP defect score of non-apical to apical segments in Takotsubo syndrome was smaller than that of the patients with acute myocardial infarction (0.1 ± 0.1 vs. 1.1 ± 0.7 , $p < 0.0001$), indicating ^{123}I -BMIPP abnormalities were exclusively observed in apical area. The ratio of summed perfusion defect scores of non-apical to apical segments in Takotsubo cardiomyopathy did not differ significantly from that of acute myocardial infarction (0.52 ± 0.6 vs. 0.57 ± 0.3 , $p = \text{NS}$). Summed BMIPP defect score in apical area of Takotsubo syndrome was larger than that of perfusion defect score (3.9 ± 2.7 vs. 1.8 ± 1.8 , $p = 0.04$). **Conclusion:** Impaired metabolic metabolism exclusively in apical region was observed by ^{123}I -BMIPP SPECT images in Takotsubo syndrome. These typical metabolic SPECT features of the disease can be utilized on differential diagnosis of Takotsubo syndrome.

E-PW114

Low Dose CT Attenuation Correction Method: Impact On Ischemia Diagnosis - An Angiographic Correlation

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Background- Aim: Myocardial perfusion scintigraphy is a valuable imaging modality in the assessment of coronary artery disease. Several technical issues, especially attenuation artifacts, can interfere with image quality and cause false positive results. With modern gamma camera systems, these artifacts can be corrected with the usage of low dose CT transmission maps. The aim of this study is to evaluate the effectiveness of low dose CT attenuation method in ischemia diagnosis. **Materials and Methods:** Thirty (30) patients underwent a Tc 99m sestamibi stress - rest myocardial perfusion scintigraphy and a coronary angiography (CA). The scintigraphic procedure was performed according to EANM myocardial perfusion imaging guidelines. The imaging was performed in a Philips Brightview XCT gamma camera. The results of non-attenuation corrected images (nonACMPI), as well as the photon low dose CT based attenuation corrected images (ACMPI) were compared to the angiographic results. The CA results were considered positive for stenosis of 70% for right coronary (RCA), circumflex (LCX) and left anterior descending (LAD) arteries and for 50% stenosis of the left main coronary artery (LCA). The results of the scintigraphic method were blinded to the angiographic results. **Results:** Sensitivity of nonACMPI was 55% for the detection of ischemia, while for ACMPI the sensitivity was 78%. The specificity was the same for the two methods at 50%. Regarding the sensitivity of the methods per coronary artery, the two methods showed similar sensitivity for LAD lesions (50%), AC method was mildly more sensitive for LCX lesions (80 to 64%) and far more sensitive for RCA lesions (100 to 50%). **Conclusion:** Low dose CT attenuation correction method is a valuable technique in the setting of myocardial perfusion scintigraphy procedure, improving the sensitivity of the method, especially for right coronary artery lesions.

E-PW115

Reliability of quantitative myocardial perfusion reserve prediction with IQ-SPECT/CT using a standardized uptake value

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Introduction: Myocardial blood flow (MBF) and myocardial perfusion reserve (MPR) quantified by positron emission tomography (PET) or single photon emission tomography (SPECT) fitted with a cadmium-zinc-telluride (CZT) semiconductor detector gamma-camera are widely used to predict detrimental cardiac events and diffuse micro-vascular or multi-vessel balanced ischemic coronary artery disease (CAD). However, calculating MPR requires dynamic acquisition protocols and specific medical software, and adequate testing facilities are

often limited. This study aimed to determine the clinical efficacy of IQ-SPECT/CT technology for predicting CAD. **Subjects & Methods:** 103 consecutive patients who underwent adenosine stress and at-rest myocardial perfusion imaging with ^{201}Tl examinations were selected to calculate both their MBF from dynamic SPECT fitted with a CZT semiconductor gamma-camera and their standardized uptake value (SUV) of myocardium from static SPECT using a IQ-SPECT/CT method. The MPR in the entire left ventricular myocardium was measured by dividing the stress MBF by at-rest values from dynamic SPECT. The increased ratio corresponding to MPR was calculated by dividing the stress SUV mean value by the at-rest SUV mean from the static images. Correlation between quantitative values obtained from dynamic SPECT and static SPECT imaging were verified. **Results:** Increased ratio, stress SUV mean, and at-rest SUV mean all showed a statistically significant correlation with MPR ($r=0.555$, $p<0.001$), stress MBF ($r=0.501$, $p<0.001$), and at-rest MBF ($r=0.449$, $p<0.001$), respectively. **Conclusion:** This study suggested that the quantitative values easily calculated with IQ-SPECT/CT imaging might be as reliable for assessing diffuse balanced ischemic CAD as the values obtained through conventional complicated protocols.

E-PW116

Semi-quantitative evaluation of myocardial perfusion and left ventricular function: comparison between the standard Anger and novel CZT camera with angiographic validation

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Introduction: Conventional Anger camera systems for single-photon emission computed tomography (SPECT) myocardial perfusion imaging have been widely used in the evaluation of patients with suspected or known coronary artery disease (CAD). The novel gamma cameras with semiconductor Cadmium-Zinc-Telluride (CZT) detectors demonstrated to allow an improvement in terms of image accuracy and acquisition time of SPECT imaging. **Aim:** We conducted a retrospective study to compare the diagnostic accuracy of CZT camera (D-SPECT) and conventional SPECT in detecting myocardial perfusion and functional abnormalities according to coronary angiographic findings in patients with suspected or known CAD. **Materials and Methods:** 93 consecutive patients referred to gated stress MPI for clinical evaluation of suspected or known CAD and with available angiographic data were included. Linear regression was used to evaluate the correlations between perfusion and functional parameters by D-SPECT and conventional SPECT. The differences between the two methods were assessed by Bland-Altman analysis. Sensitivity, specificity, and diagnostic accuracy for the detection of coronary stenosis ($\geq 50\%$ and $\geq 75\%$ luminal narrowing) were calculated for conventional SPECT and

D-SPECT and compared with McNemar's test. A p -value <0.05 was considered as statistically significant. **Results:** An excellent correlation between summed stress score (SSS), summed rest score (SRS) and total perfusion defect (TPD) measured by conventional SPECT and by D-SPECT was observed ($r=0.88$, 0.94 , 0.95 , respectively, $p<0.001$). At Bland-Altman analysis, the mean differences in SSS, SRS and TPD were 1.3% , 1.6% and 0.3% , respectively. Linear regression analysis of LV functional analysis showed an excellent correlation between methods in end-diastolic volume (EDV), end-systolic volume (ESV) and ejection fraction (EF) ($r=0.94$, 0.93 , 0.84 , respectively, $p<0.001$). At Bland-Altman analysis, the mean differences in EDV, ESV and LVEF were -13.6% , -10.8% and 5.1% , respectively. Conventional SPECT yields a higher sensitivity than D-SPECT (92% vs 77% , respectively, $p<0.01$) in assessing coronary stenosis $\geq 50\%$, while D-SPECT yields higher specificity than conventional SPECT (64% vs 80% , respectively, $p<0.01$). The diagnostic accuracy for conventional SPECT and D-SPECT was not different (83% and 78% , respectively, $p=0.3$). Similarly, in assessing coronary stenosis $\geq 75\%$ conventional SPECT yields higher sensitivity than D-SPECT (90% vs 77% , respectively, $p<0.01$), while D-SPECT yields higher specificity than conventional SPECT (81% vs 59% , respectively, $p<0.05$). The diagnostic accuracy for conventional SPECT and D-SPECT was not different (73% and 78% , respectively, $p=0.8$). **Conclusions:** The perfusion and functional parameters obtained by novel CZT camera provides excellent correlation with those obtained by conventional camera. Quantitative measures of myocardial perfusion showed comparable diagnostic accuracy between the two methods in the detection of significant coronary artery stenosis, despite some differences in sensitivity and specificity.

E-PW117

Diagnostic impact of hybrid cardiac perfusion SPECT/CT for patients with coronary artery disease after coronary artery bypass grafting

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Introduction: Patients with coronary artery disease (CAD) undergoing coronary artery bypass grafting (CABG) occasionally experience recurrent myocardial ischemia. Because of their severe CAD and the complicated hemodynamics associated with it, conventional non-invasive imaging modalities, such as cardiac CT (CCT) and cardiac perfusion SPECT, often cannot reveal the cause of myocardial ischemia. Hybrid cardiac SPECT/CT imaging simultaneously shows myocardial ischemia distribution, coronary artery lesion distribution, and their relationship. This modality enables detailed interpretation for such patients. This study aimed to assess the diagnostic impact of hybrid cardiac SPECT/CT imaging for patients with CAD and suspected myocardial ischemia after CABG. **Methods:** A total of 152 consecutive patients between April 2016 and March 2018, who were suspected of myocardial ischemia after CABG and underwent rest and stress cardiac perfusion SPECT, were included in this study. Among them, 115 patients (69 ± 11 years, 99 men and 16 women) who received cardiac SPECT using Discovery NM 530c,

CCT using Revolution CT, and hybrid cardiac SPECT/CT imaging using CardIQ Fusion were analyzed. In the cardiac perfusion SPECT images, the myocardial ischemia diagnoses were determined, and SSS, SRS, and SDS were quantified using a 17-segment model with a 5-point-grading system. In the CCT images, all coronary artery segments, including coronary artery bypass grafts, were assessed and coronary artery stenosis diagnoses (significant coronary artery stenosis: $\geq 70\%$) were determined. In the SPECT-only analysis, culprit lesions were determined based on the most standard coronary artery distribution map. In the SPECT/CT fused analysis, culprit lesions were determined based on the patients' actual coronary artery distribution. Diagnostic results for culprit lesions were compared between SPECT-only analysis and SPECT/CT fused analysis. **Results:** SSS, SRS, and SDS were 12 ± 9 , 9 ± 8 , and 3 ± 3 , respectively. Out of 2247 coronary artery segments, the number of significant stenosis segments was 851 (38%). SPECT/CT fused analysis yielded more accurate interpretations than SPECT-only analysis (interpretation change in 36% of patients). SPECT/CT fused analysis indicated that patients with LITA-LAD or RITA-LAD and patients with a bypass to PL had frequent myocardial ischemia in the diagonal artery territories (43%) and LCX territories (32%), respectively. Myocardial ischemia by diagonal branch stenosis was the most significant cause of interpretation change between SPECT-only and SPECT/CT fused analyses ($p = 0.00005$). **Conclusions:** Hybrid cardiac SPECT/CT imaging can better facilitate the interpretation of the complicated hemodynamics in patients with CAD after CABG, yielding more accurate interpretations than SPECT-only analysis.

E-PW118

Added Value Of Semi-quantitative Scoring For The Interpretation Of Rubidium-82 Pet Myocardial Perfusion Imaging

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Purpose: Semi-quantitative assessment of PET myocardial perfusion imaging (MPI) has the potential to decrease variation in scan interpretation, but is not widely applied due to discrepancies with visual interpretation leading to distrust and the need for camera specific databases. Our aim was to determine the reproducibility of semi-quantitative scores and their added value to visual interpretation of Rubidium-82 (Rb-82) PET MPI. **Methods:** We retrospectively included 30 consecutive patients who were referred for rest/regadenoson-stress Rb-82 PET/CT MPI (Discovery 690 PET/CT, GE Healthcare). Data processing was performed by two technologists and repeated by one technologist to determine the inter- and intra-operator reproducibility in calculating the semi-quantitative summed difference scores (SDS). Next, two pairs of expert readers visually interpreted the scans for occurrence of ischemia after which one pair repeated this to enable calculation of the inter- and intra-operator reproducibility. The semi-quantitative and visually assessed outcomes were then compared. $\text{SDS} \geq 3$ was considered to be indicative for ischemia.

In addition, SDS cut-off values predicting either ischemia or non-ischemia were determined based on the visual interpretation. **Results:** The inter- and intra-operator reproducibility of processing the scans before calculating SDS were almost perfect (both Cohen's kappa=0.87). The inter-observer agreement of the visual interpretation was moderate (Cohen's kappa=0.56) whereas the intra-observer agreement was substantial (Cohen's kappa=0.79). Visual interpretation resulted in 6 ischemic and 24 non-ischemic findings. The use of $\text{SDS} \geq 3$ resulted in more scans labeled as ischemic ($n=13$) than visual interpretation ($p=0.02$). Moreover, all scans with $\text{SDS} \geq 9$ ($n=4$) were visually interpreted as ischemic whereas all scans with $\text{SDS} \leq 4$ ($n=17$) were interpreted as non-ischemic. **Conclusion:** Semi-quantitative scores are highly reproducible. They can assist visual interpretation of Rb-82 PET MPI. Scans with $\text{SDS} \leq 4$ or $\text{SDS} \geq 9$ may even not require visual interpretation.

E-PW119

Diagnostic performance of quantitative ¹³N-ammonia PET/CT measures of coronary flow reserve and myocardial blood flow for the assessment of functional significance of coronary stenoses

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Aim: Cutoff values of coronary flow reserve (CFR) and stress myocardial blood flow (MBF) by ¹³N-ammonia positron emission tomography combined with computed tomography (PET/CT) for the assessment of functional significance of coronary stenoses vary in different clinics. Therefore the goal of this study was to determine the optimal cutoff values for stress MBF and CFR for the detection of coronary stenoses $\geq 50\%$ and to evaluate the diagnostic performance of the method in patients with suspected coronary artery disease (CAD). **Material and Methods:** 81 patients (68 with known CAD, 13 - control group) underwent dynamic ¹³N-ammonia stress-PET/CT and invasive coronary angiography (ICA). The absolute values of regional and segmental MBF at stress and at rest were derived by PET/CT; subsequently the regional and segmental CFR were also calculated. **Results:** We analyzed 243 coronary arteries (CA), including 137 with significant ($\geq 50\%$) stenoses, 68 intact CA in patients with CAD, 39 intact arteries in control group. Using a receiver-operating-characteristic (ROC) curve analysis optimal cutoff value for stress MBF was ≤ 2.09 ml/min/g and for CFR was ≤ 2.50 with a very good model quality: for MBF the area-under-the-ROC curve (AUC) = 0.86 and for CFR AUC = 0.89 with a certain advantage of CFR. Using the obtained cutoff values, the diagnostic performance of PET/CT for the detection of CAD (group of patients $n=81$) were assessed: sensitivity, specificity and diagnostic accuracy for regional and segmental CFR were 84%, 92% 85% and 88%, 69%, 85% respectively; for regional and segmental MBF - 85%, 69%, 83% and 84%, 61%, 80% respectively. **Conclusion:** The optimal cutoff values for the detection of significant coronary stenoses are $\text{CFR} \leq 2.50$ and stress MBF ≤ 2.09 ml/min/g. Dynamic ¹³N-ammonia PET/CT showed a high accuracy in the detection of CAD, with the best ratio of sensitivity and specificity achieved by using regional CFR values

≤2.50. Detection of obstructive lesion of a single artery is characterized by high sensitivity and lower specificity. These results might be determined by the decrease of CFR due to not only by obstructive CA lesions, but also by diffuse type microcirculatory or endothelial dysfunction.

E-PW120

Myocardial blood flow and coronary flow reserve assessment in patients with three-vessel coronary artery disease

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FEDERATION.

Purpose: To assess the myocardial flow reserve in patients with three-vessel coronary artery disease (MVCAD) by dynamic SPECT using CZT-based gamma camera. **Material and Methods:** 25 patients (20 males and 5 females; mean age 63.3 ± 12.6 years) with MVCAD with a lesion >70% in at least 2 major epicardial vessels according to invasive coronary angiography. Control group: 7 men and 2 women (25 ± 4 years) without any cardiac diseases (healthy volunteers). All patients and volunteers underwent myocardial perfusion SPECT (with ^{99m}Tc -MIBI) using cadmium-zinc-telluride based gamma camera. All scintigraphic images were acquired on the hybrid SPECT/CT unit (GE Discovery NM/CT 570C). The reconstructed dynamic image as well as CT attenuation correction maps were processed by 4DM Reserve application (University of Michigan, Ann Arbor, MI, USA). The values of stress and rest MBF were calculated semi-automatically by a net retention model. The value of CFR was calculated as MBF ratio (MBF stress / MBF rest). We estimated coronary flow reserve for the heart as a whole (gCFR) as well as for the three coronary artery territories (LAD, LCx, RCA) - regional coronary flow reserve (rCFR). **Results:** The average value of the gCFR index was lower in a MVCAD group 1.32 (1.01;1.72) than in control group 1.82 (1.79;2.19); $p < 0.001$. Regional coronary flow reserve also significantly ($p < 0.001$) differed between patients with MVCAD and healthy volunteers group: 1.34 (1.08;1.81) versus 2.05 (1.75;2.21) for the LAD; 1.27 (0.92;1.58) versus 2.24 (1.73;2.44) for the LCx; 1.1 (0.92;1.58) versus 1.58 (1.42;2.43) for the RCA, respectively. The average values of coronary blood flow in the rest not differed in these groups. The global and regional MBF values were significantly higher at stress study comparison with rest. Coronary blood flow values at stress study in the group of patients with multivessel coronary artery disease were significantly lower in comparison with the control group: 0.43 (0.27;0.6) versus 0.73 (0.57;1.04) for the LAD; 0.48 (0.31;0.58) versus 0.82 (0.66;1.02) for the LCx; 0.32 (0.3;0.51) versus 0.76 (0.68;1.07) for the RCA and 0.43 (0.28;0.58) versus 0.74 (0.70;0.97) for the global MBF, respectively. ROC analysis showed that the $\text{gCFR} \leq 1.78$ allows to identify MVCAD with a sensitivity and specificity 95.7% and 61%, respectively; area under curve was equal 0.79. **Conclusion:** Dynamic myocardial rest-stress SPECT using CZT-based gamma camera allows for identifying low myocardial flow reserve in patients with three-vessel coronary artery disease. It can be helpful in assessment of severity of myocardial perfusion abnormality in these patients.

1711 Wednesday, October 17, 2018, 10:00 - 11:30, Hall A

e-Poster Walk 13 - Radionuclide Therapy / Thyroid: Local and Systemic Therapy of Malignant Tumours

E-PW121

SPECT/CT-based Dosimetry for a Multicentre Trial of Selumetinib Enhanced Radioiodine Treatment of Differentiated Thyroid Cancer: Preliminary Results

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Background: The SEL-I-METRY trial (EudraCT No 2015-002269-47) is a multicentre phase II Molecular Radiotherapy trial, to investigate the potential of the MAP kinase inhibitor selumetinib (AZD6244, ARRY-142886) to re-sensitise advanced iodine-refractory differentiated thyroid cancer to radioiodine uptake. This is the first multicentre trial to assess the role of ^{123}I and ^{131}I SPECT/CT-based lesion dosimetry in predicting response to radioiodine therapy, as an exploratory endpoint. **Methods:** A network of 8 UK centres has been set-up to perform standardised quantitative ^{123}I and ^{131}I SPECT/CT imaging. Patients' ^{123}I whole-body and regional SPECT/CT scans are acquired at baseline and following a 4 week course of 75mg selumetinib twice daily. Patients that show evidence of new sites of iodine uptake or a 30% increase in uptake in existing iodine-avid lesions undergo a further 2 - 3 ^{123}I SPECT/CT scans for up to 72±4 hours following administration. The activities measured from these images are used to produce time-activity-curves (TAC) for absorbed dose calculations to predict the therapeutic ^{131}I absorbed dose. Patients receive ^{131}I therapy at a fixed activity of 5.5 GBq and cease Selumetinib treatment 2 days after the ^{131}I administration. Dosimetry is performed on 3-4 SPECT/CT scans acquired up to 144±24 hours following ^{131}I administration. Iodine-123 and ^{131}I SPECT/CT-based lesion TAC and estimated absorbed doses were compared in a preliminary assessment of results for patients that have proceeded to radioiodine therapy. **Results:** To date 3 patients have received radioiodine therapy. Eight lesions were visible on both the ^{123}I and ^{131}I scans. The percentage biological retention of ^{131}I at therapy was on average $233 \pm 151\%$ higher than that predicted from the ^{123}I scans in the 24 hour scan. Diffuse lung uptake and 2 extra bone lesions were evident on the ^{131}I scans compared to the ^{123}I scans. In 5 of the lesions there was no washout phase of ^{123}I within the 72 hours of scanning. However at ^{131}I therapy the average effective half-life of radioiodine washout was 34.3 ± 15.6 hours. Because the ^{131}I uptake and retention were higher and shorter respectively, the estimated average absorbed doses for the 8 lesions were comparable at 53.3 ± 47.4 Gy and 47.0 ± 33.3 Gy for ^{123}I and ^{131}I respectively and correlated within a 90% con-

fidence interval ($p=0.053$). **Conclusion:** For the therapeutic ^{131}I , the uptake was consistently higher and the retention shorter than predicted from the ^{123}I scans. Treatment response will be assessed in due course. (Research supported by AstraZeneca and Genzyme Corporation)

E-PW122

The value of Ga-68 DOTA-TATE PET/CT scanning in the Assessment of Vandetanib Treatment Response in Advanced Medullary Thyroid Cancer

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Introduction: Medullary thyroid cancer (MTC) represents an aggressive form of thyroid malignancy. 13-15% of patients of MTC presents with distant metastasis (DM) and have a 10-year survival of approximately 20%. Treatment options are limited in metastatic MTC. Vandetanib, a kinase inhibitor approved in April 2011 as an efficient treatment option for the treatment of locally advanced or metastatic MTC. The aim of the study is to compare the efficacy of Ga-68 DOTA-TATE PET/CT (TATE) scan versus biochemical markers (calcitonin and CEA) in regards to assess treatment response to Vandetanib. **Method:** We retrospectively evaluated 80 MTC patients from the files registered to hospital information system between March 2015 and April 2018 and found 7 patients, who received Vandetanib treatment and included in the study. All 7 patients had pre-treatment TATE scans, 5 of whom had post-treatment TATE scans. All patients had pre-treatment and post-treatment serum calcitonin (CT), and carcinoembryonic antigen (CEA) levels. Statistical evaluation is not performed because of limited number of patients. **Results:** There were 6 males and 1 female patients with a median age, 55 y (ranged 48-71), who were treated with Vandetanib (300mg orally per day), at least 6 months because of advanced and progressive MTC. In pre-treatment situation, all patients had an elevated (>500 pg/ml) CT levels despite of normal CEA levels in two and multiple metastasis (6 patients had lymph node, 4 patients had bone, 3 patients had liver and 1 patient had lung metastasis) on imaging modalities (TATE and/or MRI scans). Among these patients, TATE scans were only positive in 5 patients and negative in 2 patients with liver metastasis seen on MRI. After the treatment, biochemical response (at least 50% decrease of either CT levels or CEA levels) was observed in 4 of 7 patients, 2 of whom had post-treatment TATE scans revealed partial regression of the disease. The other 2 patients without post-treatment TATE scanning had post-treatment MRI scans with stable disease. The remaining three patients had a progressive disease both on tumor markers and TATE scanning. **Conclusion:** Ga-68 DOTA-TATE PET/CT scanning is a useful and decisive imaging modality to determine the response of Vandetanib treatment in MTC, particularly when CT and CEA levels are fluctuating or inconsistent results.

E-PW123

Radium 223 in the real world setting: Results from a multicentre retrospective study in the Triveneto Italian region

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Purpose: Radium223 (^{223}Ra) has been introduced for the treatment of metastatic castration resistant prostate cancer (mCRPC) with bone disease, based on the results of a randomized trial versus placebo showing a reduction of the risk of death and a prolongation of overall survival (OS). Our aims are to evaluate survival, response and outcomes for patients receiving ^{223}Ra in a real world setting. **Methods:** We developed a multicentre retrospective trial including patients with mCRPC treated with ^{223}Ra in the Triveneto regions. Key inclusion criteria are: histologic diagnosis of PC, presence of symptomatic bone lesions without visceral metastases, therapy with ^{223}Ra for at least one cycle. **Results:** Since its introduction, 158 patients received ^{223}Ra . Median age was 72 years old (range 52-82), median baseline PSA was 335.6 mg/dL (range 0.33-4552), median baseline ALP was 256 UI/mL (range 19.2-3028). 70 patients underwent radical prostatectomy, 60 received definitive radiotherapy. 46 patients had baseline lymph node disease. 41 (26%) patients received ^{223}Ra in first line setting, 37 (23%) in second line, 33 (20%) in third line, 47 (30%) in forth or further line of treatment. After a medial follow-up time of 9.5 months, 75 patients had died. Median number of cycle of ^{223}Ra therapy was 6. Median OS was 14.2 months, median progression free-survival (PFS) was 6.2 months. 71 (45%) patients achieved progression as best response during therapy; overall response rate (ORR) was 11%; clinical benefit rate was 28%. Previous radical prostatectomy or docetaxel exposure did not influence OS or PFS in a significant way; ECOG performance status maintains its prognostic role (ECOG PS 0 vs 1 $p=0.0062$; 0 vs 2 $p=0.0002$). A neutrophil to lymphocytes ratio (NLR) >3 significantly impact on OS ($p<0.001$) and PFS ($p=0.05$). Patients with a baseline ALP value ≥ 220 had a worse OS and PFS ($p<0.001$, for both). At the same time, patients with a reduction of the ALP value during treatment achieved a better OS ($p=0.029$) and PFS ($p=0.002$). There was no significant difference according to the line of therapy (0 vs ≥ 1 , $p=0.490$). Collected side effects did not differ from available data from pivotal trial (data not shown). **Conclusion:** At our knowledge, this is the largest real world report on ^{223}Ra in mCRPC. Our data confirms the published data for OS and PFS, finding no difference according to treatment line and confirming the emerging data about NLR. Moreover, the study confirms safety and efficacy of ^{223}Ra in an unselected cohort of patients.

E-PW124

A retrospective analysis of 115 Dutch mCRPC patients treated with Radium-223; analyzing success-rate and factors that contribute to therapy completion

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Background: Radium-223 (Ra-223, Xofigo®) is an alpha emitting radio-isotope used in the treatment of metastatic castration-resistant prostate cancer (mCRPC) in the Netherlands. The treatment consists of six intravenous doses at a 4-week interval. Clinical trials have shown that Ra-223 increases overall survival with an average of 3.6 months, but there is little data concerning efficacy outside the context of clinical trials. Furthermore, the reasons for therapy discontinuation are poorly known and it is unclear which factors contribute. Therefore the aim of this study was to gain insight in the frequency of therapy success and to identify variables that may be associated with therapy completion or premature discontinuation. **Methods:** We retrospectively analyzed 115 mCRPC patients who received Ra-223 between October 2013 and December 2017. Two groups were defined: (A) patients who have received all 6 doses (B) those who received 1-5 doses. The number of Ra-223 doses and the reason for discontinuing Ra-223 were registered. Prostate-specific antigen (PSA), PSA doubling time (3 months prior to Ra-223), lactate dehydrogenase (LD) and alkaline phosphatase (ALP) in addition to the hematologic status, consisting of hemoglobin, platelets and leucocytes levels were evaluated prior and during Ra-223. Additionally, previous use of chemotherapy was compared between the two groups, as well as the total Gleason score and the severity of bone metastases. **Results:** Forty-six patients (40%-group A) received 6 doses and sixty-nine patients (60%-group B) received 1-5 doses. The most common reasons for Ra-223 discontinuation were disease progression (45%), toxicity (20%) and death (16%). Patients in group A showed significant higher Hb, and lower LD/ALP at baseline and were less heavily pretreated with chemotherapy. Also, patients in group B showed a strong and continued increase in PSA and LD levels from the first injection of Ra-223 on, whereas patients in group A only showed a stable PSA and LD level or mild increase. **Conclusion:** This study showed that patients who discontinued Ra-223 received more intense therapy prior to Ra-223, had higher levels of ALP and LD and lower Hb at baseline, suggesting more advanced disease. During treatment, a pattern of continuous PSA and LD increase was associated with inability to complete the Ra-223 regimen, whereas patients with a mild increase were able to complete the treatment.

E-PW125

The administration of Radium-223 dichloride in Patients with castration resistant prostate cancer (mCRPC) and bone metastases is feasible and safe in “real-life” setting: single center experience

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Purpose/Introduction: Radiation therapy with radium-223 dichloride has demonstrated ability to improve overall survival, reduce symptomatic skeletal events in men with castration-resistant prostate cancer (CRPC) and bone metastases, with a good safety profile. Herein, we report on the safety and feasibility of radium-223 dichloride administration in mCRPC patients, in a “real life” setting. **Subjects & Methods:** In this open-label, uncontrolled, non-randomized, phase IV trial, radium-223 dichloride was given to patients with CRPC and ≥ 2 bone metastases in 4-week cycles. The patients were treated with injections of radium-223 dichloride [55 kBq/kg body weight (BW)] every 4 weeks (Q4W) for up to six injections. Between January 2017 to December 2017 all the patients treated with radium-223 dichloride were enrolled. Safety was determined via adverse event (AE) reporting, and biochemical bone markers (alkaline phosphatase, ALP) and the change in bone scans were assessed for treatment feasibility. **Results:** Overall 25 patients received the radium-223 dichloride (median age 75, 55-84y). All patients were previously treated with abiraterone acetate, enzalutamide, or taxanes in 72%, 20%, 40%, respectively. All patients complained pain at the bone metastatic sites (median BPI 2, 2-8). The ECOG was 0-1 in 63%. The mean number of administered cycles was 5.4 (mean dose at the first cycle 4429 vs last cycle 4241 KBq). The change in laboratory exams is showed in Table 1.1, 1.2, 1.3. The median follow-up was 5.3 months. Two patients (2/25) were transfused for symptomatic anemia. Nausea, anorexia, constipation and weight loss occurred in 30%, 28%, 17% and 18% of the cases, but are present mainly during the first 12 weeks. At last follow-up 16 patients completed the scheduled therapy, 5 still ongoing, 2 developed a clinical progression, 1 died for causes not drug-related. The 3-month bone scans showed stable disease and progression in 21 (87%) and 3 (12%) of cases, respectively. However, the 6-month bone scans showed a progression rate of 71%. **Discussion/Conclusion:** Radium-223 dichloride was well tolerated in mCRPC patients. At the recommended dose, in a real life setting we confirmed the safety profile described in the literature. The fluctuation of biomarkers (ALP and PSA) was as expected, and as previously described, confirming a good safety profile. The clinical outcomes recorded were consistent and overlapping with those reported in randomized clinical trial.

E-PW126

First evidence for a dose-response relationship in hepatic holmium-166 radioembolization

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Introduction: Radioembolization is an intra-arterial therapeutic procedure with the aim to deliver a tumoricidal dose to tumors while sparing the healthy liver tissue. Since treatment with holmium-166 (¹⁶⁶Ho)-microspheres can be preceded by a scout dose of identical microspheres that are imageable using SPECT, the treatment can be personalized based on pre-treatment quantification. To this end, a dose-effect relationship needs to be established, which is the aim of this study. **Subjects & Methods:** Patients who were treated in the clinical phase 2 HEPAR

II study and who underwent an FDG PET scan at baseline, at three months follow-up, and a post-therapy ^{166}Ho -SPECT/CT scan, were included for analysis. The dose-response relationship was assessed by relating the change in total lesion glycolysis (TLG) between baseline and follow-up to measured absorbed tumor dose. The ^{166}Ho -microspheres activity distributions following treatment were estimated with quantitative SPECT/CT reconstructions using a pre-calibrated fast Monte Carlo-based reconstructor (UMCS), which has been previously validated for ^{166}Ho . Lesion masks were defined on baseline FDG-PET (PERCIST; threshold $2 \times \text{SUL}_{\text{mean}}$ in aortic blood pool). The masks were transferred to the corresponding ^{166}Ho -SPECT reconstructions following affine co-registration of the CT scans of the PET and SPECT acquisitions. The tumor doses were estimated using these transferred masks. The entire microsphere dose was assumed to be absorbed in the $5 \times 5 \times 5$ mm SPECT voxel. Response was categorized according to the PERCIST criteria: complete response (CR) if 100% decrease in TLG; partial response (PR) if TLG decrease $\geq 45\%$; progressive disease (PD) if TLG increase $\geq 75\%$; otherwise stable disease (SD). **Results:** In total 30 patients with a total of 88 lesions were included. The lesions were categorized as CR ($n=31$), PR ($n=17$), SD ($n=30$) or PD ($n=10$). The corresponding median absorbed doses were 192 Gy (range 35–905) for CR, 138 Gy (6–608) for PR, 126 Gy (62–375) for SD and 78 Gy (38–204) for PD. An objective response (CR and PR) was observed in 48 lesions (55%). Doses in these lesions were significantly higher than doses in lesions without objective response (Mann-Whitney $U=604.0$, $z=-2.983$, $p=0.003$). **Discussion & Conclusion:** In this study, we have established that there is a significant effect of absorbed dose on lesion response in ^{166}Ho radioembolization, according to the PERCIST criteria. Further analysis will stratify these results according to tumor type and provide a dose threshold needed for a reliable tumor response.

E-PW127

Predictivity and dose-effect relationship of $^{99\text{m}}\text{Tc}$ -MAA-SPECT/CT based dosimetry in the treatment of advanced hepatocellular carcinoma (HCC) treated by SIRT with resin ^{90}Y -microspheres

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The goal was to evaluate the predictive role of $^{99\text{m}}\text{Tc}$ -MAA-SPECT/CT based dosimetry for advanced HCC, with the cohort of the SARAH trial¹. **Methods and Material:** Among the 184 patients from the SARAH trial who received SIRT, 121 were included in the survival analysis and 109 for tumour response, according to available corresponding data. Baseline CT, MAA-SPECT/CT and ^{90}Y -SPECT or PET /CT, 6 months follow-up CT were centralized and reviewed. A 3-scale visual agreement (optimal, sub-optimal or not optimal) was defined between imaging datasets. MAA-based dosimetry was done according to the MIRD formalism. The liver and lung were manually delineated on the CT, the injected activity was considered distributed in

liver and lung. The tumour was segmented by manual threshold on the SPECT. The absorbed-dose was calculated by a dose point kernel approach², these indices were extracted from tumour-absorbed-dose histograms: average absorbed-dose, D20 (least dose irradiating 20% of the volume), D50 and D80.

Results: The median tumour-absorbed-dose was 112 Gy (IQR 67.8–220). Patients who received ≥ 100 Gy ($n=67$) had significantly longer survival (median 14.1 months (95% CI 9.6–19) vs. 6.1 months (95% CI 4.9–6.8) in patients receiving <100 Gy, $p<0.0001$). Among them, those with a good visual agreement ($n=24$) had the longest median OS (25 months 95% CI 9.6–34). Objective response (OR) and disease control (DC) rates were 20.5% and 63.7%. DC was significantly associated with higher tumour-absorbed-dose (median 121 Gy (IQR 86–190) vs. 85 Gy (IQR 58–164) in non-DC patients, $p=0.0204$), while OR was not (median 133 Gy (IQR 76–238) vs. 104 Gy (IQR 72–175) in non-OR patients, $p=0.2$). A tumour-absorbed-dose > 100 Gy was the best predictive factor of prolonged survival according to a multivariate analysis (<0.0001). The tumour dose-control data was successfully fitted by a linear quadratic survival model. **Conclusion:** The tumour-absorbed-dose based on $^{99\text{m}}\text{Tc}$ -MAA-SPECT/CT is a statistically significant predictive factor of survival and tumour control for the treatment of advanced HCC with resin ^{90}Y -microspheres. **References:** 1. Vilgrain V, Pereira H, Assenat E, et al. Efficacy and safety of selective internal radiotherapy with yttrium-90 resin microspheres compared with sorafenib in locally advanced and inoperable hepatocellular carcinoma (SARAH): an open-label randomised controlled phase 3 trial. *Lancet Oncol.* 2017;18(12):1624–1636. 2. Sanchez-Garcia M, Gardin I, Lebtahi R, Dieudonné A. A new approach for dose calculation in targeted radionuclide therapy (TRT) based on collapsed cone superposition: validation with (^{90}Y). *Physics in medicine and biology.* 2014;59(17):4769–4784.

E-PW128

Lu-177 PSMA Radioligand Therapy as Salvage Treatment in Metastatic Castration-Resistant Prostate Cancer

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Purpose: The aim of this study was to analyze the efficacy and safety of Lu-177 PSMA radioligand therapy (PRLT) as a salvage treatment in patients with metastatic castration-resistant prostate cancer (mCRPC), i.e., applying repeated therapy cycles using high cumulative radioactivities for progression after the initial 3 PRLT cycles. **Methods:** In this retrospective study, 85 patients with mCRPC who underwent salvage Lu-177 PRLT, were included. These patients had demonstrated an initial response to PRLT. The median cumulative activity was 37 GBq (25.0–61.2 GBq) applying 4–9 cycles (median 6). Response to therapy was determined as per RECIST as well as according to molecular imaging criteria using Ga-68 PSMA PET/CT. Toxicity was evaluated with the assessment of laboratory parameters, including complete blood counts and renal function tests, using CTCAE 4.03. **Results:** PSA-decline was noted in 40/85 (47.1 %) patients. Based on Ga-68 PSMA PET/CT, complete remission was observed in 3 (3.5 %),

partial remission in 31 (36.5%), stable disease in 19 (22.4 %) and progressive disease in 32 (37.6 %) patients. RECIST revealed 3 (3.5 %) complete remissions, 25 (29.5 %) partial remissions, 29 (34.1 %) with stable disease and 28 (32.9 %) disease progressions. The median progression-free survival (PFS) from the start of salvage therapy was 8 months. Grade 3/4 pancytopenia was noted in 4 patients (4.7 %) due to progressive diffuse bone marrow involvement. No significant nephrotoxicity or xerostomia was evident during long-term follow-up. **Conclusions:** Salvage Lu-177 PSMA radioligand therapy for progressive metastatic castration-resistant prostate cancer is safe, feasible and effective even after progression post the initial 3 PRLT cycles.

E-PW129

⁶⁸Ga DOTATOC PET/CT for treatment response of Peptide Receptor Radionuclide Therapy using ¹⁷⁷Lu and ⁹⁰Y-DOTATOC

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Purpose: In this work the relation between the absorbed doses and the modifications in ⁶⁸Ga-PET/CT images (acquired before and after therapy) was investigated in lesions. The aim was to explore the role of PET to evaluate the response of therapy. **Subjects and Methods:** For this study a sample of 42 patients enrolled in a PRRT clinical trial with alternation of ¹⁷⁷Lu and ⁹⁰Y-DOTATOC was considered. Each patient underwent a dosimetry study for organs at risk and for lesions at the first therapy cycle (injection of ¹⁷⁷Lu-DOTATOC) by means of 5 sequential SPECT/CT acquisitions (at 1h,4h,24h,40h,70h p.i.). Dosimetry was performed with the software OLINDA1.0. ⁶⁸Ga-DOTATOC PET-CT scans were acquired before therapy and after therapy (up to 6 months after the last injection). Variations between basal and follow-up values for SUVmax (maximum value for SUV), volume (threshold 40% of SUVmax), meanSUV, and TLG (product between meanSUV and volume) were calculated for each of the 127 lesions analysed. SUVmax, meanSUV, volume and TLG variations were classified into two class: TC (Tumour Control) and NTC (Not Tumour Control), similarly to PERCIST response criteria (TC if CR or PR, NTC if SD or PD) in solid tumours. Absorbed doses to lesions were divided into 2 classes, considered low and high dose collections. **Results:** Median (25th percentile, 75th percentile) values for volume and absorbed dose lesions were: 11.2 (7.3, 20.9) ml and 31.3 (16.7, 74.6) Gy. The 75th percentile of lesion doses (75Gy) was considered to divide data into two classes (D<75Gy; D≥75Gy). The classification provided a percentage of TC for (D<75 Gy, D≥75 Gy) respectively: (31%, 39%) for SUVmax, (14%, 45%) for volume, (28%, 45%) for meanSUV, (25%, 45%) for TLG. Pearson's correlation test showed no agreement between absorbed dose and variation of SUVmax (R=-0.1), volume (R=-0.1), meanSUV (R=0.1) and TLG (R=-0.1). **Conclusions:** Classification between Tumour Control and Not Tumour Control, based on PERCIST-like criteria, showed higher probability of TC for larger absorbed doses. However, no correlation was found between dose and variation of SUVmax, meanSUV, volume and

TLG. The lack of correlation might be due to the low value of mean absorbed dose delivered to lesions in this cohort. Further analysis should investigate correlation between ⁶⁸Ga-PET/CT in lesion and response to the therapy. Moreover, different threshold values for classification of lesions in TC and NTC and different figures of merit might show higher correlation with absorbed doses. This work was supported by the EMPIR-MRTDosimetry project.

E-PW130

Renal protection during LUTATHERA treatment using lysine and arginine solutions

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Radioactive somatostatin analogs used in Peptide Receptor Radionuclide Therapy (PRRT) are partially reabsorbed by proximal tubular cells in the kidney after glomerular filtration. Co-administration of positively charged amino acids (AA) is effective in decreasing the kidney absorbed radiation dose and risk for toxicity, increasing the dose limiting threshold. Published clinical experience and ENETS guidelines recommend lysine and arginine (25g each) as optimal AA composition for renal protection infused over 4 h. Kidney dosimetry findings and short to long-term monitoring of renal function following treatment with LUTATHERA in the Phase III NETTER-1 study and Phase I/II Erasmus MC study (published data) were evaluated in relation to different AA solutions for renal protection: 2.5% lysine-arginine in 1L vs commercially available solutions containing similar amounts of these two AA in 2L. **Methods:** Patients treated with LUTATHERA (7.4 GBq x 4 treatments at 8-week intervals) were co-administered AA solutions from 30 minutes before LUTATHERA onset for 4 hours. Erasmus MC patients (n=223) received 2.5% lysine-arginine in 1L of 0.225% NaCl, whereas NETTER-1 patients received 2L of Aminosyn II 10% (Hospira, Inc) (n=66) or Vamin 18 (Fresenius Kabi) (n=50) solutions for parenteral nutrition with 18-24g of lysine and arginine content. **Results:** Mean kidney absorbed doses estimated for a cumulative LUTATHERA administered activity of 29.6 GBq was 19±9 Gy in the NETTER-1 dosimetry substudy (n=20 patients) and 20±5 Gy in the Erasmus MC study (n=223 patients), suggesting that the different AA solutions used in the two studies provided an equivalent kidney radiation exposure. This is also confirmed by the low incidence of renal function toxicities, as determined by creatinine clearance values during treatment and a median follow-up period of 22.44 (0.4- 41.1) months for NETTER -1 and 25 (0-142) months for Erasmus patients, with no treatment-related Grade 3 or 4 kidney toxicity observed in these two studies. Aminosyn II 10% or Vamin 18 were associated with increased incidence of nausea or vomiting compared to 2.5% lysine-arginine solution

(25% and 10% of nausea and vomiting respectively reported in Erasmus MC, vs 59% and 46% in NETTER -1). **Conclusions:** Solutions containing lysine and arginine used for renal protection in PRRT with LUTATHERA effectively decrease the kidney absorbed radiation dose. The absence of unnecessary components, adequate osmolality, lower infused volume (1L versus 2L) and lower incidence of nausea and vomiting, make 2.5% lysine-2.5% arginine solution the best option for patients receiving LUTATHERA.

Scientific e-Posters

EP-01

e-Poster Area

Physics: Data Analysis & Management

EP-0001

Determination of Respiratory Motion Ranges of Lung Lesions Using Data-Driven Gating in PET

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Purpose/Introduction: Respiratory gating methods in PET have been demonstrated to improve quantification and localisation of lesions located in the lungs. In this respect, data-driven gating (DDG) is a promising alternative to conventional hardware-based methods. In this retrospective study we analysed the motion extent of lung lesions as determined by DDG PET in order to define typical ranges for different locations inside the lungs. **Subjects and Methods:** Single bed position of [18 F] FDG PET/CT list mode datasets of the lungs (5 - 10 minutes duration, free breathing, Biograph mCT, Siemens Healthcare, Erlangen, Germany) of 30 patients with at least one PET-active lung or mediastinal lesion were retrospectively analysed. Gating signals were determined using a centre-of-mass-based DDG approach. End-expiratory and end-inspiratory PET images were reconstructed without attenuation correction using an amplitude-based gating scheme, and the size, location, and 3D motion extent of all lesions were determined. **Results:** 117 PET-active lesions were identified. Of these, 69 were classified as small (< 2 cm apparent diameter), 34 as medium-sized (< 4 cm diameter), and 15 as large; no significant differences in respiratory motion shifts were seen for different sizes. Highly significant differences were determined in superior-inferior direction between apical (3.7 ± 2.4 mm, $n=26$), medial (5.9 ± 3.8 mm, $n=67$), and basal locations (12.0 ± 8.0 , $n=25$), while basal lesions had significantly larger shifts in anterior-posterior directions (3.4 ± 2.5) than either medial (2.3 ± 2.4 mm) or apical lesions (1.9 ± 1.5 mm). Lesions in the anterior part of the lungs moved significantly more into the anterior direction during inspiration (2.1 ± 1.3 mm, $n=20$) than posterior lesions (0.3 ± 3.0 mm, $n=29$). The largest determined shifts determined were 7 mm in lateral, 10 mm in anterior-posterior, and 30 mm in superior-inferior directions, respectively. **Discussions/Conclusion:** Data-driven gated PET was successfully used to characterise respiratory motion ranges of lung lesions in a larger collective of patients. The results are much in line with values from literature obtained using CT- or MRI-based methods; however, due to inherent longer scanning durations in PET, the amount of scanned respiratory cycles is usually higher than in conventional scans, resulting in statistically more robust motion estimation.

EP-0002

Deep Learning Pre-Clinical Medical Image Segmentation for Automated Organ-Wise Delineation of PET

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Aim: Micro-PET-CT allows the non-invasive monitoring of biological processes, disease progression and therapy response. Morphological information provided by the CT allows organ and tissue delineation for subsequent quantification of physiological information depicted by PET. Extensive reviews of PET-CT segmentation highlights the plethora of proposed solutions. Without automated anatomical identification, analysing PET data relies on time-consuming observer-dependent error-prone manual volume-of-interest (VOI) delineation. Deep learning with convolutional neural networks (CNNs) has achieved state-of-the-art performance for automated medical image segmentation. To train a deep CNN from scratch requires expert annotations of large medical datasets which is a tedious, expensive task along with expensive computational resources (GPUs). A promising alternative has recently been proposed to use transfer learning and fine-tune a CNN that has been pre-trained using, for instance, a large set of labelled natural images. To the authors knowledge this resource saving automated segmentation approach has not been assessed in Micro-PET-CT. **Methods:** An off-the-shelf pre-trained VGG16 architecture was utilized consisting of 16 trainable layers organized in blocks. A 5-block convolutional base of neurons with 3×3 receptive fields (alternated with max-pooling layers which increase the receptive field of neurons). Following each convolutional layer is a ReLU activation function. The last fully connected layers of the classification network are replaced with fully convolutional layers to allow dense pixel-wise predictions (FCN) with end to end training. A total of 28 mice were used for the study ($0.25 \times 0.25 \times 0.25$ mm). The brain was manually segmented with VivoQuant using both the PET and CT images. The central sagittal 2D slice and one slice either side (r-l) were extracted for each animal. 17 mice ($\approx 60\%$) served as a training set, image augmentation using rotations and skews resulted in $\approx 5k$ images to fine tune the network weights. Testing was performed on the remaining images from 12 mice (36 images). **Results and Conclusion:** The DICE coefficient serves as a measure of the percentage of overlap between the reference manual contour brain segmentation and that predicted by the FCN. The mean DICE value found for the test mice of 0.902 is comparable to an automated machine-learning based state of the art approach when tested on phantom data [1] and well within the intra-operator variability of manual segmentation. Fine tuning a Deep FCN for preclinical image segmentation serves as a promising low cost method. Future work will extend the method to three dimensions and multiple organs. **References:** 1) Berthon (2016) ATLAAS: Phys-Med-Biol-61:4855-4869

EP-0003

Evaluation of imaging biomarkers in the detection of bone metastases in patients with prostate or breast cancer

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Purpose/Introduction: Bone scintigraphy (BS) is a standard method of whole-body imaging to identify bone metastases (BM) associated with various types of cancer. We aimed at finding the most relevant malignancy prediction imaging biomarkers in BS for prostate and breast cancers to develop a computer-aided diagnosis (CAD) system for measuring changes in uptake of malignant hotspots. **Subjects & Methods:** A dataset containing 156 BS obtained with ^{99m}Tc Methylene Diphosphonate from 156 patients with prostate (76) or breast (80) cancer was retrospectively evaluated. From this dataset, 40 BS were set apart as an independent validation set. Gold standard for BM was clinical and was obtained after thorough examination of information available. Uptake hotspot candidates were segmented by an automatic thresholding method and 70 descriptors were extracted to characterize size, shape, intensity, location and context of each candidate, as well as patient's sex and age. Classification of malignant hotspots and selection of relevant descriptors were performed by random forest algorithm. Three training datasets were used: prostate cancer patients, breast cancer patients and global group (all). Initial features were automatically reduced to only relevant ones by a recursive feature elimination guided by mutual information, while maintaining similar classification area under curve (AUC). **Results:** Random forest algorithm trained with the global group dataset resulted in an overall 75% sensitivity to identify BM (AUC = 0.853). Prostate cancer metastases were better identified with global classifier (sensitivity = 84%) than breast cancer metastases (sensitivity = 62%). The feature selection process conducted separately on prostate and breast cancer datasets resulted in different selections of most important descriptors. In the prostate cancer dataset, the descriptors based on the intensity, location and heterogeneity of the hotspot uptake were the ones with best discriminating power (AUC = 0.831, sensitivity = 82%). In the breast cancer dataset, patient's age, location of the hotspot, texture, and context of intensity distribution of the symmetrically located region were the best descriptors (AUC = 0.881, sensitivity = 92%). Sensitivity and AUC values were determined on the validation dataset. **Discussion/Conclusion:** Texture and context features for breast cancer and intensity, location and heterogeneity of hotspot uptake in prostate cancer originated good accuracy in identifying BM, and thus, they should be used in automated CAD systems. **Financial support:** This work is supported by the project LISBOA/NORTE-01-0247-FEDER-017685 - BTSCAD (Bone Tumor Scan - CAD) under the PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund (ERDF).

EP-0004

A Novel Technique to Validate Poisson Resampling Software

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Aim: Poisson resampling software has become a very powerful tool in nuclear medicine as it allows the simulation of reduced count images. This has obvious benefits for research and optimisation as images representing reduced injection activity or reduced scan time can be retrospectively simulated without

the need to rescan patients. Previous testing of the software has relied on analysing acquired floods. However these may have non-uniformities which could affect statistical testing and such images generally do not include very low count densities. This is relevant to consider as bone scans for example have approximately 50% of pixels in the 1-10 counts/pixel range. We have developed a novel method for testing and validating Poisson resampling software. **Method:** Noiseless test images were created where every pixel has the same count value. Individual images containing 100, 50, 20, 10, 5, 2 and 1 count(s) per pixel were created and then Poisson resampled with a range of resampling fractions (10% - 90%). The theoretical effect of Poisson resampling applied to such noiseless images should give a binomial distribution of counts where the mean is equal to $n \times p$. Here, n is the number of counts in each pixel of the original image (effectively the number of binomial trials) and p is the probability of success given by the resampling percentage. The distributions of pixel values in the resulting images were compared against the expected binomial distribution using chi-squared tests. **Results:** The Poisson resampling software showed excellent agreement with the expected binomial distributions for the noiseless test images. Chi-squared analysis showed no statistical significance between the resampled images and the expected binomial distribution for all counts per pixel and all resampling percentages (all $p > 0.05$). **Discussion:** It is not always appropriate to examine the Poisson nature of the resampled image as count variations in acquired images can not only arise from Poisson randomness but also from inherent non-uniformities in the gamma camera detector. Although such software is often referred to as 'Poisson resampling', it is actually binomial in nature akin to rolling a dice or tossing a coin. **Conclusion:** We have developed a robust and reliable testing procedure for Poisson resampling software by examining the binomial nature of the algorithm. This independent validation technique can test that Poisson resampling software correctly generates expected noise characteristics even down to 1 count/pixel. This is reassuring given the increasing applications of such software.

EP-0005

The initial evaluation of a data-driven respiratory motion correction method for whole body PET using continuous bed motion

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Aim: Data-driven respiratory gating methods eliminate the requirement for hardware-based respiratory devices typically used to correct PET images for respiratory motion. Several fully automated data-driven methods have been developed, but very few have demonstrated robust accuracy on acquisitions that extend axially beyond a single PET field of view. A fundamental limitation of typical data-driven methods is the difficulty in identifying a consistent relationship between the polarity of the respiratory signal and the physical direction of motion. We have produced a data-driven method for whole body PET acquisitions that uses continuous bed motion to maintain accu-

racy throughout anatomical regions where motion is expected. **Method:** Listmode PET data was converted into a time-series of spatially filtered, time-of-flight volumes, and the time varying anterior-posterior displacement estimated for the entire acquisition. The axial acquisition range was then divided into a series of overlapping regions, and each region analysed with a frequency domain data-driven gating method, initialized with the spectral information of the anterior-posterior displacement signal. An optimization process combined each region and assigned a consistent relationship between the respiratory signal polarity and the physical direction of motion throughout the acquisition. We evaluated 86 FDG oncology patient data sets acquired from mid-thigh to mid-brain. Respiratory signals from the data-driven method were compared with signals from a hardware based device at different anatomical regions, and motion corrected images were compared. **Results:** For all patients, a high correlation between the data-driven and hardware based respiratory signals was found in anatomical regions where motion was clearly seen, with a mean correlation of 0.81 (+/- 0.1) between the bladder and the aortic arch. Anatomical regions where poor correlation was found demonstrated very low or no detectable motion. Cases were also observed where, in some anatomical regions, more respiratory induced displacement was identified in the data-driven gated images than in the hardware gated images. **Conclusion:** We have implemented a data-driven respiratory motion correction method for whole body, continuous bed motion PET which performs as well as a hardware-based gold standard in anatomical regions where motion is expected.

EP-0006

In vivo Gd-nanoparticles image-based quantification with SPECT and k-edge spectral CT

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Introduction: Gadolinium nanoparticles (NP) combined with radiotherapy is currently under investigation for oncology treatment. Indeed, NPs concentrated in a tumor could enhance its radiosensitization. The noninvasive *in vivo* quantification of NP concentration is therefore a crucial task for radiotherapy treatment planning as this would help to determine the delivered dose. Image-based quantification could be achieved, for example, with k-edge spectral CT, also called spectral photon counting CT (SPCCT), for direct Gd detection, or with nuclear medicine scanners, as SPECT and PET, for detection of NPs coupled with a radioactive tracer. This work shows the feasibility of Gd-NP *in vivo* quantification with a preclinical SPECT/CT scanner. We also propose *in vitro* results on a preclinical prototype SPCCT scanner and its comparison to SPECT. **Methods:** The *in vitro* and *in vivo* SPECT images were obtained on preclinical nanoSPECT/CT (Bioscan Inc., Washington D.C., USA) and corrected for scatter, attenuation and partial volume effect. The absolute image calibration for activity were performed on a 5 mL volume with concentration 0.72 ± 0.01 kBq/mL of ¹¹¹In measured with a gamma counter (Wallac Wizard 1470 Gamma Counter,

GMI inc.). Conversion factor between ¹¹¹In and Gd for *in vitro* were cross checked on Inductively Coupled Plasma Mass Spectrometer (ICP-MC) measurements. For the *in vivo* analysis, the image activity measurements were cross checked with a gamma counter. The gadolinium content was recalculated from the initial parameters of the synthesis of the nanoparticles with ¹¹¹In. For the SPCCT (Philips Healthcare, Haifa, Israel) *prototype*, we also performed the same type of measurements. Only *in vitro* results are yet available. **Results:** The *in vitro* results show that activities above 1 MBq could be measured on nanoSPECT/CT images with accuracy below 10%. The *in vivo* results on SPECT proved the necessity of attenuation, scatter and partial volume corrections: the discrepancy of *in vivo* measurements without corrections was ~40% while it was less than 10% after all corrections. Thus, these activity measurements provide the *in vivo* Gd quantification from SPECT images within a similar accuracy. The SPCCT machine provides the direct measurements of gadolinium NPs, and is in agreement with SPECT *in vitro* measurements. **Conclusions:** The *in vivo* quantification of Gd nanoparticles is possible from SPECT images with about 10% accuracy. The preliminary results obtained *in vitro* show the linear correspondence between the concentration of nanoparticles measured using SPCCT and SPECT images.

EP-0007

The value of ^{99m}Tc-MAA SPECT/CT for lung shunt estimation in ⁹⁰Y radioembolization: a phantom and patient study

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Purpose: To evaluate the accuracy/precision of lung shunt fraction (LSF) estimated from ^{99m}Tc planar and SPECT/CT phantom imaging, and within this context, to compare the corresponding LSFs from ^{99m}Tc-MAA patient studies. Additionally, LSF from pre- and post-therapy imaging were compared. **Methods:** A liver/lung torso phantom filled with ^{99m}Tc to achieve three LSFs was scanned by planar and SPECT/CT imaging. To facilitate processing of patient data, a workflow was implemented within commercial software to automatically calculate LSF with SPECT and CT-based auto-contouring to define liver/lung volumes including subtraction of the inferior 2 cm of the lung to account for liver motion. Planar imaging-based LSFs for 40 patients, obtained from their medical records, were retrospectively compared with SPECT/CT (with and without corrections) based calculations. Regions had been manually defined on anterior liver and posterior lung by a technologist for the planar calculation. Additionally, in a subset of 20 patients, the pre-therapy estimates were compared with ⁹⁰Y PET/CT based estimates. **Results:** For the phantom, improved accuracy in LSF estimation was achieved using SPECT/CT with attenuation and scatter correction (within 13% of the true value) compared with planar imaging (up to 44% overestimation with anterior liver/posterior lung; up to 129% overestimation with geometric mean). The results in 40 patients showed a similar trend with planar imaging significantly over-

estimating LSF compared to SPECT/CT. This difference was due to both the lack of attenuation correction and the lack of the exclusion region in the planar calculation, with scatter correction having less impact. There was no correlation between LSF and the delay between ^{99m}Tc -MAA administration and scanning, but off-target uptake was visualized more frequently in patients with a longer delay. The mean lung absorbed dose predictions for the 28 patients who underwent therapy was 9.3 Gy (range 1.3 - 29.4) for planar and 3.2 Gy (range 0.4 - 13.4) for SPECT/CT. For the patients with post-therapy imaging, the mean LSF from ^{90}Y PET/CT was 1.0%, (range 0.3 - 2.8). This value was not significantly different from the mean LSF estimate from ^{99m}Tc -MAA SPECT/CT (mean 1.0%, range 0.4 - 1.6; $p=0.968$), but was significantly lower than the mean LSF estimate based on planar imaging (mean 4.1%, range 1.2 - 15.0; $p=0.0002$). **Conclusion:** The improved accuracy demonstrated by the phantom study, agreement with ^{90}Y PET/CT in patient studies, and the practicality of using auto-contouring for liver/lung definition suggests that ^{99m}Tc -MAA SPECT/CT with corrections should be used for LSF estimation.

EP-0008

Correlations and Analysis of Image Quantification Method Choice for Tumor/Artifact Differential Diagnosis in Theranostic Imaging of NET

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Purpose: Somatostatin receptor scintigraphy (SRS) is an essential step in neuroendocrine tumors (NETs) theranostics, tailoring the eligibility for Peptide Receptor Radionuclide Therapy. Precise tumor quantification could be essential for a personalized therapeutic approach. The present study aims to analyze different quantitative processing methods to be chosen for the next steps of a prospective PhD NETs SPECT/CT SRS versus PET/MRI research. **Material & Method:** 72 prospectively acquired NETs patients SRS images were qualitatively and quantitatively assessed for biodistribution pattern and pathological uptakes. Each patient received a 10.57 MBq/kg bw ^{99m}Tc Tektrotyd dose, prepared from Polatom Tektrotyd kits. Radiolabeling efficiency was assessed using instant thin layer chromatography (ITLC). **Study design:** Early dynamic (60 images, 1 image/second, 128x128 matrix, Zoom 1) acquisition, static (10 minutes/image, 256x256 matrix, Zoom 1), whole body (WB) and SPECT images were acquired at 10 minutes, 2, 4 and 24 hours. Regions of interest (ROI) for each hot area (either pathological or suspected artifact) were defined, uptake was quantified (counts/pixel) and indices were calculated: I_1 =tumor/liver, I_2 =tumor/spleen, I_3 =tumor/lung, I_4 =tumor/right thigh, both for maximum and mean values. Uptake kinetics graphs for all indices were compared and

are presented, as well as tumor heterogeneity graphs. Statistical correlations were calculated to decide best indices. **Results:** Radiochemical efficiency exceeded 98% in all cases. A homogeneous pattern was found in 91.6% tumor ROIs. The uptake indices (for maximum values) with lower variability were I_1 and I_2 , respectively I_1 : 0.51-3.61 (mean 1.58, variance 1.09), I_2 : 0.47-4.54 (mean 1.56, variance 1.18), I_3 : 1.41-19.47 (mean 5.799, variance 25.32) and I_4 : 2.33-23.42 (mean 8.62, variance 45.2). A strong, statistical significant, Spearman (rho) correlation between tumor and spleen uptake index I_2 was found, with R being 0.8123, p-value 1E-05, suggesting that this could be the index of choice for further studies, especially in the case of extensive liver metastasis; Kendall (tau) coefficient was 0.6174, p-value 0.0001. For I_3 and I_4 , the values were not statistically significant correlated. Different biodistribution patterns were observed related to the patient physiology and/or preparation protocol for the examination (liquid diet and laxatives before the examination exclude colon elimination artifacts but may result in gallbladder intense hot spot artifact; administration of a cholecystokinetic could be helpful in differential diagnosis but requires checking on 24-hours images). **Conclusions:** Best suited indices, from our study, seem to be tumor/spleen and tumor/liver. Heterogeneity graphs and uptake kinetics follow-up to 24 hours could be useful in artifact differential diagnosis.

EP-0009

Optimisation of Analysis of [^{18}F]FMISO Uptake in IPF

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Aim: It is important to find a method to measure disease progression and therapy effects in IPF patients. For this purpose, we have investigated the use of the hypoxia tracer [^{18}F]FMISO, which has previously mainly been used in tumour studies. We compared various quantification methods, based on static or dynamic PET data. **Materials and Methods:** PET/CT data were acquired as dynamic studies split into three scans; one 20-30 min scan starting at the time of injection, and two 15-30 min scans starting 100 and 200 min after injection, respectively. Volumes-of-interest (VOIs) were defined for diseased (IPF-D) and normal appearing (IPF-N) lung regions in the IPF patients (N=10) and also in non-diseased lung regions of patients with lung tumours for comparison (CTR-N) (N=5). Tumour VOIs were also defined (CTR-T). SUV values were obtained from the last scan for each patient, with and without air-fraction correction (AFC). The full dynamic data sets were analysed using the Patlak method (PL) as well as compartmental modelling (CM). The PL analysis was performed using data acquired after 15 and after 100 min. The CM analysis was done using models with 2 and 3 tissue-compartment (TCs). Four kinetic analysis methods were applied to dynamic data including correction for tissue blood

volume (V_p), with and without AFC, and results were compared. **Results:** There were statistically significant differences in SUV ($p < 0.01$) between the three groups (IPF-D, IPF-N, CTR-N) before AFC, but not after. We compared K_i values (representing tissue uptake rate) from PL and CM analysis, resulting in R^2 values of 0.329 (PL-100 vs. 2TC), 0.816 (PL-15 vs. 2TC) and 0.924 (PL-15 vs. 3TC). The k_s values (representing irreversible binding rate) for the IPF patients appeared to be biased due to the non-negativity constraint. We therefore derived corresponding values (k_s^*) based on the PL-derived K_i values, to allow for negative values. The k_s^* values [min^{-1}] for each group were: -0.0001 ± 0.0015 (IPF-D), -0.0002 ± 0.0018 (IPF-N) and 0.0020 ± 0.0013 (CTR-N). There was no significant difference in k_s^* values with and without AFC. **Conclusions:** The difference in SUV values, observed between different groups when AFC was not applied, was due to the difference in lung density. The most appropriate analysis methods for the dynamic [^{18}F]FMISO lung data were the 15-min PL and the 3TC CM. Our chosen outcome parameter was k_s^* , which is independent of blood-flow, blood volume and air-fraction, and is not biased due to the non-negativity constraint.

EP-0010

Validation of a fully automated atlas based segmentation tool for bone scintigraphy

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Purpose/Introduction: Bone scintigraphy continues to be widely used in the routine evaluation of malignant and benign disease. However, it is often seen as a qualitative (visual) measure of osteoblastic activity. Automated methods may help physicians to quantify and classify bone lesions. This implies automated identification/segmentation of anatomical bone structures. Our aim is to develop an automated and accurate segmentation tool for bone structures. **Subjects & Methods:** We propose an automated bone segmentation methodology that can be divided into two main steps: (1) the bone scintigraphy is spatially aligned with a normal template/atlas previously built from a normal database; (2) the consequent geometrical transformation is inverted and applied to the atlas segmentation to obtain the entire patient skeletal components segmentation. To test this approach, we randomly and sequentially selected 32 bone scintigraphies (16 male and 16 female patients). All images were manually segmented twice by three experienced observers (obs 1, 2, 3) and automatically segmented using the proposed computational solution. We considered axial (skull and spine) and appendicular (humerus, scapula, pelvis and femurs) skeleton separately. To compare the segmentation agreement the Dice's coefficient (DC) was used to measure the "proportion of overlapping". **Results:** In the axial skeleton, inter-observers DC averages were 0.934 (1vs2), 0.929 (1vs3) and 0.936 (2vs3); compared to automated solution, the averages were 0.944 (obs1), 0.951 (obs2) and 0.942 (obs3). In the appendicular skeleton the DC averages were respectively 0.893 (1vs2), 0.881 (1vs3), 0.895

(2vs3) between observers; and 0.894 (obs1), 0.906 (obs2), 0.893 (obs3) between observers and automated solution. In the axial skeleton, the intra-observer DC averages were 0.947, 0.949 and 0.932; and in the appendicular skeleton were 0.911, 0.923 and 0.905, respectively for observers 1, 2, 3. Inter-observers DC were very high, both in axial and appendicular skeleton. In the axial skeleton, inter-observers DC were slightly higher between the observers and the automated solution than between the three observers. In the appendicular skeleton, only in one case the DC was slightly higher between observers than between observers and automated solution. Intra-observers DC were very high in all cases. **Discussion/Conclusion:** Our proposed automated solution is, at least, as accurate as experienced observers for segmentation, with no intra-observer variability. This automated segmentation tool automatically identifies skeleton structures and may contribute to computer-aided diagnostic methodologies. **Financial support:** This work is supported by the project LISBOA/NORTE-01-0247-FEDER-017685, from PORTUGAL2020.

EP-0011

Y-90 PET radiomics modeling analysis for response prediction within hours of radioembolization in liver cancer patients

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Aim: Evaluate if lesion radiomics characteristics extracted from post-therapy Y-90 PET can predict lesion response in radioembolization of liver cancer patients. Robust tools for early outcome prediction can potentially be used to guide clinical decisions, for example, external beam radiotherapy boosting of lesions that may have a poor prognosis after Y-90. **Methods:** First, Y-90 PET/CT phantom studies were performed to establish the robustness of the different radiomics features. In 20 patients with primary and metastatic liver lesions, Y-90 PET/CT was performed within few hours of radioembolization with glass microspheres. Time-of-flight PET/CT reconstruction parameters were optimized based on Y-90 phantom studies and included 1 iteration 21 subsets of OS-EM with resolution recovery. Seventy-two lesions were outlined on baseline CT or MRI by a radiologist and transformed to co-registered Y-90 PET/CT. Lesion specific categorization as responding (CR, PR) and non-responding (PD, SD) at 3 months follow-up was determined according to RECIST (available for all 72 lesions) criteria and mRECIST (available for 31/72 lesions) criteria. PET images were input to an in-house developed (Matlab) radiomics toolbox, that runs as an extension on a commercial system, to extract 44 features (quantifying lesion first-order (global) and second-order (textures) histogram statistics). PET images with and without pre-processing of dynamic range correction with square-root transformation was evaluated. Radiomics model was based on multivariate logistic regression with shrinkage regularization (LASSO). Nested 5-folds cross-validation and bootstrapping were used for optimal parameter/feature selection and guarding against overfitting risks. The area under the receiver-operating characteristics curve (AUC) was used to analyze feature associations and assess radiomics model predictive power. **Results:** Despite relative poor

quality of Y-90 PET compared to FDG-PET, repeated acquisitions and changes in reconstruction parameters demonstrated that most features are reproducible and robust (COV < 20% for 31/44 features) in our phantom analysis. In patients, lesion specific response rate as assessed by RECIST was 25% and mRECIST 41%. The radiomics features showed more stability post square-root transformation. The modified LASSO model identified three relevant lesion radiomics features (global: [variance, skewness] and texture: [small zones emphasis]), with lesions presenting more heterogeneous PET uptake exposed to higher risk of failure. The resulting model achieved an AUC of 0.714 (95%CI: 0.705–0.723) with RECIST and 0.736 (95%CI: 0.730–0.742) with mRECIST on bootstrap resampling. **Conclusion:** Results demonstrate the potential of using radiomics, derived from PET within a couple of hours after radioembolization, for clinical prognosis. These encouraging results must be confirmed with larger datasets.

EP-0012

The Potential for Quantitative SPECT of ^{223}Ra - A Monte Carlo Study

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Purpose: The aim of this study is to investigate the potential for and limitation of activity quantification of ^{223}Ra using SPECT.

Subjects and Methods: The SIMIND Monte Carlo program was used to simulate essentially noise-free gamma-camera projections (20 % energy window centred at 82 keV) using a MEGP collimator. Two sets of geometries were considered; one consisting of single spheres (0.6 mL to 120 mL) centrally in an elliptical phantom and one using an anthropomorphic computer phantom (XCAT) with three inserted spheres (34 mL, 70 mL and 100 mL). Sixty projections were simulated over a full rotation (128×128 matrices) and scaled to an acquisition time of 55 s per projection before Poisson-distributed noise was added. The spheres in the elliptical phantom were set to contain 1 MBq of ^{223}Ra (in equilibrium with its daughters) and 10 noise realisations were performed for each image. For the anthropomorphic phantom, the activity concentration was varied between 0.5 kBq/mL, 1 kBq/mL, 2 kBq/mL and 4 kBq/mL without activity in the background and with activity in the background (large intestine and skeleton, total activity 4.2 MBq in phantom), with 5 noise realisations each. Also the essentially noise-free projections were considered. Reconstruction was performed using OS-EM (40 iterations, 10 angles per subset) with compensation for attenuation, scatter (ESSE) and collimator response (including septal penetration). The activity concentrations in the spheres were estimated for the various geometries using VOIs encompassing the whole spheres and compared with the activity concentrations defined in the simulation. **Results:** The recovery for spheres in an elliptical phantom was (mean±SD) 0.90±0.01 for the 22 mL sphere and reached 0.96±0.02 for 120 mL. For the background-free XCAT phantom, the recovery was 0.71±0.07, 0.86±0.14 and 0.82±0.05 for 34 mL, 70 mL and 100 mL, respectively, for an activity concentration of 0.5 kBq/mL. The

corresponding numbers for 4 kBq/mL were 0.83±0.08, 0.88±0.03 and 0.90±0.02. For noise-free projections, the recovery was consistently higher with values of 0.90, 0.93 and 0.94. When adding background, the recovery decreased further for the spheres with low activity concentration, being 0.66±0.24, 0.73±0.09 and 0.76±0.06 for the concentration 0.5 kBq/mL, while for the highest concentration studied (4 kBq/mL) the results were almost equivalent with the no-background case. **Conclusions:** Estimation of ^{223}Ra concentration works well for high activity concentrations, but further development is needed for reliable activity estimation at lower activity concentrations with respect to both bias and repeatability.

EP-0013

Automated segmentation of [F-18]FET-PET/CT brain images: The impact of non-brain tissues

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Aim: In most of the [F-18]fluoro-ethyl-L-tyrosine positron emission tomography (FET-PET) brain images, non-brain tissues such as skin have intensities overlapping with intensities of tumor tissues. Thus, for better delineation of the tumor, non-brain tissues should be removed before segmentation. In our study, we compared automated segmentation results of FET-PET brain images with and without non-brain tissues. **Materials and Methods:** A mean activity of (186±7) MBq of [F-18]FET was injected intravenously into eight patients with brain tumors. Dynamic [F-18]FET-PET measurements were performed for 45 min in list mode. To separate the brain from the computed tomography (CT) images, a method based on combining expectation/maximization segmentation and mathematical morphology was used. The resulting binary mask was then successfully aligned and multiplied by the PET images frame by frame to isolate the brain within the PET data. Both FET-PET images with and without non-brain tissues were segmented using the k-means clustering algorithm. Because k-means needs to specify the number of clusters in advance, WB-index was utilized to determine the optimal number of clusters automatically. Finally, the optimal number of clusters for 300 slices of 8 patients before and after brain extraction were evaluated and tested for significance with the McNemar's test. A level of significance of p<0.05 was applied. **Results:** For the optimal number of clusters, a significant difference between the images with and without non-brain tissues was found (p=0.005). The WB-index suggested different optimal number of clusters for 167/300 slices and thus different time activity curves before and after brain extraction. In 107/167 slices the optimal number of clusters was decreased after removing the non-brain tissues. For the 133 slices with the same optimal number of clusters before and after removing the non-brain tissues, in nearly 100% of these cases, the partitioning of clusters and time activity curves differ. The calculation load was reduced by a factor of 0.3 to 0.5,

because after removing the non-brain tissues the number of voxels per slice was decreased. **Conclusion:** Segmentation of dynamic [F-18]FET-PET brain images is impacted by non-brain tissues. Differences in tumor delineation were found between images with and without non-brain tissues. Therefore, to obtain relevant and accurate segmentation results, brain extraction as a preprocessing step is desirable.

EP-0014

Proton treatment plan accuracy verification with off-line PET/CT on PMMA phantom

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Purpose: To verify the proton therapy accuracy, PET/CT image is usually used as an approach for supervising. In this research an accuracy evaluation process based on Monte Carlo is constructed. Treatment plan is simulated to generate a prediction PET image and compared with measurement PET on depth and lateral profile. The consistency of the treatment plan and execution will be evaluated by calculating the depth and lateral position error. This comparing process will be constructed to evaluate the treatment accuracy in single beam irradiation.

Method: Irradiation is operated on PMMA (C₅H₈O₂) phantom, this phantom is a transparent and homogeneous cube with size 20*20*30cm³. There are 2 dose groups of 2Gy and 4Gy, each dose group have 7 dose depths from 5cm to 20cm step by 2.5cm, the radiation field is 5*5cm². The irradiation time is 1-2 minutes, cooling time after irradiation is set as 10 minutes, PET signal is acquired by Biograph mCT device from Siemens, the acquisition time is 30 minutes, and image reconstructed by 2D-OSEM algorithm. Prediction and measurement PET distribution are compared on both depth and lateral profile. In depth profile position verifying, 272 points are sampled inside the radiation field, each sample point can get a pair of PET-depth curve, find out the position of 50% maximum on curve distal fall off edge, and then comparing the position error of prediction and measurement PET. For all the sampling position error, the mean error and standard deviation can be calculated. In lateral profile position verifying, scoring layers are set to different depth, on each layer there are two 50% contours for lateral profile, the position error of the contours can be sampled uniformly along the border of radiation field. Totally 66 points are sampled on a layer, and the mean position error of a layer is calculated. The location of scoring layers set start from 2.5cm depth, end at the dose central depth, step by 2.5cm. Average all the lateral error on all the scoring layers, then get a global lateral error for one irradiation case, **Results:** depth and lateral error for dose group of both 2Gy and 4Gy are no more than 1mm. **Conclusion:** The prediction PET distribution and measurement PET distribution have a depth error smaller than 1mm, and lateral error smaller

than 1mm. The comparing method in this research can be used to evaluate accuracy of proton radiotherapy plan.

EP-0015

May Texture Parameters Derived from Baseline Fluorine-18 Methyl-Choline PET-CT Be Expression of Biological Features of Prostate Cancer?

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Introduction: Fluorine-18 methyl-choline (¹⁸F-Choline) PET-CT plays a central role in staging, restaging and monitoring treatment in patients with prostate cancer (PC). The use of texture analysis in nuclear medicine may be promising in predicting tumor aggressiveness, response to treatment or disease-free survival in many neoplastic conditions. Aim of our study was to investigate the relationship between histopathology or laboratory features of PC patients at the initial diagnosis and texture-analysis derived parameters at baseline ¹⁸F-Choline PET-CT.

Subjects and Methods: A retrospective analysis was performed on a sample of 25 patients with PC who underwent ¹⁸F-Choline PET-CT for initial staging, exclusively before treatment, between June 2016 and February 2018. All included patients showed Gleason scores (GS) ≥6 at diagnosis; baseline prostate-specific antigen (PSA) values were collected from all patients. Patients were further divided into two groups according to GS≤7 (n=6, group 1) or GS>7 (n=19, group 2). Median PSA was 10.66 ng/ml (range 7-174). Whole prostate volume was delineated by drawing a VOI using LifeX Software® (www.lifexsoft.org), tested for reliability, and then several PET parameters were extracted: intensity (SUVmean, SUVmax, SUVpeak) and advanced texture analysis (i.e. entropy, homogeneity, SRE, LRE, LGZE, HGZE) parameters. Results were correlated with patients' GS and PSA. **Results:** Among all the intensity and textural features tested, three advanced texture parameters significantly differed between the two groups according to GS: Short-Zone Emphasis_{GLZLM} (GLZLM_SZE; *p*=0.037), Grey Level Non Uniformity for Zone_{GLZLM} (GLZLM_GLNUz; *p*=0.037) and Zone Length Non-Uniformity_{GLZLM} (GLZLM_ZLNU; *p*=0.018). Particularly, median GLZLM_SZE was 0.62 [interquartile range (IQR) 0.59-0.69] for GS≤7 and 0.58 (IQR 0.55-0.60) for GS>7; median GLZLM_GLNUz was 23.62 (IQR 14.47-113.57) for GS≤7 and 9.54 (IQR 5.37-12.89) for GS>7; median GLZLM_ZLNU was 271.41 (IQR 76.38-476.84) for GS≤7 and 46.30 (IQR 21.90-72.41) for GS>7. Those parameters tended to be lower when GS>7. Neither intensity nor texture indices were linearly correlated with PSA values. **Conclusion:** Although preliminary, our data suggest some texture parameters may be expression of the tumor differentiation grade according to the Gleason Scoring; conversely, conventional intensity parameters were not effective in depicting the tumor biology. Therefore, texture-analysis derived parameters may be more predictive than conventional intensity ones in stratifying PC aggressiveness. Further investigations are required to validate these results and to relate them with the tumor prognosis.

EP-0016

Automatic Segmentation of Respiratory Gated PET

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Background: There is an ongoing interest in integrating 4D PET data into radiotherapy treatment planning. To date numerous techniques have been developed for segmenting 3D PET images. One approach to tumour delineation of 4D PET is to independently apply such a segmentation algorithm to each 3D frame in turn. Alternatively if it were assumed that the size of the tumour is consistent across all phases of the respiratory cycle then it may be possible to make use of all data to inform the delineation process at each stage of the respiratory cycle. It was hypothesised that doing so would result in a more accurate delineation. The fuzzy logic adaptive Bayesian (FLAB) technique uses a statistical model of tumour and background voxel populations to classify voxels appropriately [1]. The algorithm iteratively determines an underlying prior probability model of voxel classification, parameters characterising the distribution of voxel values for each classification, and ultimately the most likely classification of each voxel. **Methods:** The FLAB algorithm was extended to the case of 4D PET data. In brief, a volume of interest (VOI) was manually defined to encompass the tumour and surrounding background on each frame. The VOI contents were registered to a common frame of reference. Within an iterative loop of the algorithm each individual 3D frame was treated as a subset of the full data. An underlying prior probability model applicable to all frames was updated after consideration of each frame. The algorithm was tested on images of a NEMA IQ phantom filled with 50MBq ¹⁸F and mounted on a QUASAR respiratory motion platform. Data were acquired for 5 minutes over a single bed position and reconstructed into 10 frames over the respiratory cycle. Segmentation was performed on spheres ranging from 17–37mm diameter using both 4D and 3D FLAB. Volume accuracy, sensitivity and positive predictive value were assessed. **Results:** The algorithm was developed and found to converge to a solution. Volume accuracy and sensitivity were in general greater for 4D FLAB in comparison to sequential application of 3D FLAB but not significantly so. The positive predictive value of the segmentation was not improved. **Conclusion:** An existing segmentation algorithm has been extended specifically to segment 4D PET data with no user interaction following an initial identification of the tumour. **References:** 1. Hatt M et al. A fuzzy locally adaptive Bayesian segmentation approach for volume determination in PET. *IEEE Trans Med Imaging*. 2009;28:881–93.

EP-0017

Comparison of the reproducibility of two suitable validity indices for [F-18]FET-PET brain images

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Aim: Clustering is widely used in automated medical image segmentation. The quality of clusters generated by a clustering algorithm is assessed with different cluster validity techniques. Therefore, several clustering validity indices have been proposed. In this study, we compared I and WB indices, two indices suitable for [F-18]fluoro-ethyl-L-tyrosine positron emission tomography ([F-18]FET-PET), with regard to the ability of the indices to reproduce the same clusters after removing one cluster from the data. **Materials and Methods:** The k-means clustering algorithm was applied to dynamic [F-18]FET-PET brain images of eight patients. Because the number of clusters must be predefined for the k-means algorithm, WB and I cluster validity indices were utilized to determine the optimal number of clusters automatically. From the optimal clusters, one cluster was removed and k-means was applied for the remaining data to examine the ability of the indices to reproduce the same clusters after removing one cluster. Correct reproduction (successes) was defined based on 2 features: (1) production of the expected number of clusters, and (2) less than 1 % changed voxels per cluster after removing one cluster. Successes achieved by each index were investigated slice by slice for all patients. To compare two indices with regard to the chosen optimal number of clusters, McNemar's test ($p < 0.05$) was used. **Results:** Median and ranges of suggested optimal number of the clusters for WB and I indices were 4 [3,6] and 3 [3,7] clusters, respectively. Although the optimal number of clusters given by both indices were the same for 242/400 slices, the results showed that there is a significant difference between WB and I indices ($p = 0.017$). In addition, by removing one cluster the success rates of WB were 77% and 75% for features 1 and 2, respectively, while I index was successful in 71% and 69% of cases with respect to the features 1 and 2. **Conclusion:** Significant differences in suggested optimal number of clusters were found between WB and I validity indices. WB index has a tendency to recommend higher number of clusters. Moreover, the success rates showed that the use of the WB index yields a higher reproducibility.

EP-0018

Radiomics based analysis of prostate cancer's osseous tumour burden assessed by [¹⁸F]-PSMA-1007 and [⁶⁸Ga]-PSMA-11 PET/CT

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Introduction: Prostate cancer is the most frequent cancer entity in men and has a remarkably early tendency of spreading cells to other organs, especially bone and bone marrow. Up to 70 % of patients undergoing prostatectomy surgery after diagnosis exhibit disseminated tumour cells in the bone marrow. To improve patients' treatment regimes, there is an urgent clinical need to predate the detection of bone lesions, by revealing premetastatic patterns rather than just fully-grown metastases.

We regard premetastatic patterns as intraosseous aggregations of tumour cells, which are not revealed to the naked eye, but can potentially be detected by advanced image analysis methods. In the presenting study, we have developed a novel algorithm capable of assessing intra osseous PSMA distribution. **Materials and Methods:** A total number of 52 PET CTs (25 patients scanned with [^{68}Ga]-PSMA-11, 27 patients with [^{18}F]-PSMA-1007) were retrospectively analysed. Nuclear medicine and radiology specialists performed a consensus reading, classifying the scans in two subgroups: one with bone lesions, the other one without serving as controls. The algorithm drives a bone mask from the CT images (i), applies it to the co-registered PET data excluding non-bone information (ii) and finally calculates conventional and radiomic parameters (iii) in an automated way. Radiomic parameters are obtained using the Grey Level Occurrence Matrix (GLCM) and normalization steps coping for intra-individual differences of tracer distribution, that are not cause by tumour formations. **Results:** Non-metastatic bone's SUV did not significantly ($p > 0.05$) differ between [^{18}F]-PSMA-1007 (mean-SUV: 0.19) and [^{68}Ga]-PSMA-11 (mean-SUV: 0.18). Bone SUV did not significantly differ between controls scanned with either [^{18}F]-PSMA-1007 (mean-SUV: 0.16) or [^{68}Ga]-PSMA-11 (mean-SUV: 0.14). For [^{18}F]-PSMA-1007, bone PSMA heterogeneity was significantly greater ($p < 0.05$) in the bone lesion group (mean: 142.19), compared to controls (mean: 133.16). The same was true for [^{68}Ga]-PSMA-11 (controls: 131.65, bone lesions: 148.55, $p < 0.05$). Controls' bone heterogeneity was not significantly different ($p > 0.05$) between [^{18}F]-PSMA-1007 and [^{68}Ga]-PSMA-11. **Conclusion:** In this study we could demonstrate that [^{18}F]-PSMA-1007 and [^{68}Ga]-PSMA-11 PET-CT are equally suitable for the assessment of bone metastasis. Additionally we could show that intra osseous PSMA heterogeneity enables the detection of bone metastases. Moreover, PSMA heterogeneity is independent of the tracer choice ([^{18}F]-PSMA-1007 or [^{68}Ga]-PSMA-11) and thereby potentially suitable for the detection of premetastatic patterns, which still has to be evaluated.

EP-0019

Automating DICOM retrieve from PACS with free and open-source software

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Aim: To automatize the retrieve process of DICOM images to automatically download a large population of patients for research needs. **Material and Methods:** The free and open-source Orthanc PACS software was used to handle query and retrieve operations. A standalone application was developed in the JAVA language to drive the Orthanc server using its RESful API. The developed software handles: Definition of the list of patients: Each patient can be defined by providing one or multiple search attributes (name, ID, accession number, study date, modality, study

description). The software can provide the matching results in the PACS before starting the retrieve operation, to fine-tune the retrieve list. Definition of a series filter: For each study found, additional series filters can be set to download only specific series (filter to retrieve or exclude some specific series description/number or modality). Scheduling option to start the retrieve operation during the night when the network bandwidth usage is lower. Report generation of the retrieve operation with summary of all retrieved elements (in the interface and/or in CSV). The full software is available for all operating system (Windows, MacOS or GNU/Linux) and published using the free and open-source GPL license with step by step documentation, as part of project <http://petctviewer.org/>. **Results:** The Orthanc-server was installed and declared in the PACS by a physician with the help of the network manager of the hospital in Dijon (France), in just one afternoon, using the provided user manual. The developed plugin did not require any additional installation in the operating system. The testing operation was made by setting a patient list of 108 patients (defined by the first letter of last name and first name and the study date). A series filter (using series description value) was used to download only PET and CT series (i.e. discarding secondary captures, dose reports...). The operation was scheduled to start at 10pm, outside of working hours. The automatic retrieve process successfully downloaded 102 out of 108 patients. All downloaded patients were complete without any unwanted series. The 6 missing patients were due to erroneous input (wrong study date in the search parameter) or unattended series description: They were all retrieved with a second call with corrected input. **Conclusion:** This free and open-source tool allows the automatic mass retrieval of DICOM studies, hereby saving physicians and physicists from performing multiple manual query/retrieve.

EP-0020

Validation of GATE Monte Carlo simulations for Siemens PET/CT and PET/MR systems

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Aim: The objective of this work is to validate a Monte Carlo (MC) simulation model for two commercially-available, whole-body PET systems. The MC models will be used in future to evaluate the performance of different image reconstruction methodologies at low acquired counts. **Material and Methods:** GATE (GEANT4 Application for Tomographic Emission) was used as the MC toolkit for the modeling of the Siemens Biograph 64 TruePoint TrueView (TPTV) PET/CT and the Siemens Biograph mMR PET/MR (mMR) systems. In both cases, we included detailed models of the detector electronics, system geometry and the physical processes involved in the data acquisition. The performance of both system models was validated following the NEMA (National Electrical Manufacturers Association) NU 2-2012 protocol. We compared the simulation results with the measured values for sensitivity, count rate, and noise equivalent count rate (NECR). **Results:** The calculated (reference value from measurements) sensitivity for the mMR was 13.8 (15.0) kcps/MBq and 14.4 (13.9)

kcps/MBq at the center of the field-of-view and at 10 cm radial offset, respectively. The NECR peak was 178 kcps @ 23.8 kBq/ml (184 kcps @ 23.0 kBq/ml) and the scatter fraction at the NECR peak was 38.5 (37.9) %. For the TPTV, the sensitivity was 8.0 (8.1) kcps/MBq and 7.9 (8.2) kcps/MBq at the centre of FOV and at 10 cm radial offset, respectively. The NECR peak was 151 kcps @ 27 kBq/ml (161 kcps @ 31 kBq/ml) and the scatter fraction at the NECR peak was 24.8 (32.5) %. **Conclusion:** Both PET/CT and PET/MRI models showed a good accordance (< 10 %) with the measured reference values. The application of these models for the evaluation of different image reconstruction algorithms in simulated numerical phantoms is work in progress. **Acknowledgments:** The financial support of the Austrian FWF Project I3451-N32 is gratefully acknowledged.

EP-0021

Automating de-identification and sharing DICOMs with a free and open-source software

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Aim: To build a free and open-source software to automate the mass de-identification of datasets of patients, taking into account the specificities of PET/CT. **Material and Methods:** The free and open-source Orthanc PACS software was used to handle DICOM network communications and to de-identify patients/studies and series following the NEMA 2017c guideline with fine-tunable options through the RESTful API of Orthanc. A standalone application was developed in the JAVA language to drive the Orthanc server using its RESTful API to de-identify DICOM files respecting constraints of PET images, as part of project <http://petctviewer.org/>. The developed software handles: Single or batch de-identification of studies. Manual or automatic definition of de-identified names and/or IDs. De-identification profile adapted to PET series (retaining patient's weight, height, acquisition time, injection time, injected dose) or following the full NEMA guideline (for CT, MRI...). Recognition and automatic removal of secondary capture images (to avoid patient identification hardprinted in the pixels of some image). Local download of de-identified studies (ZIP) and remote sharing service with FTP, SFTP or WebDAV protocol. Report generation about the de-identification process (retracing original identity and de-identified key). **Results:** The Orthanc server was installed and declared in the PACS by a physician with the help of the network manager of the hospital in Dijon (France), in just one afternoon, using the provided user manual. The de-identification software is provided as a standalone executable tool with no installation requirement. The anonymization feature was successfully tested with up to 80 PET/CT studies in a single anonymization procedure. De-identified patients were sent to a third center (located in Nice) using a private ownCloud server (WebDAV protocol)

from the same anonymization software. All de-identified studies were successfully read (preserving SUV values), both on commercial and on open-source workstations. **Conclusion:** A free and open-source software is available for mass DICOM de-identification and sharing of PET/CT images. This package is provided as part of the free and open source PET/CT viewer project (<http://petctviewer.org/>)

EP-0022

41% of SUVmax threshold is highly reproducible even if obtained with different software for PET/CT segmentation

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Purpose/introduction: The aim of this work was to compare the variability in measuring the Metabolic Tumour Volume (MTV) of known lesions obtained with 4 different software (SW) for PET segmentation. **Subjects & Methods:** MTV of 24 known lesions were analysed by the same imaging expert with 4 SW: ROVER (ABX GmbH), LifeX (Universite Paris-Saclay), Fiji (petctviewer.org) and MIM (MIM software Inc.) For each lesion three different segmentation algorithm were used: 41% of SUVmax (PER), 2.5 SUV (FIX) and the proprietary segmentation algorithm (PSA). Each MTV was normalised to the average of the four SW and is reported as mean±standard deviation and range. **Results:** MTV for PER were: ROVER (0.99±0.04, range: 0.90-1.05); LifeX (0.99±0.03, range: 0.93-1.06); Fiji (1.02±0.04, range: 0.93-1.14); MIM (1.00±0.03, range: 0.92-1.06). MTV for FIX were: ROVER (1.15±0.38, range: 0.66-2.30); LifeX (0.92±0.21, range: 0.35-1.40); Fiji (0.93±0.27, range: 0.26-1.40); MIM (1.00±0.33, range: 0.22-2.23). MTV for PSA were: ROVER (Adaptive Threshold) (0.74±0.14, range: 0.30-0.98); LifeX (NESTLE Algorithm) (0.93±0.21, range: 0.34-1.30); MIM (Gradient Threshold): (1.33±0.31, range: 0.90-2.23). The mean, median, standard deviation e range of all MTV, expressed in cc, were (61.67±82.64, median: 20.26 range: 4.76-291.61), (145.97±174.26, median: 72.12 range: 6.24-719.10) and (73.10±91.59, median: 28.57 range: 5.21-325.18) for PER, FIX and PSA respectively. **Discussion/Conclusion:** PER is a robust and reproducible procedure to evaluate the MTV of PET-CT lesion even if using different software with variability below 10%. The FIX showed a high variability related to the positioning and shape of the initial VOI used for segmentation. The PSA showed a great variability related to the different segmentation algorithm emphasising the fact that different PSA are not inter-changeable. MTV measured with PER are systematically lower than with FIX.

EP-0023

A new denoised deconvolution analysis in ^{99m}Tc Mag3 renography

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Aim: To obtain the relative kidney uptake and renal transit times thanks to a new deconvolution process of noisy renal time activity curves. **Material and Methods:** The method relies on a

previous work of fitting and filtering noisy renogram curves with Legendre polynomials (LP). The mathematical background consists of a convolution of a LP matrix of unknown coefficients with a measured input function (IF). IF was obtained using a region of interest drawn over the heart or the distal aorta near the iliac bifurcation. The deconvolution operation gave the transit curve (TC). After trimming, a plateau was determined at the initial part of the TC curve to obtain the relative renal uptake information. Minimum (MinTT), maximum (MaxTT) and mean (MTT) transit times were also computed. We used a renal database (<http://www.dynamicrenalstudy.org>) which contains Monte-Carlo (MC) simulated studies and real patients' data. The MC studies provided Gold Standard with different levels of injected activity, renal clearance and noise in the anterior and posterior views. The new method was compared to the conventional matrix method implemented in a commercial software (Hermes) and to the Fourier deconvolution after preprocessing the IF and the renal curves with the Legendre method mentioned above. **Results:** A perfect agreement, demonstrating the correct removal of the vascular contribution, was observed between the measure of the uptake and its ground-truth values for the MC gold standard datasets. In particular an excellent stability with respect to the level of noise in the images was observed for the Legendre method. For the rest of the studies (comprising MC and patient data), slope (R^2) of the linear regression between the new method and Hermes output was for example: 0.82 (0.96) for uptake, and 0.71 (0.72) for MTT. Furthermore Mean (SD) for the Bland-Altman analysis was: -0.15 (0.51) for the MTT. Similar results were observed for the Fourier deconvolution after preprocessing of the curves with the Legendre method versus the matrix method in Hermes. **Conclusion:** The Legendre deconvolution method directly provides smooth renal transit curves and therefore facilitates the computation of the transit and uptake parameters that reveal much less sensitive to noise in the data compared to the usual matrix deconvolution. Furthermore, the analysis can be applied regionally on kidney.

EP-02

e-Poster Area

Physics: Neurology - Data Analysis & Quantification

EP-0024

Error propagation properties of 5 partial volume correction algorithms for [18 F]THK5351 PET imaging

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Aim: Partial volume correction (PVC) improves the quantification of brain PET images in ideal situations. Error propagation (EP), however, while often seen in clinical situations, have not been fully investigated. Therefore, we evaluated EP properties (EPPs) of 5 PVCs such as Müller-Gärtner (MG), Labbé (LABBE), Geometric transfer matrix (GTM), Regional voxel-based (RBV) and Iterative Yang (IY). **Materials and Methods:** Simulated PET images of [18 F]THK5351 were generated based on anatomical and binding data from real MRI and PET images of a healthy control (HC) and an Alzheimer's disease (AD) patient. Two simulated PET images (HC and AD) of 7.0 mm FWHM resolution were reconstructed with FBP3D. To evaluate EP due to mismatches of PVC-conditions, errors in FWHM, registration and segmentation of prior anatomical data were included into the PVC processing. FWHM and registration errors between PET and anatomical images in the axial, and segmentation-error of hippocampal volume for only HC were set from 4.0 to 8.0 mm, -7.3 to 7.3 mm, and -50.0% to 70.0%, respectively. For all error conditions and PVCs, the percent difference (%diff) of PVC-corrected SUVR against the true (PVC-SUVR) were calculated in hippocampus, whose % diff of uncorrected SUVR (AD) against the true was -53.5%, parahippocampal gyrus, and cortices structures such as temporal, occipital and parietal regions. Finally, these EPPs were compared across PVCs and regions. **Results:** In case of 1 mm underestimation of FWHM (6.0 mm), %diff of hippocampal PVC-SUVR (AD) in all PVCs were less than -9.4%, and %diff of parahippocampal PVC-SUVR (AD) in MG was the worst performing PVC technique across all regions. %diff of PVC-SUVR in GTM was similar to those in RBV and IY for all conditions of FWHM error and subjects. For -2.4 mm global shift, %diff of hippocampal PVC-SUVR (AD) by MG, LABBE, GTM, RBV and IY were -20.2%, -19.6%, -28.7%, -29.3% and -29.7%, respectively. Even though registration error was small, the error caused large %diff of PVC-SUVRs in all conditions and PVCs. For all PVCs, segmentation error also influenced hippocampal PVC-SUVRs but had little effect on other regions. In case of -30.0% segmentation-error, %diff of hippocampal PVC-SUVR by MG, LABBE, GTM, RBV and IY were 9.1%, 11.7%, 10.2%, 10.2% and 10.2%. **Conclusion:** The results suggest PVC is so sensitive that even minor errors (esp. in segmentation and registration) may greatly affect SUVR, and we should be careful with image processing when performing PVC on clinical brain PET images.

EP-0025

Parent fraction estimation methods for improved dynamic [11 C]PiB PET quantification

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Aim: Reliable estimation of the metabolite corrected plasma input function is required for accurate quantification using tracer kinetic modelling. However, due to fast metabolism of [11 C]-Pittsburgh-Compound-B([11 C]PiB), estimation of the parent fraction is challenging. The aim of this study was to evaluate the performance of different approaches for estimating the parent fractions. **Materials and Methods:** Seventeen [11 C]PiB scans, including test-retest scans (n=6; 2 Alzheimer's disease patients

and 4 healthy controls) were studied. Ninety minutes dynamic [^{11}C]PiB scans were acquired with continuous arterial sampling. In addition, for each scan 3 to 7 manual samples were available at various times. Metabolite corrected plasma input functions were derived using parent fractions obtained by several different strategies (using data from the 17 PET scans):-(1) measured parent fractions(MP); (2) a population approach taking one average parent fractions for each time point(POP); (3) by fitting all subject's measured data by a double exponential as function of time for each patient; (4) parent fractions described as function of the plasma/blood ratio for each patient(PBP) and (5,6,7) using approaches 2, 3 and 4, but for morning and afternoon scans (time specific approaches) separately. The latter analyses were performed, as a difference in [^{11}C]PiB parent fractions was seen depending on time of scanning. Volume of distribution(V_T) was estimated for each input function by fitting the data using a reversible two tissue compartmental model with fitted blood volume fraction(2T4k_ V_B). To evaluate the performance of each input function, test-retest reliability(TRT) of estimated V_T was calculated for the 6 test-retest scans. Fit accuracy was evaluated using unbiased Akaike Information Criterion(AICc). **Results:** Average TRT ($\pm$ SD) of V_T for individually measured parent fractions was $-7.7\pm 10.9\%$. TRT for other implementations ranged from $1.66\pm 8.97\%$ when using POP to $37.2\pm 31.5\%$ for time specific PBP. Best performing approaches were MP ($r^2=0.75$, slope= 0.75 , intercept= 1.68 between test and retest V_T) and POP ($r^2=0.82$, slope= 0.71 , intercept= 1.47 between test and retest V_T). V_T derived from input functions using MP versus POP had a good correspondence but low correlation ($r^2=0.67$, slope= 1.00 , intercept= 0.37). Differences in AICc were negligible. **Conclusion:** Population average estimates may be used as a surrogate for measured parent fractions. Plasma-to-blood ratio based approaches did not provide reliable parent fraction estimates. Methods specific to time of scanning did not provide better TRT than POP implementation. This suggests that differences observed in the parent fractions with respect to time of scanning could be due to uncertainty or bias in the measurements.

EP-0026

Automated Striatal Analysis of ^{18}F -DOPA PET images of patients with suspected Parkinson's Disease

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Purpose: 6- ^{18}F fluoro-L-DOPA (FDOPA) is a positron-emission-tomography (PET) tracer used to assess the presynaptic dopaminergic function in patients with Parkinson's disease (PD) and in differential diagnosis of PD with essential tremor and other Parkinsonian syndromes. We have developed an automated striatal analysis application for FDOPA images and built a database of quantitative reference values for reliable and meaningful quantification of FDOPA data. **Methods:** First, a standard FDO-PA template in the Montreal-Neurological-Institute (MNI) space was generated using 30 FDOPA datasets with a range of striatal uptake. Then, striatal volumes-of-interest (VOIs) were created on

each side of the brain (caudate, anterior and posterior putamen) by smoothing and slightly enlarging the corresponding standard automated anatomical labeling (AAL) volumes to ensure complete enclosure of anatomical structures independent of residual interpatient variability after stereotactic normalization. Given a new exam, the PET-FDOPA image is first registered using a 12-parameter affine transform with the standard template followed by automatic-placement of striatal and reference VOIs on the registered PET image. Manual adjustments of VOIs' positions are allowed to minimize any residual misalignments with standard template. Regional Distribution-Volume-Ratios (DVRs) using a predefined occipital lobe region in MNI space as reference region, putamen-to-caudate ratios, and asymmetry values are automatically computed on each VOI. Note that regional mean values are computed using only the 75% of brightest voxels within each striatal VOI. A semi-quantitative slab view is also generated and displayed for optimized visual interpretation. This pipeline was used to create a database of quantitative reference values using 45 PET/CT datasets of patients with normal FDOPA scans and with no evidence of Parkinsonian neurodegeneration (at baseline and at 18month+ follow-up). We validated the generated database through classification of 23 negative and 11 positive FDOPA cases, using one quantitative parameter at a time. A scan is classified as positive if the measured parameter is 2 standard-deviations below corresponding reference value. **Results:** Optimal classification accuracy (CA) using Youden index, and area under receiver-operating-characteristic curve (AUC) were: caudate (CA= 73.5% , AUC= 0.87), putamen (94.1% , 0.96), striatum (91.2% , 0.94), anterior-putamen (91.2% , 0.94), posterior-putamen (88.2% , 0.96), putamen-to-caudate ratio (91.2% , 0.97), caudate-asymmetry (58.8% , 0.73), putamen-asymmetry (79.4% , 0.61), striatum-asymmetry (61.8% , 0.73). **Conclusion:** We developed a software solution for analysis of FDOPA striatal uptake and used it to build a database of quantitative reference values. Measured values from new subjects are automatically computed and compared to corresponding normal ranges. Further studies are needed to determine its added value to visual read.

EP-0027

Influence of [^{18}F]LBT-999 molar activity on DAT occupancy, a comparison between rodents and human subjects

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Introduction: [^{18}F]LBT-999 is a new high affinity Positron Emission Tomography (PET) radiopharmaceutical targeting dopamine transporters (DAT) with a promising potential in Parkinson disease or Lewy body dementia. Molar Activity (MA), directly impacts the Injected Mass (IM) of radiotracer, and is therefore

critical for target occupancy, particularly for PET neuroimaging studies. With this work, we evaluated the influence of [^{18}F]LBT-999 MA, on its non-displaceable Binding Potential (BP_{ND}) to DAT, in both rodents and human subjects. **Material and Method:** This work was conducted on 8 healthy human volunteers (3 men, 5 women; 53–80y; $80.0 \pm 14.2\text{kg}$) and 20 male Wistar rats ($336.2 \pm 35.9\text{g}$). [^{18}F]LBT-999 was administered intravenously and PET dynamic measurements of BP in the striatum, differentiating caudate (BPc) and putamen (BPp) in humans, were completed. The correlation between BP and both MA and IM was explored within each species with a nonparametric Spearman test. Significance was set at $p < 0.05$. **Results:** No significant difference in MA of [^{18}F]LBT-999 was found between the clinical ($63.8 \pm 73.7\text{GBq}/\mu\text{mol}$) and preclinical ($41.5 \pm 22.3\text{GBq}/\mu\text{mol}$) explorations ($p = 0.78$, Mann-Whitney test). In rats, a significant positive correlation between BP (4.4 ± 0.9) and MA was found ($r = 0.48, p = 0.03$), whereas a negative correlation between BP and IM (0.4 ± 0.1) was close to the threshold of significance ($r = -0.39, p = 0.08$). In human subjects, IM of [^{18}F]LBT-999 was $6.7 \pm 9.13\mu\text{g}$. BP values were 6.3 ± 1.07 for BPc and 6.75 ± 1.09 for BPp. No correlation was statistically significant between either of these parameters: BPc/MA, BPp/MA, BPc/IM and BPp/IM showed Spearman coefficients and p-values of $r = 0.29/p = 0.5$, $r = -0.14/p = 0.75$, $r = -0.19/p = 0.66$ and $r = 0.24/p = 0.58$, respectively. **Discussion and Conclusion:** The present study suggests an impact of the MA value of [^{18}F]LBT-999 on its BP_{ND} in the striatum of rats. The higher the MA is, the more [^{18}F]LBT-999 uptake on its target increases. In contrast, even if the knowledge and the control of MA and IM are required for precise quantification of DAT occupancy, their values don't appear critical in human exploration. This discrepancy may be related to the fact that small animals are injected with a higher quantity of [^{18}F]LBT-999, compared to their weight (IM/subject's weight is 15 times higher in rats than in human), affecting DAT binding sites availability. Knowledge and careful monitoring of [^{18}F]LBT-999 MA will be required to accurately quantify DAT expression in vivo within preclinical neuroimaging PET studies. **Acknowledgments:** This study was supported by the French National Agency for Research ("Investissements d'Avenir" no. ANR-11-LABX-0018-01), IRON and by Cyclopharma Laboratories.

EP-0028

Impact of the reconstruction method in the localization of the seizure onset by SISCOM in drug-resistant epilepsy

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Aim: The goal of neuroimaging in epilepsy is to localize the region of seizure onset. Ictal-interictal subtraction SPECT with MRI co-registration (SISCOM) has proven to be a valuable tool in localizing the epileptogenic focus. However, there is still a lack of standardization regarding SPECT images processing. The aim of

this study is to determine the clinical impact of different SPECT reconstruction parameters in this patient group. **Methods:** We retrospectively studied 15 cases (6 male, median age 37 ± 10 years). Each patient underwent an ictal and interictal SPECT, MRI, video-EEG and PET. SPECT images were acquired using a Philips Skylight SPECT/CT (Philips). Ictal injection of the radiopharmaceutical (74 MBq of $^{99\text{m}}\text{Tc-HMPAO}$) was done manually in the first 25 seconds from the beginning of the epileptic seizure. Data was processed using 12 standard reconstructions: filtered Back-Projection method (FBP) with a butterworth filter of power 6 and cutoff frequency 0.35 (BF6,0.35); OSEM with 2 iterations, 10 subsets (OSEM2,10) using BF6,0.5 or BF10,0.5; OSEM6,8 using BF6,0.5 or BF10,0.5; and OSEM8,16 with BF10,0.3. All data was reconstructed with and without Chang's attenuation correction (AC). Ictal and interictal co-registrations with MRI were performed using SPM12 and the subtraction using our in-house software (with python 3.6). SISCOM visual analysis was performed with a z-score threshold of 2. Additionally, z-scores were computed for each anatomical region from the AAL atlas. A blind review of each image was performed by an experienced neurologist. SISCOM localization was compared with the hypothesis of seizure onset obtained using the other techniques, and whenever possible, to the post-surgical evolution. Additionally, the physician selected the most visually appealing reconstruction in each case, based on lesion conspicuity and background noise. **Results:** OSEM2,10 AC with BF10,0.5 or BF6,05 or OSEM6,8 BF6,0.5 presented the most concordant results in 83% of the patients. OSEM8,16 BF10,0.3 only presented concordant results in 25% cases and FBP BF6,0.35 only in 44% cases. Chang AC improve the mean concordance of all reconstructions (73% vs 64%). OSEM2,10 AC BF6,0.5 was selected as the most visually appealing reconstruction in 85% cases. The use of AC reduces the z-score maximums (mean value 5.2 vs 4.7). Differences up to 19% were found in the variations of maximum z-scores per patient. **Conclusions:** Reconstruction parameters play an important role in the correct localization of the epileptogenic focus. According to our results, standardization is necessary to find the parameters that more precisely locate the epileptogenic focus.

EP-0029

Quantification Methods for Evaluating [^{11}C]PiB PET in Cognitively Healthy Adults

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Introduction: [^{11}C]PiB is a positron emission tomography (PET) tracer for measuring beta-amyloid (A β) plaques deposit, related to cognitive decline in both healthy aging and neurodegenerative disease. It may help researchers examine aging, disease, and pathology in living human brains. It is critical to quantify A β burden accurately and robustly to further our understanding of disease mechanisms, to develop early diagnostic techniques, and to identify suitable indicators for treatment monitoring and efficacy evaluation. **Aim:** To compare absolute and relative quantification methods for evaluating dynamic and static brain

[¹¹C]PIB PET images in cognitively healthy subjects. **Methods:** Dynamic [¹¹C]PiB PET images were acquired in 3D mode for 90 minutes following injection (38 frames: 4×15s, 8×30s, 9×1min, 2×3min, 14×5min) using a PET/CT scanner (Discovery 600, GE Healthcare). Static PET images consisted of the average from 50–70min acquisition. The area under the time-activity curves (TAC), binding potential (BP), distribution volume ratio (DVR), standard uptake value (SUV) and ratio SUV (SUVR), of hippocampus/parahippocampal gyrus (HYP), fusiform gyrus (FUS), calcarine (CAL), amygdala (AMY) and cerebellum (CER) were calculated. BP and DVR were generated using SRTM and Logan reference analysis, respectively, with cerebellar cortex as reference. Two groups of cognitively healthy subjects, separated by 2 decades, evaluated using Mini-Mental State Examination (MMSE), were studied: G50 (n=9; 52–64 years; MMSE = 29–30) and G80 (n=3; 80–91 years; MMSE = 27–28). Data extraction used AAL-merged atlas and kinetic analysis were done with PMOD software package (version 3.8) using the full set of dynamic data (0 to 90 min after injection). For statistical analysis, the Spearman correlation and non-parametric Mann Whitney test were used in SPSS package.

Results: No statistically significant was found between groups in all regions (all $p > 0.05$) for SUV, SUVR and AUC. However, mean TAC for younger healthy subjects (TAC_{G50}) was significantly different from elders (TAC_{G80}) in all regions. Uptake was significantly lower in G80 than in G50, mainly in the first 20min after injection. Significant differences between groups were found in HYP and AMY, for both BP and DVR. In FUS, a significant difference between the groups was found for DVR. However, analyses of the healthy group differences in [¹¹C]PiB uptake behavior should be interpreted as exploratory, given our limited sample size. **Conclusion:** Concluding, dynamic quantitative analysis of [¹¹C]PiB PET are more sensitive for age differences in cognitively healthy subjects. Further investigation is ongoing to evaluate this technique in a larger cognitively healthy population.

EP-0030

Amyloid Image Quantification - To Quant or not to Quant?

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Introduction: This project evaluates ¹⁸F-florbetapir (Amyvid) data in 225 patients evaluated for Alzheimer's disease. Patient classification is based on pathological levels of beta-amyloid and is assessed visually using a binary read. Software tools provide support to clinical interpretation. **Syngo.VIA** Amyloid Plaque and Hermes BRASS allow quantitative assessment of beta-amyloid PET brain scans. Both produce a relative SUV for 6 regions to cerebellum. To aid reporting, scans were classified into type A (with typical features) or non-type A (with atypical features) for both positive and negative scans according to imaging characteristics. **Methodology:** For the first 100 studies, Kappa score (κ) was used to assess agreement between reviewers, reviewer vs. final clinical report, final clinical report vs. BRASS. The FRP and FNR were calculated to assess accuracy of BRASS in supporting clinical reads. All 225 patients were then loaded into BRASS and **Syngo.VIA**. The quantitative results were compared against

the final clinical report. **Results and Discussion:** Good agreement ($\kappa > 0.6$) was observed for all data (n=100), with very good agreement for typical/Type A scans (n=79), $\kappa > 0.8$, and a wide range for atypical/Non-Type A scans (n=21), $-0.1 \leq \kappa \leq 0.9$. For Type A scans, ROC analysis showed FPR = 2–10%. The standard statistical based scoring using BRASS criterion of $z \geq 2$ in $ROI \geq 2$ (TPR=97%, FPR=20%) or SUV_r mean = 1.18 (TPR=97%, FPR=12%) are suitable cut-offs to support reporting of type A scans by trained readers. For 225 patients, the sensitivity and specificity for type A (n=182) scans using Hermes and a threshold based criteria of SUV_r mean = 1.18 was 98.8% and 91.0% respectively. For **Syngo.VIA** Amyloid Plaque these were 96.3% and 92%. Both Hermes BRASS and **Syngo.VIA** performed well for typical scans. The sensitivity and specificity for non-type A (n=43) scans using Hermes was 83% and 47%, and using **Syngo.VIA** Amyloid Plaque was 79% and 58% respectively, suggesting that for these scans further support is necessary to assist reporting. **Conclusion:** Both Hermes and **Syngo.VIA** perform well for amyloid scans with typical features and can be used to support visual evaluation. However, they do not perform as well in atypical-non-Type A scans, which should be recognised and acknowledged visually, and quantification applied with caution. Regional based SUV_r cut-offs with ROC analysis need to be derived once a sufficient sample (at least 84 non-type A patients) is available to reduce FPR, increase TPR, increase reader confidence, improve agreement of atypical scan reporting.

EP-0031

Blood Flow Dependence of Early [¹¹C]PE2I and [¹⁸F]FE-PE2I PET SUVR Measurements Used In the Differential Diagnosis of Parkinsonian Disorders

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Introduction: [¹¹C]PE2I and [¹⁸F]FE-PE2I are PET ligands with high affinity and selectivity for the dopamine transporter (DAT). Decreased DAT availability is associated with various neurological disorders such as Parkinson's disease and an 80–100 min dynamic scan with either tracer, giving both binding potential (BP_{ND}) as a measure of DAT availability and relative delivery (R_1) as a measure of relative cerebral blood flow, can be used for differential diagnosis of patients with parkinsonian disorders. For routine clinical applications, the use of shorter acquisition times, with DAT availability estimated using standardized uptake value ratio (SUVR)-1 at peak equilibrium, has been validated for both [¹¹C]PE2I and [¹⁸F]FE-PE2I. However, early SUVR measurements may be influenced by blood flow, and the purpose of this study was to investigate any relationship between the relative tracer delivery (R_1) and SUVR-1 as well as BP_{ND} for [¹¹C]PE2I and [¹⁸F]FE-PE2I. **Materials and Methods:** Forty healthy controls (HC) were included. They underwent either an 80 min [¹¹C]PE2I (n=20) or a 93 min [¹⁸F]FE-PE2I (n=20) dynamic PET scan. Parametric BP_{ND} and R_1 images were calculated for the full data sets using a basis function implementation of the simplified reference tissue model and SUVR-1 images were calculated on a 30–40 or 15–

45 min time interval for [^{11}C]PE2I and [^{18}F]FE-PE2I, respectively. After spatial normalisation to MNI space, BP_{ND} , SUVR-1 and R_1 values in putamen were retrieved from the parametric images using a VOI template, and the relations between R_1 and BP_{ND} or SUVR-1 were assessed using linear regression. **Results:** Significant correlations were found between R_1 and SUVR-for [^{11}C]PE2I and [^{18}F]FE-PE2I, $R^2=0.34$ and 0.20 , respectively ($p\text{-value}<0.005$). However, higher correlations were found between R_1 and BP_{ND} for both [^{11}C]PE2I and [^{18}F]FE-PE2I, $R^2=0.49$ and 0.39 , respectively. **Discussion:** The correlation between R_1 and SUVR-1, as seen especially for [^{11}C]PE2I, alludes to a blood flow dependency for SUVR-1 measurements. However, an even larger correlation was found between R_1 and BP_{ND} for both [^{11}C]PE2I and [^{18}F]FE-PE2I, where this correlation should not exist. Our hypothesis is that partial volume effects may induce a similar underestimation in BP_{ND} (or SUVR-1) and R_1 values within subjects, but with a large variation between subjects, causing a spurious correlation between R_1 and BP_{ND} . This will be subject of further investigations.

EP-0032

Impact of intensity normalization on the quantification of pre-surgical PET studies in refractory epilepsy: a simulation study including functional and anatomical information

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Intensity normalization is a key factor in the quantification of brain PET studies. Conventional normalization methods such as those based on proportional scaling (PS) or histogram-based intensity normalization (HN) can yield significantly biased results. In this work, we used a realistic simulation framework to assess the performance of different intensity normalization methods on typical epileptic lesions: PS, HN and a novel iterative version of the HN method (iHN). Realistic simulations based on control patient studies with Magnetic Resonance (MR), Computed Tomography (CT) and FDG-PET were obtained using a MC model of the GE Discovery STE 4 implemented on SimSET v2.9.2. The attenuation and the activity maps were obtained from CT and MR scans and adding functional information from the PET images. Eight digital phantoms were generated by adding two lesions, one to the frontal lobe (44cm³) and another to the temporal lobe (11cm³), each with four different levels of hypometabolism (20, 40, 60 and 80%). Simulated sinograms were reconstructed using the STIR library. PS, HN and iHN methods were applied for intensity normalization between each simulated image and a database of 97 control patients included in Neurocloud-PET software. In the iHN method, the HN-normalized image is compared with the database template, excluding the potentially hypometabolic voxels from the next iteration, until the normalization factor converges. Voxel-based statistical anal-

ysis was used to compare each simulated PET with this same database, including age as a covariate. The normalization methods were evaluated in terms of the bias of normalization factor and the ratio between detected and theoretical volumes of each hypometabolic region. The calculated normalization factors were biased up to 5% when using conventional methods, while the proposed iHN reduced this bias to <1%. Our results showed that all the methods underestimated the lesion theoretical volume. Thus, for the temporal lesion, PS managed to recover 0, 26, 54 and 59% of the theoretical volume, for 20, 40, 60 and 80% hypometabolism levels respectively. Instead, HN and iHN recovered 10, 32, 57, 65 % and 20, 48, 62, 71% for the same lesion and hypometabolism levels. Similar trends were obtained for the frontal lesion. Conventional intensity normalization methods yielded biased normalization factors, thus affecting the detectability of smaller and subtle hypometabolisms. The use of the iHN method significantly reduced bias, providing better detectability and lesion recovery.

EP-0033

Dynamic Digital PET/CT for Neurology: Revisiting Imaging Uptake and Acquisition Time for the Next-Generation PET System

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Purpose: Current recommendations for neurologic PET imaging with FDG are from 2009 and are quite wide regarding details such as uptake time and acquisition durations. EANM and SNMMI recommendations suggest brain image acquisitions begin anywhere from 30 to 60 minutes post-injection with acquisition times of 15-30 minutes. Here, we aimed to evaluate brain dynamic uptake characteristics enabled by the precision and accuracy of next-generation digital photon counting PET/CT. **Materials and Methods:** PET imaging was performed continuously for 75 minutes post-injection for 10 patients participating in a response assessment clinical trial. Imaging was performed on a digital photon counting PET/CT system (Philips Vereos, dPET). Patients were injected with 185 MBq 18F-fluorodeoxyglucose (FDG). PET listmode data were reconstructed with 5 minute frames over the entire 75 minute acquisition. Additional reconstructions were run using 20 minutes of acquisition time at 40 minutes post-injection, for quantitative comparison to the 5 minute frames at the same timepoint. Uptake curves were evaluated in 22 regions of interest throughout the brain, via SUV_{max} . **Results:** Excellent image quality was achieved for the 5 minute frame duration reconstructions. We observed differences in both the absolute levels of FDG uptake between individual patients and the rates of uptake in the different brain regions. Uptake curves also showed that at 40 to 50 minutes post-injection, tissue uptake patterns were still changing and did not begin to plateau until at least 60 minutes post-injection. Quantification from the 5 minute and the 20 minute frames at 40 minutes post-injection were comparable. **Conclusion:** The introduction of digital photon counting PET may help lessen the need for long, high dose brain imaging. Here, continuous

75 minute imaging revealed that uptake kinetics in the brain only begin to stabilize about one hour post-injection. Distinct differences in intra-individual uptake rates point to the necessity of consistency in uptake time for precise and robust PET/CT imaging of the brain.

EP-0034

Flutemetamol and FDG Brain-PET Image Reconstruction Methods Affect Software-Aided Diagnosis in Patients with Neurodegenerative Diseases

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Introduction: The introduction of new developments in neuro-PET, such as digital silicon photomultiplier detectors, time-of-flight (TOF), point-spread-function (PSF) modelling and penalized reconstruction methods have resulted in improved spatial resolution and signal-to-noise ratio in reconstructed images. The aim of this study was to investigate how the improved PET image reconstructions affect quantitative measures and software-aided assessment of patient pathologies. **Materials and Methods:** Two cohorts of control subjects with PET examinations scanned on a digital TOF PET/CT scanner were included. The first cohort consisted of 12 melanoma patients without brain involvement receiving 3.8 MBq/kg of ¹⁸F-FDG and a 2-min scan. The second consisted of 10 healthy controls receiving 2.4 MBq/kg of ¹⁸F-Flutemetamol and a 20-min scan. Reconstructed images were obtained by ordered-subsets expectation maximization (OSEM; 3 iterations, 16/34 subsets, 3/5-mm gaussian post-processing filter, TOF, PSF modelling) and block-sequential regularized expectation maximization (BSREM; TOF, PSF, β -value 150). Each reconstruction was anatomically normalized into MR template space (CortexID Suite, GE Healthcare). Automated analysis of tracer uptake in regions of interest and comparison with the corresponding tracer uptake in a database of normal subjects in terms of standardized uptake value ratio (SUVR) and z-score was performed using the whole brain and cerebellum as reference areas in cohort 1 and pons and grey cerebellum in cohort 2. **Results:** TOF, PSF modelling and BSREM gradually either increased or decreased the relative uptake difference to the normal subjects' database within the software, depending on the tracer and chosen reference area, i.e. resulting in increased absolute z-scores. The study yielded comparable results to the normal database when using OSEM 3/16 5-mm reconstruction, without TOF and PSF. For FDG, mean SUVR to cerebellum was higher than the database for all improved reconstructions, whereas the mean SUVR to whole brain was lower. The number of regions per patient being assessed as pathologic (z-score < -2)—with cerebellum as reference—was 2.7 when using OSEM 3/16 5-mm compared with 7.1 using BSREM. For flutemetamol, mean SUVR was lower than the database regardless of reference area for all improved reconstructions, although the SUVR to grey cerebellum showed regional differences, e.g. the lateral temporal and occipital did not follow the overall negative trend. **Conclusion:** This study showed that software-aided

diagnosis is affected by image reconstruction methods and parameter settings. To avoid false-positive results, software-aided diagnosis should be used with caution when employing improved image reconstruction methods compared to those used for acquisition of the normal database.

EP-03

e-Poster Area

Physics: Cardiology - Data Analysis & Imaging Systems

EP-0035

Performance Variations in Myocardial Perfusion SPECT/CT: A Multicenter Gated Phantom Study in Finland

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Aim: Investigate how reliably modern SPECT/CT systems can produce homogeneous myocardial perfusion images using clinical and standard gated acquisition parameters. **Materials and Methods:** The initial results of 23 gamma cameras of public nuclear medicine laboratories in Finland that routinely perform myocardial perfusion imaging (MPI) are presented. A commercial gated heart phantom for assessing the quality of MPI was set to pump at 60 beats per minute at 50% ejection fraction (EF) during MPI SPECT/CT acquisition. The dynamic phantom contained no defects, so we expected a homogeneous perfusion. The phantom was imaged twice: 1) with the clinical stress protocol (CLINICAL) routinely used by each laboratory, and 2) with an optimal standard protocol (STANDARD). The CLINICAL protocol enables the comparison of routine images from different laboratories, whereas the STANDARD protocol enables comparisons of equipment performance across laboratories. In addition, the STANDARD imaging parameters were chosen so that count-statistics were better than in any of the CLINICAL protocols. Reconstructions and subsequent analyses of perfusion uniformity were performed similarly for each data set to limit user and software dependence during analysis. Integral uniformity ($IU = [\text{maximum} - \text{minimum}] / [\text{maximum} + \text{minimum}]$) was calculated based on the polar maps produced by QPS software (Cedars-Sinai), using mean values from 14 inner segments of the 20-segment model. The outermost segments were excluded, as the software's delineation algorithm usually contained unwanted background at the edges of the polar map. **Results:** The mean (range) IU was 14.3% (10.3% - 22.6%), for the CLINICAL protocol, whereas it was 12.8% (8.0% - 17.5%) for the STANDARD protocol. The performance of the STANDARD protocol was statistically significantly better in general (paired t-test, $p = 0.03$) and outperformed the CLINICAL protocol in 14 out of 23 laboratories (perfusion was more homogeneous). The calculated IU

values were not significantly different between manufacturers (Siemens vs. GE) or between their modern SPECT/CT cameras (Symbia, Intevo and Discovery) when tested with t-test and one-way ANOVA, respectively. **Conclusions:** Based on these results, many laboratories in Finland could improve reliability of their MPI results by having higher activity or time per view, as the longer STANDARD protocol showed significant improvement in uniformity over the CLINICAL protocol. Due to biological variation in patients, it is challenging to optimize image acquisition parameters. The gated heart phantom is reliable source of artifact free MPI SPECT/CT data, and could be used for parameter optimization in future.

EP-0036

A Simple Alternative To Compartment Models For Myocardial Flow Reserve Measurements Using Rubidium-PET

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Aim: A two-frame retention model (RM) is a simple and fast technique to estimate myocardial flow reserve (MFR) from dynamic PET myocardial perfusion images. It may serve as an alternative to complex compartment models and does not require time-consuming reconstructions of large dynamic image series, nor expensive software for compartmental analysis. Our aim was to investigate the potential use of a two-frame retention model for reliable MFR measurements using Rubidium-82 (Rb-82) PET. **Method:** We retrospectively included 31 consecutive patients who underwent a dynamic rest-pharmacological induced (Regadenoson) stress PET/CT (GE Discovery 690, GE Healthcare) with Rb-82. Dynamic data of both rest and stress examinations were processed using Corridor4DM (v2015.02.64) software. MFRs were calculated 1) using the retention model based on the ratio of the measured tracer uptake in the myocardium 4 minutes after tracer injection and the cumulative arterial blood concentration in the first 2 minutes after tracer injection, 2) using the one-tissue compartment model (CM) of Lortie et al. based on region of interest methodology and modelling. The latter model served as a reference. For both methods, MFRs were evaluated for the three vascular territories: left anterior descending (LAD), left circumflex artery (LCX) and right coronary artery (RCA), and for the whole myocardium. We calculated the Spearman's correlation coefficient between the MFR values using RM and CM. Furthermore, the standard deviation of MFR differences (Δ SD) was determined. Based on current literature, Δ SD < 10% was considered for clinical adoption of RM. **Results:** Mean $\pm$ SD MFR measurements using CM were 2.16 ± 0.48 , 2.08 ± 0.48 , 2.36 ± 0.61 and 2.19 ± 0.47 for the LAD, LCX, RCA and the whole myocardium, respectively. For the RM we found 2.21 ± 0.41 , 2.14 ± 0.46 , 2.16 ± 0.37 and 2.18 ± 0.40 , values that are close to the CM results. The correlation coefficient between the measured MFRs was 0.84, 0.90, 0.80 and 0.88 for the LAD, LCX, RCA and the whole myocardium, respectively. Further, we found Δ SD equal to 10.0%, 10.1%, 10.4% and 9.1%, respectively. **Conclusion:** MFR measurements with Rb-82 PET using a two-frame retention model generate values that are close to

values acceptable for use in clinical practice. Fine-tuning of the retention model may lead to even more consistent results. Our results show that a simple flow model is a serious alternative to complex compartment models. It has the advantage of simplicity for routine application compared to compartmental analysis.

EP-0037

Semi-Automatic Mouse Left Ventricle Delineation in 18 F-FDG PET Gated Images

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Introduction: In the context of 18 F-FDG PET cardiac gated study in mice, a semi-automatic MATLAB® algorithm was designed to rapidly and semi-automatically delineate the left ventricular (LV) of mice and to extract ejection fraction, LV volume, cavity volume and the volume of the infarcted region. As a proof of concept, the algorithm was used to test the relation between the LV ejection fraction and the volume of the infarcted region.

Methods: The algorithm, written in MATLAB® environment, takes advantage of the cylindrical symmetry of the LV. The heart was manually isolated and aligned to its LV long axis. For each slice the center of mass of the activity was calculated and a line was traced from the center for every angles. For each line, we assumed that the maximum of activity was in the LV and its boundaries were defined as 95% of the maximum activity on each side. This was repeated for every slice under a predefined minimum threshold of activity. To test the algorithm, myocardial infarction in male C57BL/6J mice of 12 weeks was induced by permanent ligation of the left anterior descending artery. Mice were injected with 10 MBq 18 F-FDG. PET acquisition was performed 60 minutes post injection for 30 minutes. Eight bin gated reconstruction was obtained. The images were normalized regarding the weight, the time of injection and the activity injected. **Results:** The algorithm was successfully applied to PET gated images. A first group of seven mice presented a defect ratio < 0.1 of the LV volume (0.05 ± 0.03) whereas a second group of nine mice presented a LV defect ratio ≥ 0.1 (0.51 ± 0.12). Mice in the first group showed an average ejection fraction of $71 \pm 14\%$ compared to $29 \pm 7\%$ for the second group ($p < 0.01$). The average volume of the defect region was 52.4 ± 20.9 mm³. The average of the LV of mice in the first group was 60.4 ± 7.7 mm³, smaller than mice of the second group 98.7 ± 16.8 mm³ ($p < 0.01$). This resulted in an inverse correlation between ejection fraction and defect ratio ($R = 0.87$), with a linear relation $y = -0.82 \cdot x + 0.72$. **Conclusion:** A semi-automatic method of segmentation was designed and successfully tested. A correlation was observed between the defect size and ejection fraction.

EP-0038

Minimization Of Temporal Sampling For Myocardial Blood Flow Quantification Using Rubidium-82 PET

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Introduction: Temporal sampling of dynamic Rubidium-82 (Rb-82) PET influences myocardial blood flow (MBF) quantification. Both the length and number of time frames influence the measured time-activity curves (TACs) that are used as input for compartmental analysis to obtain MBFs. A large number of time frames imply time-consuming reconstructions which may hamper clinical implementation. Our aim was to determine a temporal sampling protocol with a minimum number of time frames that still results in reliable MBF measurements using Rb-82 PET. **Subjects & Methods:** We retrospectively included 30 consecutive patients (15 with an ejection fraction (EF) <45% and 15 with an EF ≥45%) who underwent dynamic rest and pharmacological induced (regadenoson) stress Rb-82 PET/CT (GE Discovery 690, GE Healthcare). Data were reconstructed using 26 time frames (12x5s, 6x10s, 4x20s, 4x40s). Activity concentrations during stress were determined in the left ventricle, the three vascular territories (LAD, LCX and RCA) and in the whole myocardium for each time frame using Corridor4DM software (INVIA, v2016). Next, we simulated the TACs for different temporal sampling protocols varying between 20 and 12 frames. MBFs of the three vascular territories and the whole myocardium were determined with TracerKinetic software (Rstudio) using the Lortie 1-tissue compartment model. MBFs based on 26 frames were used as reference values. MBFs deviating <10% were considered reliable. Temporal sampling protocols were considered for clinical validation if in 95% of the simulated scans all four MBFs deviated <10%. **Results:** In the protocols with 20 frames (12x5s, 6x10s, 2x120s) and 16 frames (12x10s, 2x30s, 1x60s, 1x120s) all MBF deviations were <10%. In the protocol with 14 frames (9x10s, 3x30s, 1x60s, 1x120s) 97% of the simulated scans produced MBF deviations <10%. The protocol with 12 frames (9x10s, 1x30s, 2x120s) resulted in MBF deviations <10% in 90% of the simulated scans which was considered unacceptable for clinical validation. **Conclusion:** Temporal sampling protocols with fewer than 26 frames can still produce reliable MBF measurements using Rb-82 PET. The minimal number of time frames that can be considered for clinical validation is 14.

EP-0039

An investigation for quantitative myocardial blood flow with Tc-99m MIBI by a patlak plot analysis in rat.

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Background: We aimed to investigate the use of dynamic cardiac planar images to estimate myocardial blood flow (MBF) by a patlak plot analysis using time-to-peak (TP) map and compared it by the microsphere technique in rat. Positron emission tomography is considered the gold standard method, but is not available everywhere. By contrast, myocardial perfusion imaging (MPI) with single-photon tracers is more widely available. We reported that MBF estimation by a compartment model analysis using TP map could facilitate absolute MBF measurement in rats; however, a complicated mathematical calculation was necessary to perform the compartment model analysis. The TACs of input function and whole heart, both of them have a single peak in the first few phase of the acquisition. Where, the peak

of whole heart may represent the activity from the left ventricle because the tracers may not be accumulated in the myocardium during the initial phases. We proposed using a patlak plot analysis for the time-activity curve (TAC) of myocardium, which obtained by a subtraction of left ventricle activity from whole heart activity, and hypothesized that this method could facilitate the measurement of absolute MBF by MPI in rat without the complicated mathematical calculation. **Methods:** Sixteen normal rats were studied. Dynamic planar images with Tc-99m MIBI were obtained on a gamma imaging system for small animals (Inveon Multimodality System, Siemens, Germany), and input function and cardiac regions of interest were set using the TP map. The myocardial TAC was calculated with the following formula: myocardial activity = (whole heart activity) - (left ventricle activity). Moreover, left ventricle activity was obtained by curve fitting technique on the TAC of input function and whole heart in the first few phases. The MBF was estimated by a patlak plot analysis with the Renkin-Crone model and by the microsphere technique. **Results:** The average of the left ventricle activity fraction in the whole heart activity was 57%. The MBFs with the patlak plot analysis and microsphere technique were significantly correlated. The Pearson's correlation coefficients was 0.67 ($p < 0.005$). **Conclusions:** MBF estimation by a patlak plot analysis using TP map could facilitate absolute MBF measurement in rats.

EP-0040

Reduced time acquisition for Thallium myocardial perfusion scintigraphy with novel large field cadmium-zinc-telluride SPECT/CT - An equivalence study.

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Purpose: Dedicated cadmium-zinc-telluride (CZT) camera allow reduction of time and radiopharmaceutical activity without compromising quality of Myocardial Perfusion SPECT (MPS). CZT-SPECT/CT with large field of view are now available, and present a better resolution than conventional Anger camera. We hypothesized that dose or time reduction is also achievable with this equipment without compromising image quality. This study aimed to determine the equivalence between conventional protocol and reduced time protocol of MPS acquired on CZT/SPECT. **Materials and Methods:** MPS realized on DISCOVERY-CZT after injection of 1,5MBq/kg of ²⁰¹Thallium, (50 secondes/projection, 32 projections) from December 2017 to March 2018 were retrospectively analyzed. Data were post-treated with list-mode to simulated 74 and 50% of total counts statistics. After anonymization, stress images were analyzed with QGS/QPS software by three different readers blind for post-treatment information. Main objective was to assess the equivalence in number of segments lower than 70%, between the full sequence and both the sequence reduced to 74% and 50%. Equivalence was demonstrated if the CI95 of the difference fell within equivalence margins, set to 1 segment. A hierarchical gatekeeping procedure was applied. Agreement

between the 3 observers was assessed by the Lin's CCC (Concordance Correlation Coefficient). **Results:** The study included 103 patients with an average of 66 years. The average number of segments lower than 70% identified was respectively 6.0, 6.0 and 6.5 for the full sequence, 74%-sequence and 50%-sequence (range was 0-14 for the 3 sequences). The number of pathologic segments identified was respectively 0.8, 0.8 and 0.9 for the 3 sequences (range 0-8). Agreement between the observers was good for the number of segments lower than 70%, with a CCC=0.90 for full sequence, 0.89 for 74%-sequence and 0.88 for 50%-sequence. Therefore, we have pooled the 3 values and used the average of the parameter to assess the equivalence. Agreement was poor on the number of pathologic segments (between 0.6 and 0.7) and was excellent for FE (resp. 0.97, 0.96 and 0.97 for full, 74% and 50% sequences). Equivalence was demonstrated for both sequences. Regarding the full/74%-sequence, mean difference was 0.06 (CI95: [-0.15;0.27]) and considering an equivalence margin of 1 segment, the associated p-value <0.001. Regarding the full/50%-sequence, mean difference was 0.518 (CI95: [0.28;0.76]) and the associated p-value <0.001. **Conclusion:** With novel CZT-SPECT/CT, dose or acquisition time can be reduced by 50% with an equivalence in number of segments lower than 70% and a good agreement between the observers.

EP-0041

Myocardial functional imaging in mice: development of a voxel based and cluster analysis software

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Introduction: Most current software used for cardiac analysis evaluate the left ventricular perfusion and function on an individual basis. As part of a study of cardiac function in mice, we wanted to compare left ventricular perfusion and metabolic images quantitatively between different groups. Therefore, we designed an algorithm to statistically compare voxel per voxel left ventricle PET images and able to define and display significant voxels and voxels clusters. **Methods:** On PMOD® software, a mask of the heart was generated based on the average of left ventricular images from a 130 18F-FDG cardiac PET database. The algorithm was designed to import images to the MATLAB® environment as a 3D matrix and automatically realign, mask and normalize before voxel-wise analysis. A two-tailed two-sample t-test with a 5% false positive threshold was performed between the two groups for each voxel of the matrix, followed by a false discovery rate correction at 5%. The significant voxels were clustered using MATLAB's Image Processing toolbox and plotted to examine their morphological position. As proof of concept, we tested this algorithm on 22 male C57BL/6J mice at 12 weeks of age. Myocardial infarction in mice was induced by permanent ligation of the left anterior descending artery. Mice had an intravenous 10MBq 18-FDG injection. The PET scan was performed 60min post injection during 30min. The images were normalized regarding the weight, the time of injection and the activity injected. **Results:** Eight control mice were compared to 14 infarcted mice. For each group, correct realignment was

verified, and the average of the normalized masked images was displayed for visual inspection. On our mice, out of a total of 916 voxels tested, 381 were significantly different between the two groups after the false discovery rate correction. These significant voxels were distributed in two clusters which were well-defined visually. The significant volume between the two groups was estimated at 43mm³ volume, representing 38% of the mask. **Conclusion:** The algorithm was able to quantify the heart defect in infarcted mice group compared to the control group. Further developments would include adding spatial normalization to the image pre-processing.

EP-0042

Influence of Photon Count-Level on Semi-Automatic Image Assessment in Myocardial Perfusion Imaging

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Purpose: The SMARTZOOM multi-focal collimator from Siemens Healthcare was developed to improve the gamma-photon sensitivity in myocardial perfusion imaging without truncating the field of view. As part of the IQ-SPECT package, it may be used to reduce radiopharmaceutical dose to patients, as well as acquisition time, which in turn leads to reduced photon count-levels. When semi-automatically assessing images in MPI using software packages which apply comparison to normal data (e.g. Corridor 4DM or Emory Cardiac Toolbox), it is unclear what the influence of adapting / non-adapting count levels of patient and normal data is. Consequently, the aim of this study was to evaluate the influence of dose reduction in semi-automated MPI scoring, with focus on different strategies for the choice of normal data (count-matched, full-count). **Methods:** 50 patients underwent Tc-99m-sestamibi one-day stress/rest SPECT/CT. Multiple levels of count reduction were generated using binomial thinning. Using Corridor 4DM, summed stress score (SSS) was calculated using either count-matched or full-count normal data. Studies were classified as low-risk (SSS<4) or intermediate/high-risk (SSS≥4). **Results:** For both strategies rate of reclassification was significant at roughly 67% dose and below. Count-reduction using count-matched normal data increases false-normal rate and decreases sensitivity. With full-count normal data, count reduction increases false-hypoperfusion rate, leading to decreased specificity. Overall, matching counts of normal and patient data leads to lower reclassification rate. **Conclusion:** Significant bias may result arising from the interplay between the count-level of normal data relative to the actual patient data. Specifically, if the count level of patient data is reduced and normal data held constant, reclassification towards hypoperfusion prevails. Conversely, if count levels of normal and patient data are matched, reduction of patient counts results in preferential reclassification of studies to normal perfusion. The latter strategy leads to lower reclassification rates. However, some might prefer the former strategy (bias towards false positives over bias towards false negatives) and accept the moderately higher total number of re-classified studies.

EP-0043**Cardiac motion artifacts from patient breathing in myocardial perfusion imaging, importance of breathing method.**

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Introduction: Small cardiac motion during patient breathing can induce artifacts in myocardial perfusion imaging (MPI). The visibility of these artifacts in reconstructed images depends mainly on motion amplitude. New detector technologies in heart dedicated cameras, e.g. use of cadmium zinc telluride (CZT) crystal, has considerably enhanced the spatial resolution and also reduced the scanning time in MPI. For such high resolution images, even small artifacts in the reconstructed image can be skeptical in subjective assessments. In this study, the effect of patient cardiac motion from breathing was evaluated using quantitative methods as well as by an expert physician. The aim was to study if the breathing method can affect the level of cardiac motion artifact in MPI. **Method:** A cohort of 10 patients underwent MPI at clinical physiology department at Sahlgrenska university hospital. In order to reduce the dose burden to patient, two days protocol is used in our department, where the stress study is performed at first day and the rest study at second day. All patients in this cohort were scanned using heart dedicated system DSPECT (Spectrum Dynamic Medical[®]). At second day, i.e. rest study, patients were scanned with normal breathing first. Two additional scans were also performed for each patient: First with chest and second with abdominal breathing in supine position. Images were reconstructed on spectrum working station using default settings for iterative reconstruction algorithm recommended by the manufacturer. QGS/QPS (Cedars-Sinai[®]) software were used for quantitative assessment of segment scoring and an expert physician performed the subjective assessment. Kappa test was used to find the correlation between image qualities from these three breathing methods for both quantitative and subjective evaluations. **Result:** Weighted kappa test showed 78 %, 77%, and 65% agreement for normal- vs chest-breathing, normal vs abdominal-breathing, and chest- vs abdominal-breathing, respectively. **Conclusion:** Quality of DSPECT images can be affected by artifacts from breathing motions, but the impact of these artifacts are not significantly different between different breathing methods. Therefore, patients can breathe normally during MPI.

EP-0044**CT-Attenuation Correction of MIBG Scoring in Conventional and IQ system for Quantitative Analysis of Cardiac Sympathetic Nerve Function**

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Purpose and Introduction: Iodine-123-metaiodobenzylguanidine (I-123 MIBG) SPECT has been used to determine sympathetic nerve activity and to provide us information for a regional innervation of the heart. However quantitative SPECT scoring is still uncommon because the inferior attenuation ar-

tifact is often found in I-123 MIBG SPECT image. Therefore, we performed SPECT/CT-attenuation correction using IQ-SPECT/CT in a short-term acquisition protocol to test the hypothesis the I-123 MIBG SPECT scoring can be useful in clinical setting.

Subjects and Methods: The subjects include 247 patients who underwent I-123 MIBG imaging. The early- and delayed-phase cardiac images were obtained. I-123MIBG imaging was analysed in IQ-SPECT/CT and conventional collimator and quantitative SPECT/CT scoring and heart-to-mediastinum ratio (HMR) was calculated by the ratio of mean counts between heart and mediastinum areas of interest drawn on a planar image by means of automated software analysis. SPECT images were obtained by IQ-SPECT system with CT-attenuation correction. The cardiac sympathetic nerve function was assessed by QPS (Cedars-Sinai Medical Center, Los Angeles, CA) quantitatively, using the standard 17-segment and 5-point scoring system. Subjects were divided into 3 groups according to HMR and QPS defect score. A contingency table analyses was used for the analysis. IQ-SPECT scoring was compared to HMR. IQ-SPECT scoring in dementia patients was examined. **Result:** Median HMR and summed score in the delayed phase was 2.2 (range; 1.0-4.6) and 9 (range; 0-50). Very high defect score (>20) was observed in 98% of the low HMR group. Although the high HMR group showed low defect score (≤ 10) in 80% of the patients. The significant relationship between QPS defect score and HMR was observed in the delayed phase (χ^2 value 163, $p < 0.0001$). IQ-SPECT completed the acquisition of SPECT imaging in about 5 minutes ($n=22$). In part, conventional SPECT took 16 minutes ($n=225$). Interior decreased uptake was significantly improved by the CT-attenuation correction using IQ-SPECT/CT. The quantitative QPS scoring showed significantly close relationships with MHR values ($P < 0.0001$). IQ-SPECT in a short time acquisition protocol was applied to the patients. SPECT scoring with IQ-SPECT identified subjects with Levy body disease (49 ± 4 vs 4 ± 3 , $p < 0.0001$). Conventional collimator showed a close relationship between SPECT scoring and HMR ($p < 0.0001$). **Conclusion:** IQ SPECT scoring of I-123 MIBG with CT-attenuation was feasible and inferior attenuation was improved. Quantitative SPECT scoring with IQ-SPECT/CT was achieved by a short-time acquisition protocol. Quantitative SPECT scoring might be a possible marker of evaluating severity of I-123 MIBG defect.

EP-04**e-Poster Area****Physics: Quality Control, Performance & Standardization****EP-0045****Standardisation of ⁶⁸Ga PET/CT imaging resolution for multi-centre study**

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Introduction: Gallium-68 PET/CT imaging is an emerging modality not yet standardised for multi-centre studies. The aim of

this work was to study the impact of resolution on recovery coefficients (RCs) and propose a method to standardise PET spatial resolution for inter-centre comparison. **Materials and Methods:** A line source phantom and a NEMA-2012/IEC-2008 phantom with ^{68}Ga specific activity of 8 kBq/ml in spheres were prepared and acquired on a GE Discovery 690 PET/CT with EARL accreditation parameters (two 5-minutes steps overlapping on spheres). Images were reconstructed with the 3D OSEM algorithm (3 iterations, 18 subsets, TOF and resolution recovery correction) using different Gaussian post-filters with full width at half maximum (FWHM)=[0, 4.0, 6.8, 11.1, 13.6] mm. Resolution, characterised by the FWHM, was determined on the line source phantom images for all filters. RCs were measured with Pmod 3.4 in spheres delineated on NEMA phantom PET images according to constructor volumes. Assuming that partial volume effect is proportional to sphere surface, RCs were plotted as a function of inverse sphere radius. The correlation of RC slope with PET resolution was also investigated, using a linear model. Flawless NEMA phantom PET images (without statistical noise) were simulated with Scilab 6.0.0 in order to mimic experimental measurements and validate results. **Results:** With the line source phantom images, measured resolution for the five filters was FWHM=2.5, 4.7, 7.3, 11.4 and 13.8 mm. With the NEMA-2012/IEC-2008 phantom measurements, we demonstrated a linear relationship between RC and inverse sphere radius for each resolution ($R^2 \geq 0.99$). RC line slopes were linearly correlated to image resolution ($R^2 = 0.99$). Trends were confirmed by Scilab simulation even if a systematic error was observed due to ideal simulation conditions. **Conclusion:** Linearisation of RC curves and quadratic sum of Gaussian FWHMs allowed direct determination of spatial resolution and of the needed post-reconstruction filter to reach comparable resolution for multi-centre studies, a first step towards ^{68}Ga PET/CT standardisation.

EP-0046

Standardizing image quality for ^{68}Ga -DOTA-TATE PET/CT.

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Aim: In recent years, the use of ^{68}Ga -DOTA conjugated PET tracers has become common practice. The 2017 European Association of Nuclear Medicine procedure guideline on PET/CT tumor imaging with ^{68}Ga -DOTA-conjugated peptides recommends a dose ranging between 100-200 MBq (at least 100 MBq), also depending on characteristics of the PET scanner and patient body weight. The relationship between patient weight or patient-dependent parameters and image quality is not known for ^{68}Ga -DOTA in contrast to ^{18}F -FDG where evidence exists for a quadratic dose regimen. The aim of this study is to propose a dose regimen based on a patient-dependent parameter that standardizes image quality and yields sufficient image quality for visual assessment. **Methods:** 21 patients scheduled for a diagnostic ^{68}Ga -DOTA-TATE PET/CT were prospectively included, patient weight ranged from 50-120 kg. According to local protocol a dose of 1.5 MBq ^{68}Ga -DOTA-TATE per kilogram body weight was administered. After 60 minutes scans were acquired on a Siemens Biograph mCT PET/CT in whole body listmode, 6

minutes/bed position (mbp). Listmode events were randomly sampled to obtain six reconstructions (1-6 mbp) for each patient. Image quality was assessed by the signal-to-noise ratio in a volume of interest within a homogeneous part of the liver (SN-Rvoi). SNR was normalized (SNRnorm) for variation in injected dose and mbp by dividing the SNRvoi with square root (dose x mbp (DTP)). The patient-dependent parameters body mass, length, body mass index, body mass per body length and lean body mass were correlated with SNRnorm. All images were visually graded (4-point scale) for image quality by three experienced nuclear medicine physicians. **Results:** A first analysis for quantitative (N=11) and visual (N=9) assessment. All patient-dependent parameters show a poor correlation ($R^2 < 0.4$) with the SNRnorm. Mean SNRvoi's of the 1-5 mbp scans are significantly ($p < 0.05$) lower compared to the reference scan of 6 mbp. After normalization, no significant ($p > 0.05$) difference in SNR between the mbp's was found. Comparing the mean visual score of the 2-5 mbp scans with the reference scan shows a significant lower score for the 2 and 3 mbp scans. Images with a SNRvoi of 5.8 were scored visually as sufficient. A DTP of 450 MBqxmin would lead to an average SNRvoi of 5.8. **Conclusions:** No relationship between patient-dependent parameters and image quality is found. A DTP of 450 MBqxmin is required for visually sufficient image quality.

EP-0047

Evaluation of Multi-Center PET/CT Quality Assurance: Multi-Paradigm Software Enables Automated PET Quality Control

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Context: PET quality assurance (QA) is becoming increasingly important as well as more complex, following the technological and radiopharmaceutical progress in PET imaging. Consequently, PET quality control (QC) has to handle an increasing heterogeneity of devices and diversity of clinical applications. However, actual PET QC focuses on equipment and good practice, while QC of individual datasets stays costly in terms of time and resources, and thus often lacks adequate diligence. **Aim:** Our aim is to promote automated PET QC of individual datasets and demonstrate its importance and feasibility as integral part of PET imaging. First objective was to develop a software prototype for automated PET QC on diverse data sets. Second objective was to demonstrate feasibility and benefits of such software. In particular, the automated QC should enable an in depth evaluation of data from a nationwide PET survey organized by the Swiss Society of Nuclear Medicine (SGNM-SSMN). **Materials and Methods:** The software implements a multi-paradigm approach based on an in-house software development tool. Among a range of modern design patterns, the software implements an embedded rule-based system to support decisions and reconfigurations of itself at runtime. A total of 453 datasets originating from 18 different PET/CT systems at 14

Swiss sites was available for QC. According to a detailed study protocol, each site was requested to provide a range of various image reconstructions from multiple acquisitions of two differing phantoms. The software was applied in a single run to all datasets, producing an individual quality report for each dataset and a database making all results available for further evaluation.

Results: The automated QC correctly classified the diverse datasets according to acquisition protocol, reconstruction protocol and type of phantom used. Corresponding protocol adherence verification and quantitative evaluations were performed. The system rejected 7% of the data sets because of serious violations of protocol. Another 57% of the datasets were categorized as of restricted use, because of a variety of minor violations of protocol or a mismatch between quantitative specifications and actual data. Only 36% of the data sets fully passed QC. The resulting database proved to be essential for further evaluations as published elsewhere. **Conclusion:** The results indisputably prove the need, the feasibility and the benefits of automated PET QC. More intelligent software is a prerequisite for rigorous PET QC of individual datasets, especially given the increasing diversity of PET imaging applications.

EP-0048

PET/CT scanner qualification in onco-haematological Clinical Trial: comparison between nationwide experience

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Purpose/Introduction: The aim of this work was to compare the Clinical Trial Qualification (CTQ) adopted by the Italian Foundation on Lymphoma (FIL), the Grupo Espanol de Linfomas/Transplante Autologo de Medula Osea (GELTAMO) and the International Extranodal Lymphoma Study Group (IELSG). **Subjects & Methods:** Local personnel acquired Uniformity (UQP) and Image Quality (IQ) NEMA/IEC phantoms filled with ¹⁸F. The images were uploaded to a central server and analysed within Cuneo CoreLab. Background activity concentration (the average of activity concentration in a large homogenous ROI) in UQP (BACUQP) and in IQ (BACIQ) and sphere to background ratio (SBR) in the IQ phantom were compared to expected values. Recovery coefficient (RC) were calculated in the IQ phantom. Inter-scanner variability (ISV) of BACUQP, BACIQ and SBR was estimated as the 95% confidence level of difference between measured and expected values. Criteria for fulfilling the CTQ are a ISV less than 10% in BACUQP and RC coefficient within EANM limits.

Results: 68/89 (76%) Italian PET/CT scanners fulfilled the CTQ. For qualified scanners the CTQ was reached at the first round in 35% of the cases, while in 31%, 16% and 18%, two, three or more than three iterations, were required, respectively. The ISV were 21.1%, 62.0% and 61.7% for BACUQP, BACIQ and SBR respectively. 25/26 (96%) Spanish PET/CT scanners fulfilled the CTQ. For qualified scanners the CTQ was reached at the first round in 24% of the cases, while in 40%, 16% and 20%, two, three or

more than three iterations, were required, respectively. The ISV were 20.8%, 36.4% and 57.5% for BACUQP, BACIQ and SBR respectively. 22/29 (76%) worldwide PET/CT scanners fulfilled the CTQ. For qualified scanners the CTQ was reached at the first round in 59% of the cases, while in 27%, 0% and 14%, two, three or more than three iterations, were required, respectively. The ISV were 21.9%, 38.2% and 43.9% for BACUQP, BACIQ and SBR respectively. **Discussion/Conclusion:** The CTQ is a robust and reproducible procedure to verify inter-scanner calibration but has several limitations. Indeed, the BACIQ is at least two or three times larger than BACUQP demonstrating that the uniformity phantom, used to achieve CTQ, is more accurately prepared by local sites. SBR demonstrated a great variability (ISV from about 43.9% to 61.7%) because it accounts both for variability in phantom preparation and in reconstruction algorithm tuning.

EP-0049

Quantitative PET: Count Number Adaptations of Organ and Site specific Acquisition Protocols are a Key Determinant of comparable PET/CT Measurements

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Aim: The ever-growing diversity and complexity of PET/CT systems make it increasingly difficult to define common acquisition protocols for quantifiable and comparable PET measurements in clinical routine and, above all, in multicenter clinical trials. We aimed to analyze the dependency of quantitative PET on technical variability, in order to improve acquisition and reconstruction protocols. The results formed the base for selected clinical acquisitions protocols, tailored to particular PET/CT systems. **Materials and Methods:** Image noise was examined in 422 PET/CT datasets from 18 PETCT systems participating in a Swiss multicenter phantom study. 215 of these measurements contained also hot spheres for recovery curve (RC) analysis. The study protocol combined different acquisition durations and low- and high-resolution image reconstructions with filtered back projection (FBP), ordered subset expectation maximization (OSEM), and vendor specific point spread function (PSF) based reconstruction. Data was analyzed with regard to exposure, defined as the product of background activity concentration and acquisition time. This produced results comparable in relation to the number of available decays per volume, independently from the actual activity concentration. Quality assurance (QA) limits for RCs were taken from guidelines issued by the Federal Office of Public Health in Switzerland. Additionally, RC shapes were quantitatively analyzed. **Results:** Passing the given QA limits depended highly on adequate exposure by keeping image noise levels low. Also, the minimal exposures required to fulfill the given QA limits differed between PET/CT systems, acquisition protocols and reconstruction algorithms. Despite higher image noise levels, quantifiability of FBP data was affected less by low count numbers than OSEM or PSF data. Insufficient count numbers led to faulty and incomparable image quantification,

and consequently also erratic RCs. From the gathered data, we were able to propose limits for minimal exposure for ten different PET/CT devices and for common clinical protocols, suitable for whole body and organ-specific high-resolution acquisitions.

Conclusions: In order to reproducibly generate comparable and quantitative data, count numbers in PET/CT acquisitions must be specifically adapted to the clinically necessary image resolution, reconstruction method and the PET/CT system used. Therefore, optimal PET/CT acquisition times vary with the required exposure and with the expected activity uptake in target organs. This in turn argues against fixed acquisition times and mandates site and organ specific acquisitions protocols. Adapting exposure to a site's distinct technical factors appears to be a relevant element of PET/CT standardization in the context of multi-center trials.

EP-0050

Improving Standards Of Diagnostic Reporting In PET-CT: An Evaluation Of Factors Influencing Doctors' Performance On The National NHS England PET-CT Programme

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Aim: 1) To identify and empirically measure type and number of reporting 'errors' in diagnostic PET-CT reports 2) To identify and evaluate likely reasons for variation in doctors' performance. **Materials and Methods:** The study examines two unique, merged datasets for 120 doctors: 1) Quantitative performance data from the National NHS England PET-CT Clinical Audit Programme pertaining to number and category of 'error' [discrepancy reports] found in audited reports between 2010 - 2016 2) Quantitative attitudinal data from a longitudinal survey to doctors reporting on the National NHS England PET-CT Programme 2013 - 2018 [National Programme]. Descriptive statistics were used to examine frequency and distribution of discrepancies in diagnostic reports. Regression techniques were applied to test for association between variation in doctors' performance with: activity volume, doctors' engagement [attitude toward audit], doctors' experience [measured as years reporting PET-CT, and as years reporting on the National Programme], 'rater' variability [defined as relative stringency or leniency with which an auditor rates diagnostic reports]. **Results:** Two distinct trends were observed in the performance data: 1) a positive skew in the frequency of errors, with some reporters increasingly associated with a higher percentage of discrepancy reports 2) a U-shaped pattern in the total percentage of discrepancies recorded across years which varied from 16% of all reports in 2010 to 3-5% in 2014 before increasing back to 13% in 2016. Proposition that positive skewness might be due to the higher absorptive capacity of some doctors which enabled them to learn more quickly from audit feedback. However, no reason for a U-shaped distribution of discrepancy reports was immediately evident. Robust regres-

sions found positive associations with: 1) doctors' engagement in the audit process which explained up to 14% of variation in the model across 3 years 2) doctors' experience measured by years reporting on the National Programme which explained up to 8% of variation in model and 3) 'rater' variability which accounted for up to 46% of variation in the model between 2011- 2014 but only 6% in 2016. No support for an association with activity volume or experience measured as years reporting PET-CT. **Conclusion:** The U-shaped variation in doctors' performance was partially explained by the change of auditor and the introduction of reporters with less experience of the National Programme. Regular auditor feedback and induction for new reporters irrespective of years of experience outside the National Programme, could significantly reduce the number of discrepancy reports.

EP-0051

Multicentre PET Standardization for an Amyloid Image Repository

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From January 2017 until February 2018, a series of 12 phantom acquisitions were collected from different PET scanners in Spain, in order to check uniformity before starting a multicentre study for the amyloid neuroimaging repository of the PET-ADDs Consortium. **Objective:** To report the findings of a multicentre PET/CT phantom study for scanner standardization. **Methods:** Sites were required to complete a form, to acquire a PET/CT image of a Jaszczak phantom with hot spheres (contrast 10:1, diameters from 10 to 31 mm) following a detailed procedure and to submit the images for centralized evaluation. Average SUV in a spherical volume of interest in the background area of the phantom was used to determine SUV bias. A 10% deviation was established as acceptance criterion. SUV recovery coefficients (RC) for the six spheres were measured on 50% isocontour VOIs. Mean (SUV50) and maximum (SUVmax) values were recorded for each VOI. For a preliminary evaluation, RC values were compared to the EARL programme acceptance criteria, interpolating EARL RC for the Jaszczak diameters. **Results:** Datasets from 9 different scanner models were collected (42% from GE, 8% from Philips and 50% from Siemens). Five out of the 12 sites (42%) were out of the SUV bias tolerance of $\pm 10\%$. It is noteworthy that a deviation of 100% was found in one of the sites. These centres were asked to repeat the phantom scan and/or to take corrective actions (recalibration of the PET system). Regarding RC values, none of the SUV RC values of any centre was below the EARL acceptance criteria. However, only for one site all the RC values fell within the EARL limits and the remaining tomographs had 1 to 6 RC values above the tolerance. For the smallest sphere, observed RC values for SUVmax ranged from 0.42 to 0.81 (EARL acceptance 0.34-0.57) and RC SUV50 ranged from 0.28 to 0.55 (EARL acceptance 0.27-0.43). Centres were not asked for additional reconstructions and the tolerance limits are being reconsidered with available data for prospective site inclusion. **Conclusion:** This study has enabled the identification of SUV calibration errors in 42% cen-

tres. Uniformity of RC values was observed, despite the tolerances of EARL were not fulfilled. Therefore, we conclude that a multicentre study requires a previous qualification for accurate quantification.

EP-05

e-Poster Area

Inflammation & Infection: Musculoskeletal Infection and Inflammation

EP-0052

Visual Versus Semiquantitative Analysis In ^{99m}Tc -HMPAO-labelled Leukocytes Scan To Diagnose Osteoarticular Infection

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Purpose: to compare the contribution of visual vs. semiquantitative analysis in ^{99m}Tc -HMPAO labelled white blood cells Scintigraphy (WBCS) for diagnosing osteoarticular infection.

Subjects & Methods: 88 patients (p) were studied to rule out osteomyelitis. Planar images in WBCS were acquired at 30min, 4 and 24h after labelled leukocyte reinjection. All images were assessed visually and semiquantitatively and compared with the final diagnosis established by culture and/or clinical follow-up of more than 12 months in all patients. Visual analysis: studies were classified as “negative for infection” if no uptake was seen in both 4h and 24h planar images or when the uptake was decreasing over time, and “positive for infection” when at least one focus of abnormal uptake, characterized by a time-dependent increase in radioactivity or an increase in size from 4h to 24h planar images, was observed. Semiquantitative analysis: in all images a region of interest (ROI) was drawn over the area of suspected infection and copied to presumed normal reference tissue. The mean counts per pixel in these ROIs were recorded to calculate target/background (T/B) ratios in both 4h and 24h images. The scan was considered negative for infection when the T/B ratios were similar or decreased with time; and was considered positive when the T/B ratio increased with time. Images were classified using different thresholds of increase ($\Delta\%$) in T/B ratio over time: ≥ 10 and $\geq 20\%$. $\Delta\% = (T/B_{24h} - T/B_{4h}) / T/B_{4h}$. The following data were analyzed: sensitivity (S), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (Ac). **Results:** The final clinical diagnosis showed infection in 23p and no infection in 65p. •Results obtained (%) in visual analysis: S:82.6; Sp:95.3; PPV:86.4, NPV:93.9 and Ac:96.1 •Results obtained (%) in semiquantitative analysis in groups with different $\Delta\%$: **$-\Delta\% \geq 10\%$:** S:47.8; Sp:75.4; PPV:40.7, PV:80.3 and Ac:68.2 **$-\Delta\% \geq 20\%$:** S:39.1; Sp:95.4; PPV:75, NPV:81.6 and Ac:80.7 **Conclusion:** The visual analysis obtained greater diagnostic precision than the semiquantitative method, which did not contribute to the diagnosis.

EP-0053

Semiquantitative Analysis In ^{99m}Tc -HMPAO-labelled White Blood Cells Scintigraphy For The Screening Of Osteoarticular Infection

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Purpose: to evaluate the usefulness of the semiquantitative analysis and its influence on the estimation of the post-test probability in white blood cells scintigraphy (WBCS) for the screening of the osteoarticular infection. **Subject & Methods:** 82 patients (p) were separated into two groups: Group 1, with joint prostheses (51p), and Group2, without prosthesis (31p). Planar images in WBCS were acquired at 30min, 4h and 8h post-reinjection of labelled leukocytes. In all scans, semiquantitative analysis was performed by drawing a ROI over the suspected infectious foci. Whenever possible, this ROI was mirrored automatically on presumed normal reference tissues. The mean counts per pixel in these ROIs were recorded and lesion-to-reference background (L/B) ratios were calculated both at 4h and 8h images. When the L/B ratios were similar or decreased with time the scan was considered negative for infection; when the L/B ratio increased with time, the scan was considered positive. Images were classified using different thresholds of percentage variation ($\Delta\%$) in L/B ratio over time: ≥ 10 and $\geq 20\%$. The $\Delta\%$ was calculated with these formula: $\Delta\% = (L/B_{8h} - L/B_{4h}) / L/B_{4h}$. The results were compared with the final diagnosis by culture and/or biopsy in 38p or clinical follow-up of 12 months in 44p. We analyzed sensitivity (S), specificity (Sp), positive and negative predictive values (PPV and NPV), diagnostic accuracy (Ac) and positive and negative post-test probability (P + and P-) for each $\Delta\%$. **Results:** The final diagnosis was: •Group1: infection in 7p and no infection in 44p. •Group2: infection in 12p and no infection in 19p. The values in the semiquantitative analysis were: **Conclusion:** The best diagnostic results were obtained in joint prostheses, determining that a $\Delta\% \geq 10\%$ seems to be enough to obtain high S and NPV, therefore, with a negative result we can rule out infection with greater impact on the post-test probability. The semiquantitative analysis seems to have a limited role in the rest of osteoarticular infections, although a $\Delta\% \geq 20\%$ should influence the positive post-test probability.

EP-0054

Effectiveness of Immunoscintigraphy with ^{99m}Tc -Antigranulocyte Antibody (Besilesomab) in Musculoskeletal Infection: Seven Years of Clinical Experience

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Purpose: Evaluate the effectiveness of the immunoscintigraphy with ^{99m}Tc labelled monoclonal antigranulocyte antibody (^{99m}Tc -besilesomab) in patients with suspected osteomyelitis.

Subjects and Methods: Retrospective study, it includes 106 procedures performed with suspected osteomyelitis (from February 2012 to October 2017). Initially, all patients underwent a three-phase bone scan scintigraphy (740 MBq of ^{99m}Tc -HDP) with immediate imaging acquisition, 5 minutes and 2 hours after its administration. Several days later, a immunoscintigraphy (740 MBq of ^{99m}Tc -besilesomab) was performed with the acquisition of planar images, 4 and 24 hours after its administration. Patients suspected of osteomyelitis were included, most of them with joint prostheses and other orthopedic hardware devices (78%). The final diagnosis it is based mainly on surgical reports (53%), microbiological confirmation (51%), pathological reports, other diagnostic imaging techniques (CT and MRI) and clinical follow-ups along at least 6 months. It has been excluded all those cases without enough data in the clinical history to reach a definitive diagnosis. It has been determined the sensitivity, specificity, accuracy, precision and negative predictive value of the test calculated according to the total number of procedures ($n = 106$) and for three defined patient groups: joint prostheses implanted ($n = 59$), orthopedic hardware of any type ($n = 83$) and patients suspected of osteomyelitis without orthopedic hardware ($n = 23$). **Results:** In the totality of the performed procedures, the ^{99m}Tc -besilesomab planar immunoscintigraphy showed a correct diagnosis in 95 cases (accuracy and precision of 0.89), indicating a sensitivity of 0.83, specificity of 0.93 and negative predictive value of 0.89. The group of patients with orthopedic hardware implanted showed a sensitivity and specificity, positive and negative predictive values similar to the total (0.82, 0.94, 0.90 and 0.88 respectively). In the patients who were exclusively carriers of joint prostheses, the sensitivity data were lower than the total (0.75) with a specificity of 0.91. The group of suspected patients of osteomyelitis without implanted orthopedic hardware revealed a better sensitivity and similar specificity compared with the rest of the groups and with the total (0.87 and 0.93 respectively). **Conclusions:** The clinical application of the immunoscintigraphy with ^{99m}Tc -besilesomab shows a diagnosis accuracy and precision in the suspicion of bone infection.

EP-0055

First-in-man Study in Bone Imaging with the New CZT SPECT Camera (VERITON®)

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Introduction: Based upon the breakthrough of cardiac CZT cameras, there is now an interest to apply this same technology to other SPECT imaging targets. Recently, an organ specific CZT-SPECT scanner (VERITON® Spectrum Dynamics, Caesarea, Israel) that utilizes a focused body/organ and contouring detector technology has been introduced, interesting for bone-imaging. In this study, we compare bone SPECT imaging between a conventional gamma camera and the VERITON® camera. **Subjects**

and Methods: With the approval of the ethical committee, on patients undergoing the routine clinical procedures as part of their clinically referred care, bone SPECT imaging have been acquired with a conventional gamma camera and the VERITON® camera, with no additional injection of radiopharmaceutical to patients. The bone HMDP SPECT data was acquired for 10min in body contouring mode using 12 CZT detectors and 240 to 300 projections per detector. The images were reconstructed using OSEM iterative algorithm with resolution recovery, CT prior, 2.46mm voxel size, 8 iterations, 8 subsets and Chang attenuation correction. **Results:** To date, bone SPECT imaging have been acquired in 18 patients (age 64+/-17) suspected of bone inflammatory or metastases and injected with 625.70 (+/-70) MBq of ^{99m}Tc -HMDP. Initial experience with the CZT-SPECT system has shown that it is possible to acquire bone SPECT image in approximately 10 minutes, same time required by a conventional SPECT system, but with a better resolution. Similar diagnosis was done in all the patients in both modalities. **Conclusion:** CZT technology has the potential to provide high resolution SPECT images with potentially lower time acquisition and/or radiation dose to the patient than when using conventional gamma camera technology. Further investigation is necessary to demonstrate the benefits of applying this new CZT-CT64 technology to SPECT bone-nuclear imaging.

EP-0056

Utility of the SPECT-CT in the detection of causes of post-surgical raquiagia

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Purpose: To analyze the usefulness of SPECT-CT in patients with spinal pain and previous history of spinal surgery. **Subjects and Methods:** We retrospectively analyzed the scintigraphic studies, performed during the last two years in our center, on 67 patients with spinal pain (46 women and 21 men), previously operated on the spine. The interval between the surgery and the scintigraphic study was: less than one year in 11 patients, between one and two years in 17 and more than two years in 39. All requests were made to rule out the main surgical complications: infection, osteosynthesis material mobilization and pseudoarthrosis. All of them underwent a bone scan with ^{99m}Tc -HDP (planar images in two phases and SPECT-CT in the metabolic phase) and a ^{67}Ga -scintigraphy (planar images and SPECT-CT if planar were positive). We divided positive results into four groups: infection, material mobilization, pseudoarthrosis and degenerative pathology (joint facets, interdiscal). **Results:** Twenty seven of the 67 patients studied had a negative scintigraphic study with double tracer, being in 24 of them true negatives. There were 3 false negative results which were subsequently operated on, because of low-grade infection. This give us a negative predictive value of 89%. Twenty of the 67 patients were subsequently operated on. Seventeen of them presented a previous positive scintigraphic study (8 degenerative pathologies, 6 mobilizations, 2 infections and 1 pseudoarthrosis), which

gives us a sensitivity of 85% in the detection of postoperative rachialgia causes. In 16 of the 20 patients operated on (80%) the identified area as causing pain was within the fused segment.

Conclusion: SPECT-CT is very useful in the study of postoperative rachialgia, presenting a high NPV to rule out the main surgical complications, and a high sensitivity in the detection of bone etiology of pain.

EP-0057

Comparative diagnostic accuracy of MRI and ^{99m}Tc Ubiquitin SPECT-CT in suspected post-operative spinal infection

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The diagnosis and localization of post-operative spinal infection remains a challenge for physicians as change in morphological feature after surgery renders MRI interpretation challenging. ^{99m}Tc -Ubiquitin has shown promising role in musculoskeletal infections, however, its role in diagnosing post-operative spinal infections has yet not been fully explored. **Purpose:** The purpose of this study was to evaluate and compare the diagnostic value of ^{99m}Tc labeled Ubiquitin SPET/CT scan and magnetic resonance imaging (MRI) in diagnosing post-operative spinal infection. **Methods:** From December 2013 to November 2017 patients with a clinical suspicion of infection in patients having prior spinal surgery, were included in the study. The ^{99m}Tc -Ubiquitin SPET/CT and MRI of the spine were performed within a 2-week time span. Imaging results were compared to the histopathology, culture and /or follow up data, for final clinical diagnosis. **Results:** Thirty-eight patients were included of whom 23 patients were diagnosed with active infection. MRI showed an overall sensitivity of 66.67 % and specificity of 85 %. Diagnostic accuracy was 76.32 %. ^{99m}Tc -SPECT-CT showed sensitivity of 72.22 % and specificity of 90%. While diagnostic accuracy was 81.58%. Inter-observer agreement was better with SPECT/CT compared with MRI as well. **Conclusions:** As compared to MRI, ^{99m}Tc -Ubiquitin SPECT/CT has slightly superior diagnostic value for detecting post-operative spinal infections.

EP-0058

Review Of The Results Of 18F-FDG PET / CT Studies Performed To Diagnosed Patients Of Histiocytosis

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Objective: To retrospectively evaluate the results of 18-FDG PET / CT studies performed on patients with histiocytosis, evaluate their use in the identification of new lesions and assess the therapeutic response. **Material and Methods:** Between 2013 and 2017, 22 PET / CT studies were performed on 10 patients diag-

nosed with histiocytosis for initial staging and treatment monitoring (3 girls, 3 boys between 2-13 years and 4 adults between 46-58 years old). The results of the PET / CT were reported and were reevaluated with CT, MRI, histology and clinical follow-up of the patient. **Results:** Of the 10 patients, 6 had type I Langerhans histiocytosis, 3 type II and 1 patient with mixed type. The extension it was monosystemic unifocal in 6 patients and multifocal monosystemic in 4, evolving one with multisystemic of low risk (lymphatic and multiple cutaneous affection). The systems with disease were lymphatic, cerebral, osseous, pulmonary, meningeal and nasopharyngeal. Of the 22 PET-CT studies, 6 were TP, 14 TN, 2 FP. Among the TP: in 3 cases the PET / CT detected more lesions than the CT, in one the PET also rejected the suggested disease in CT and NMR at the perirenal level that was shown negative and in another the PET / CT detected two lesions in the lung with a secondary metabolic behavior, a relationship with histiocytosis and a secondary one a bronchogenic cancer confirmed by biopsy. The FP were due to positive adenopathy in PET / CT and splenic involvement, which was followed by pathology care. There was 1 TN in a pathological echogenic sternal lesion, which was followed up with CT and after negative biopsy. In treatment monitoring there were only discrepancies between the PET / CT result and CT in two studies, demonstrating in the follow-up the absence of disease as described by PET. **Conclusions:** PET / CT is a useful tool, together with other diagnostic tests, in personal injuries and in monitoring, the therapeutic response of patients with histiocytosis.

EP-0059

Effect Of Microbiologic Characteristics Of Causative Micro-organisms On Patterns Of Labeled WBCs Uptake In Osteomyelitis

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Objective: To study the correlation between the scintigraphic pattern on labeled WBC scan and microbiology of the causative bacterial organisms in cases of non-vertebral osteomyelitis. **Methods:** Retrospective analysis of 25 cases referred to nuclear medicine department in Kuwait's general hospital. Bone scans and labeled WBC scans were cross-referenced with microbiological culture and inflammatory laboratory markers. **Results:** Total of 16 patients were eligible for this study, seven females and nine males. The diagnosis of osteomyelitis was confirmed on all patients based on their clinical, laboratory and positive culture results. Of these, seven patients had gram positive while nine patients had gram negative bacterial infection. The majority (85.7%) of gram-positive organisms had positive scans whereas only one-third (33.3%) of patients with gram-negative organisms had a positive scan. **Conclusion:** The pattern observed in this study shows that the false negative results of labeled-WBC scans are mainly noted in patients with gram-negative as opposed to gram-positive bacterial infections. This observation may be due to the anti-chemotactic factors that

gram-negative organisms are known to secrete, which may prevent the migration of labeled WBCs to the site of infection decreasing the accumulation of labeled WBCs and resulting in a false-negative scan.

EP-0060

Three Phase Bone Scintigraphy and SPECT-CT Findings of Spondylodiscitis

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The vertebral corpuses, intervertebral discs, paravertebral structures and spinal canal can be affected by infectious-inflammatory process named with spondylodiscitis which has potentially high morbidity and mortality rates. Staphylococci are the major cause of the disease, but other bacteria and fungi are among the other etiologic agents. Blood cultures, appropriate imaging and biopsy are essential steps for the diagnosis. Spinal infections can be aetiologically classified as pyogenic (bacterial), granulomatous (tuberculous or fungal) and parasitic (Echinococcosis). The purpose of this study is to compile the general three-phase bone scan and SPECT CT findings of patients with spondylodiscitis. **Material and Methods:** From October 2017 to March 2018, 18 patients (13 females, 5 male, mean age: 54) who were diagnosed with spondylodiscitis were included in the study. According to our clinical protocol, after the injection of the 20 ± 5 mCi (740 ± 185 MBq) Tc-99m labeled methylene diphosphonate, three-phase bone scintigraphy including perfusion images (frame/2 sec) in the first minute, the blood pool scan at 5 min and late whole body image at 3 hours together with SPECT-CT imaging of region of interest were performed to all patients. The agent we used In the area of pain blood pool scan for 2 seconds at one minute and a 5-minute view from this area after 5 minutes and usually after 3 ± 1 hours, full body scanning and SPECT-CT imaging are performed. **Results:** Rose Bengal Test for Brucella was negative for all patients in the study. Faintly increased activities in the affected area during the perfusion and blood pool images were noticed in all patients. Prominently increased activity uptake was detected in consecutive 2 vertebrae together with the intervertebral disc space in whole body images. Prominent sclerosis with endplate destruction in the affected planes of the corpus vertebra was noticed on the SPECT-CT scans. Decrease in heights of the consecutive vertebrae with disc hypodensity and narrowing intervertebral disc space were another findings. Interestingly, increased osteoblastic activity were also detected in the intervertebral disc space in addition to affected parts of the consecutive vertebrae. **Conclusion:** Although the diagnosis of the spondylodiscitis remains challenging due to an insidious onset, with subtle and misleading clinical features, three-phase bone scintigraphy with technetium-99m is very sensitive (90%) within a few days of infection onset and addition of conventional CT offers even higher accuracy in the diagnosis of the spondylodiscitis. Hence, SPECT-CT provides valuable morphological information about the underlying pathophysiological mechanisms in the increased osteoblastic activities on the bone scan.

EP-0061

Tc99m-Ciprofloxacin Scintigraphy In The Diagnosis Of Prosthetic Hip Joint Infection

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Introduction: Hip prosthesis implantation has some complications specially prosthetic infection. This study was conducted to evaluate the usefulness of Tc99m-Ciprofloxacin scintigraphy (CIP-Scan) in detection of infectious process in patients with hip arthroplasty. **Methods:** Twenty three patients (aged 24-84 years) with painful hip prosthesis underwent CIP-Scan. CIP-Scan was performed at 1, 4, and 24 h after intravenous injection of 370 MBq of Tc99m-Ciprofloxacin. Both qualitative and semi-quantitative (target-to-background ratio) methods were used to interpret the images. Target-to-background ratio was calculated based on geometric mean of region of interests. Final diagnosis of infection was confirmed by active follow-up, surgical findings, macroscopic evidence of purulent material or positive microbiological analysis. **Results:** The best results were obtained from the 4-h as well as 24-h images specially 4-h images. The sensitivity, specificity, negative predictive value, and positive predictive value were 88.9%, 84.6%, 88.8%, and 92.8% with an accuracy 91.3%. ROC curve analysis for 4-h images showed a good cut-off value: 1.43. Area under the curve was 0.86. **Conclusion:** CIP-Scan can be useful for differentiating infection from the aseptic loosening of the hip prosthesis. 4-h images were recommended for interpretation.

EP-0062

Silent myocarditis with 18F-FDG-PET/CT in systemic sclerosis

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Aim: Primary cardiac manifestation is a common complication of systemic sclerosis (SSc). In SSc the immuno-inflammatory damage leads to myocardial fibrosis and consequent myocardial dysfunction. Clinically evident heart involvement appears as a bad prognostic factor, responsible for up to 30 % of SSc-related mortality. 18F-FDG PET/CT plays an increasing role in the diagnostics of inflammatory disorders with myocardial manifestation. The aim of this study was to assess the diagnostic utility of cardiac 18F-FDG PET/CT in patients with SSc, and to evaluate simultaneously results of 2Dimensional Speckle Tracking Echocardiography (STE). **Materials and Methods:** 16 consecutive patients with systemic sclerosis (age: 59 ± 8 y, 14 female, 2 male) and 9 control patients (age: 46 ± 18 y, 4 female, 5 male) were enrolled in the study. We excluded the patients of known heart failure from different origin, and exclude patients with systemic sclerosis related secondary heart involvement. After high-fat, high-protein, low carbohydrate - diet (previous 24 hours) and

extended fasting (6 hours) cardiac 18F-FDG-PET/CT acquisition was performed in 2D mode. Within 24 hours all systemic sclerosis patients underwent comprehensive echocardiography focusing on left ventricular myocardial mechanics applying STE. The recommended 17 segment model was used to assess the 18F-FDG activity and for the calculation of myocardial strain as well. On 18F-FDG PET data the segmental myocardial 18-FDG uptake in body weight SUV (g/ml) by PMOD software was calculated and diversity index (DI: standard deviation of SUV divided with mean SUV) were calculated as well. The strain values were measured offline by speckle tracking EchoPAC software. **Results:** In eight patients (8/16) showed significantly increased 18F-FDG uptake (4.09 ± 2.47 g/ml) with significantly higher diversity index (0.13 ± 0.02) in the myocardium. In all control patients and in 8 patients with systemic sclerosis the cardiac uptake was near equal or lower than blood-pool activity. The FDG-uptake in 8 “PET-negative” systemic sclerosis patients and in control subjects were not differed significantly (1.95 ± 0.28 g/ml, DI: 0.05 ± 0.01 versus 1.81 ± 0.26 g/ml, DI: 0.05 ± 0.02 $p < 0.01$). In “PET-positive” patients global left ventricular longitudinal strain values ($17.02 \pm 3.49\%$ vs. $18.08 \pm 3.76\%$) were lower than in PET-negative cases. In 17 segmental myocardial analysis in FDG-uptake and strain abnormalities showed small differences, caused by different pathomechanism of detected inflammation and fibrosis. **Conclusion:** In systemic sclerosis 18F-FDG PET/CT is a promising imaging tool to detect early stage silent myocardial inflammation. In the active condition STE provides a simple, non-invasive modality to detect metabolic activity related subtle mechanical changes in myocardium.

EP-0063

Screening for Cancer In Autoimmune Myopathies with FDG-PET/CT

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Background: The indications and modalities for cancer screening in autoimmune myopathies (AIM) remain to be clarified. Positron emission tomography with fluorine-18 fluorodeoxyglucose integrated with computed tomography (FDG-PET/CT) was proposed as a practical alternative to conventional modalities for cancer screening in paraneoplastic settings. The studies' goal was to determine the performance characteristics of FDG-PET/CT versus conventional modalities for cancer screening in AIM.

Methods: 100 FDG-PET/CT scan results in 63 AIM subjects without history of cancer from one academic center in Montreal, Canada were retrospectively reviewed. Demographic, clinical and conventional cancer screening test (physical and gynecologic examination, blood work (complete blood count, liver function tests, urinalysis), chest X-ray, gastroscopy, colonoscopy, computed tomography of the thorax/abdomen/pelvis, mammography, endovaginal ultrasound and tumour markers) data were retrieved from electronic medical records. Subjects were classified into AIM subsets using novel classification criteria (Allenbach et al. *Neuropathol Appl Neurobiol* 2017). Diagnostic screening tests were classified whether malignancies were suspected and present (true positive), suspected and absent (false

positive), not suspected and absent (true negative) and not suspected and present (false negative). **Results:** The study cohort included 31/63 dermatomyositis (DM), 25/63 overlap myositis (OM), 1/63 immune-mediated necrotizing myopathy (IMNM), 1/63 polymyositis (PM), 1/63 orbital myositis and 4/63 unspecified myositis subjects. 3/31 (10%) DM subjects were diagnosed with malignancies: cutaneous squamous cell carcinoma (cSCC), invasive ductal carcinoma and multiple myeloma. 0/25 of the overlap myositis and 0/7 of the other subjects were diagnosed with cancer after an average follow-up period of 3.5 years. FDG-PET/CT did not detect and missed all the 3 malignancies. 13/100 (13%) false positive FDG-PET/CT scans led to 8 unnecessary biopsies and 11 additional investigations. Conventional screening detected the 3 malignancies: cSCC by physical exam, breast cancer by mammography and multiple myeloma by complete blood count. 22/62 (35.5%) false positive conventional screenings led to 10 additional investigations and 12 biopsies (including 7 investigational colonoscopy and gastroscopy biopsies). The false positive CT scans (10/50, 20%) contributed to the 10 additional investigations and to 2 biopsies. **Discussion/Conclusion:** Since the risk of cancer in AIM differs by subset, cancer screening is likely to be most useful in high-risk subsets, such as DM. In addition, FDG-PET/CT does not appear to be a useful cancer screening modality in AIM and carries potential harms associated with unnecessary invasive investigations. These results, if replicated in a larger, multi-centered study, carry significant consequences in terms of optimal management of AIM and health resource utilization.

EP-0064

Skeletal muscle volume determined by semi-automated CT segmentation in patients with idiopathic inflammatory myopathy

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Aim: Idiopathic inflammatory myopathy (IIM) is clinically characterized by skeletal muscle weakness and atrophy as well as impaired physical function. Besides inflammation, muscle biopsy may reveal reduced capillary density, degeneration, fibrosis, and histological signs of atrophy. We determined thigh muscle volume using non-invasive semi-automated CT segmentation to quantify muscle atrophy in patients with IIM. **Materials and Methods:** Lower body SPECT/CT was performed as part of a study on 99mTc-pyrophosphate muscular uptake in 84 IIM patients and 46 gender and age-matched healthy control subjects. In 71 patients, the IIM had been longstanding and was medically treated (“chronic”), 13 other IIM patients were newly diagnosed and treatment-naïve (“acute”). Muscle function was tested clinically using MMT8. Muscle volume was determined

by CT scans and semi-automated segmentation of the thigh muscle: Demarcation lines 5 cm below the trochanter major and 8 cm above the knee joint were defined manually. The muscle volume in between was automatically determined as voxels with values of 0–90 Hounsfield units. The correlation of muscle function with muscle volume was investigated by multivariate regression analysis of muscle volume per length, ^{99m}Tc -pyrophosphate uptake, age and sex. “Acute” and “chronic” subsets were also analyzed separately. **Results:** The thigh muscle volume of patients was 20% less than that of controls; i.e. 3561 ± 165 mL and 4435 ± 237 mL, respectively ($p=0.003$). Considering the length of the volume of interest, the relative difference was similar; 14.2 ± 0.6 mL/mm in patients versus 17.7 ± 0.7 mL/mm in controls ($p<0.001$). Muscle function could in part ($R^2=0.31$) be explained by a regression model that included muscle volume per length, ^{99m}Tc -pyrophosphate uptake, age, and sex; for every increase of 1 mL/mm, MMT8 increased by 0.46 ($p=0.006$). In subgroup analyses, the volume per length of acute and chronic patients was lower than in healthy controls, but did not differ; being 14.5 ± 1.5 and 14.1 ± 0.63 mL/mm, respectively ($p=0.79$). **Conclusion:** Semi-automated CT segmentation was a feasible method for determining thigh muscle volume. IIM patients had smaller muscle volume than controls, even in patients with recent onset of IIM. Reduced muscle function was in part explained by this lower muscle volume. Hence, muscle volume may be clinically relevant and should presumably be given more attention. Given the findings in patients with recent onset IIM, muscle volume determination by CT segmentation might be a clinically useful parameter that can be determined as part of SPECT/CT or PET/CT and thus contribute to the diagnostic work-up in patients with suspected IIM.

EP-06

e-Poster Area

Inflammation & Infection: Vascular and Soft Tissues Infection and Inflammation

EP-0065

Quantitative analysis of 18F-FDG uptake by PET-CT in the Diagnosis of Cardiac Sarcoidosis

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Introduction: PET-CT imaging using 18F-FDG is a very important modality to diagnose patients with cardiac sarcoidosis (CS). The aim of this study was to evaluate various quantitative parameters and assess their ability to accurately diagnose the condition within the myocardium. **Methods:** 39 patients (21 males - 18 females, mean age: 58 ± 15) with suspected CS underwent 18F-FDG imaging using a GE Discovery 710 PET-CT scanner between December 2016 and February 2018. Injected activity was 355 ± 56 MBq. All patients followed a low carbohydrate and high fat diet on the day before and an 18 hours fasting period. Prior to this scan, patients had a Rest Myocardial Perfusion Scan (MPS). CS was confirmed from abnormal imaging, biopsy and

clinical findings. Measurements of SUVmax of the left ventricular blood pool (LVBP), heart and liver were performed using the GE AW suite. A VOI covering the heart was created to measure the TLG or cardiac metabolic activity (CMA) using the LVBP SUVmax as threshold and heart SUVmax. The heart SUVmax/LVBP SUVmax and heart SUVmax/liver SUVmax ratios were calculated. The LVEF% and LV phase SD from the perfusion study were also measured using QPS-QGS (Cedars-Sinai Medical Center). Data were checked for normality and logarithmically transformed. All statistical analysis was performed using SPSS (version 23 IBM). **Results:** Heart SUVmax was 10.9 ± 5.4 and 3.7 ± 1.5 ($p<0.001$) for the positive and negative group respectively. CMA was 1532 ± 1040 and 225 ± 215 ($p<0.001$) for the positive and negative group respectively. Heart SUVmax/LVBP SUVmax was 4.7 ± 2.4 and 1.7 ± 0.7 ($p<0.001$) for the positive and negative group respectively. Multivariate data analysis for diagnosing CS showed that the ratios: heart SUVmax/LVBP SUVmax ($p = 0.000$), heart SUVmax/liver SUVmax ($p = 0.000$), heart SUVmax ($p=0.000$) and CMA ($p=0.000$) where the only significant predictors of the disease. ROC analysis showed that the area under the curve (AUC) for these parameters were: 0.920 for heart SUVmax/LVBP SUVmax, 0.953 for heart SUVmax/liver SUVmax, 0.942 for heart SUVmax, 0.956 for CMA, 0.407 LV phase SD and 0.431 for LVEF. **Conclusion:** Quantitative Parameters of FDG uptake have been shown to predict active cardiac sarcoidosis. No correlation was shown between the LV phase SD and the SUVmax.

EP-0066

Evaluation of Left Ventricular Assist Device (LVAD) Infection with 18F-FDG PET/CT: Normal Variants and Diagnostic Performance

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Objectives: Left ventricular assist devices (LVAD) are battery operated pumps used in patients with heart failure to maintain adequate systemic circulation. LVAD infections are especially difficult to diagnose and are associated to high morbidity and mortality. Nowadays, FDG-PET/CT imaging is often included in the investigation of LVAD infections. However, interpretation of FDG-PET/CT is complicated by post-operative inflammation, CT artifacts, and lack of interpretation criteria. In this study, we assess performance of FDG-PET/CT imaging to differentiate between normal and infected LVAD. **Methods:** 32 FDG-PET/CT scans performed in 14 subjects with a LVAD (HeartMate II) were retrospectively reviewed. Imaging was performed following a myocardial suppression protocol including prolonged fasting, high-fat/low-carbohydrate diet, and intravenous heparin. Qualitative and semi-quantitative assessment of FDG-PET/CT with metabolic distribution (SUVmax) and metabolic volume were performed for each component (driveline, outflow cannula, and pocket housing). Non-LVAD infections and antibiotics treatments were documented. Final diagnosis was based on a composite of outcome information, surgical observations, histopathological samples, and INTERMACS classification. **Results:** FDG-PET/CT were performed between 14 and 919 days after LVAD installation (285 ± 264 days). Four (28.6%) subjects had LVAD infection

(3 drivelines, 2 outflow cannulas, and 3 pocket housings) based on final diagnosis. Non-LVAD infections were identified on 9 scans (5 subjects). In non-infected subjects, FDG uptake appears to stabilize after approximately 1 year in all components with homogenization of the distribution over time. SUVmax were significantly higher ($p<0.001$) in infected components compared to non-infected components. Metabolic volumes were significantly higher in infected drivelines ($p<0.001$) and pocket housings ($p=0.002$) while not significantly different ($p=0.68$) for outflow cannulas. Optimal SUVmax cutoffs were 4.0 for driveline, 10.0 for outflow cannulas, and 6.5 for pocket housing. Using these cutoffs, sensitivity, specificity, and accuracy were 100%, 88%, and 78% for driveline, 100%, 100%, and 100% for outflow cannulas, and 100%, 90%, and 91% for pocket housing. Metabolic volume performed equally or better compared to SUVmax for driveline and pocket housing. For outflow cannulas, metabolic volume accuracy was inferior to SUVmax (69% vs 100%). **Conclusion:** We showed that FDG-PET/CT is an accurate modality for assessment of LVAD infections in a broad range of post implantation time interval. Knowledge of the various uptake patterns is crucial in order to provide accurate interpretation. Over time, FDG uptake in the different components becomes more homogeneous and stabilizes, suggesting that serial imaging could further improve diagnostic performance.

EP-0067

18F-FDG PET/CT in visceral leishmaniasis: uptake patterns in view of recent outbreaks in Northern Italy

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Purpose/Introduction: Visceral leishmaniasis (VL) is the most severe manifestation of leishmaniasis, a vector-borne disease. VL may present with aspecific symptoms, mimicking other disorders, but can rapidly progress into a more severe, life-threatening condition. VL is often underdiagnosed and considered an imported disease in western countries, however outbreaks of infection have been recently reported in Italy and Spain. Aim of the present study was to describe FDG uptake patterns in patients (pts) who underwent a PET/CT and were later diagnosed with VL. **Subjects & Methods:** A retrospective mono-centric Ethical Committee-approved study of pts who underwent FDG PET/CT between 2008 and 2017 and were later diagnosed with was performed. All pts presented non-specific clinical symptoms (e.g. fever of unknown origin, chronic feverish symptoms, pancytopenia, splenomegaly). FDG PET/CT scan was performed following standard EANM procedure. Semi-quantitative parameters were calculated in FDG-positive lesions: SUVmax, SUVmax spleen/SUVmax liver ratio (SLR), SUVmax focal/diffuse spleen ratio (FDR). Microbiological diagnosis of VL was confirmed in

all pts. **Results:** Overall, 23 pts matched the inclusion criteria (median age=60ys [24-82]). PET/CT was negative in 2 pts (immuno-compromised) and positive in 21/23 (6 pts spleen only, 7 pts spleen+bone marrow (BM), 4 pts spleen+BM+nodes, 1 pt spleen+BM+lung, 1pt BM+nodes, 2 pts nodes only). Splenic involvement was demonstrated in 20/21 (95%). Two different patterns of splenic uptake were established: diffuse (13/20 pts, mean spleen SUVmax=7.3±4.2 [4.0-14.1], mean STL=2.2±1.6 [1.3-6.7]) and focal over diffuse (7/20 pts, mean SUVmax=12.6±4.5 [9.5-20.5], mean STL=2.8±0.8 [2.1-4.4], mean FDR=2.1±0.8 [1.2-3.6]). Focal splenic lesions with surrounding physiological splenic FDG distribution were not observed. Extra-splenic FDG-avid findings were detected in 15/21 pts (65%): bone marrow in 13/15 pts (diffuse pattern, mean SUVmax=4.0±1.3 [2.8-6.0]), nodes in 7/15 pts and lung in 1/15 pts. **Discussion/Conclusion:** PET/CT demonstrated splenic FDG uptake in all non-immunocompromised patients with VL. Two patterns of pathological splenic FDG uptake (diffuse or focal over diffuse) were observed and were indistinguishable from splenic involvement by other disorders (such as lymphoma, sarcoidosis, tuberculosis). The most frequent extra-splenic FDG-positive site was the BM followed by nodal involvement. Considering the potential aggressiveness of the disease and the recent outbreaks registered in north-eastern Italy, VL should be considered in the differential diagnosis of FDG positive splenic findings in patients from endemic areas or reporting travels to endemic countries. Microbiological confirmation remains mandatory in all cases.

EP-0068

FDG PET / CT in infective endocarditis, our experience

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Background: Infective endocarditis (IE) is a potentially serious and lethal infection; detecting this pathology on time is crucial for proper and timely treatment. **Aim:** To evaluate the role of 18F-FDG PET/CT in the diagnosis of infectious endocarditis (IE) **Material and Methods:** We retrospective review 33 Patients (p) with clinical suspicion of IE who had undergone 18F-FDG PET/CT examinations at our center between January 2012-December 2017, 25 men, with mean ages 63.4 years. We evaluated in all patients the clinical symptoms, clinical history, presence of acute phase reactants, microbiology, echocardiography trans-thoracic or/and trans-esophageal, other images techniques such as CT or MRI and FDG PET/CT. The diagnosis of endocarditis was made according to the Duke criteria and the follow-up. **Results:** 14 out of 33 patients (42%) had a confirmed diagnosis of IE. 3p had prosthetic valve (PV), 3p with prosthetic tubes after corrective cardiac malformation surgery and 2p with pacemaker; PET/CT was positive in 8/14 (all of them with some cardiac dispositive and positive blood culture), 3p of them showed also pulmonary septic embolism. FDG PET/CT was false positive 2p/33. Echocardiography was positive in 12/14p and false positive in 4p/33. Echocardiography showed a higher sensitivity as a diagnostic tool for the detection of IE compared to FDG-PET-CT (75% vs.

53%), but less specificity 78% vs 88% respectively. Blood culture was positive in 24/33 patients, 13p with IE. Staphylococcus aureus was the frequent germs implicated in the process. FDG PET/CT also show the site of infections in others 7p with blood culture positive; one of them was a patient with native valve, with FDG PET-CT false negative at cardiac valves, but with muscular infectious embolism in lower extremities and abdominal wall. In the follow-up 7p/33 died, 2 of them with IE confirmed and the others due to multi-organs failure, secondary to systemic hematogenous infection, for multi-resistant germs. **Conclusion:** FDG PET/CT is good tool that improve diagnostic accuracy in IE, especially in patients with PV and other cardiac prosthesis and devices. FDG PET/CT also allow diagnose septic distant embolisms, even in patients with native valves IE.

EP-0069

Progressive Accumulation of Radiolabeled White Cells in Scans Performed for Suspected Vascular Prosthetic Graft Infections

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Introduction: Vascular graft infection is a serious complication which can be diagnosed using radiolabeled white cell scintigraphy (WCS). In a recent scan performed for suspected vascular graft infection (SVGI) in our department, increased white cell accumulation around the graft had cleared by 24 hours. Interpretation criteria proposed by a recent multicenter study would have incorrectly classified this scan as negative for infection. Importantly, participants in that study did not include any patients with SVGI. No research has to date investigated whether assessment of progressive white cell accumulation improves the accuracy of WCS performed for SVGI. **Subjects and Methods:** A retrospective analysis was performed of all WCS scans performed for SVGI between January 2004 and March 2018. Studies were only included if both 3-hr and 24-hr imaging were available. Initial 3-hr images were first classified as positive or negative on the basis of presence or absence of white cell activity at the site of the vascular graft. Next, by comparing 24-hr and 3-hr images, studies were scored as either positive or negative based on the presence or absence of progressive white cell accumulation: both visually, and by calculating an accumulation index using suitable regions of interest with count values corrected for decay. A composite reference standard upon which the final diagnosis was made was based on a combination of microbiological, clinical and imaging follow up. **Results:** Provisional analysis has to date been performed in 10 cases (mean age: 59.9 years, 4 females). Six of these had proven infection while in 4 infection was excluded. Visual interpretation of 3-hr images alone classified all 10 cases correctly. Visual interpretation of white cell accumulation over 24-hr classified 9 cases correctly and resulted in 1 false negative. Finally, interpretation based on an accumulation index alone correctly classified 5 cases but resulted in 3 false negatives and 2 false positives. **Conclusion:** Based on preliminary data, there is no evidence to suggest that assessment of progressive white cell accumulation up until 24 hours improves diagnostic accuracy of WCS for SVGI.

EP-0070

Mapping of ^{18}F -FDG PET/CT patterns of tuberculosis in a sub-Saharan region

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Aim: Tuberculosis (TB) is the most common infectious disease in developing countries. Positron emission tomography computed tomography (PET/CT) using ^{18}F - fluorodeoxyglucose (FDG) offers a non-invasive way to assess the whole body infection and inflammatory processes. The goal of this study was to describe the patterns of non-treated TB in a large cohort of patients undergoing baseline ^{18}F -FDG PET/CT imaging. **Methods and Materials:** Participants from two ongoing prospective studies were selected. Data from ART-naïve HIV infected participants with baseline FDG PET-CT imaging prior to ART initiation and having a GeneXpert positive pulmonary TB, as well as a similar HIV negative group from a phase-2 randomized trial that aims to measure the efficacy of host directed therapy (HDT) were assessed. In total, data were available for 154 participants. The lung involvement was assessed as bilateral or unilateral and specific lung lobes were also assessed. The highest SUV and total lesion glycolysis (TLG) in each region was measured and comparison between regions was determined. **Results:** The mean age was 35.6 ± 9.8 years (19-63), 73.4% were male and 27.9% had underlying HIV infection. Active TB was commonly seen in both lung fields (69.5%) rather than unilateral lung involvement (25.5%); [$p < 0.001$]. The left lung was more affected (60%) than the right ($p < 0.001$) in those with unilateral parenchymal involvement. Lobar involvement was distributed as follows: LUL (35.71%), LLL (12.99%), RUL (29.22%), RML (5.84%) and RLL (11.6%) and the remainder had no pulmonary active uptake. There was a significant difference in the presence of lymph nodes as well as their related SUVs and TLGs in participants with associated HIV vs those with TB alone ($p < 0.001$; $p < 0.001$ and $p = 0.03$). The highest SUV and TLG in the lung parenchyma were predictors of HIV negative status (OR=0.82201; 95%CI: 0.74494-0.90707, $p < 0.0001$ and OR=0.99128; 95% CI: 0.98258-0.99999, $p = 0.01$). **Conclusion:** Pulmonary TB in sub-Saharan Africa affects a younger and more active population. About two-thirds of those with active disease have bilateral lung involvement, particularly in the upper lobes. While unilateral lung involvement is seen in a quarter of patients, the left lung appears to be the preferential site for disease. While higher SUVs and TLGs on ^{18}F -FDG PET/CT imaging are seen in lymph nodes of HIV infected participants the reverse was seen in pulmonary TB. The higher these molecular imaging parameters, the more likely pulmonary TB is not associated with HIV infection

EP-0071

Role of ^{18}F -FDG PET-CT in the differentiation of nodal involvement in patients with Tuberculosis with or without HIV infection

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Aim: Tuberculosis (TB) is a leading cause of morbidity and mortality in South Africa. Nodal disease is often seen in both HIV infected HIV uninfected patients with TB. PET/CT with ¹⁸F-FDG can be used as a novel diagnostic method for imaging granulomatous inflammation. The aim of this study is to determine the ability of ¹⁸F-FDG PET-CT in distinguishing nodal involvement in TB with or without associated HIV infection. **Methods and Materials:** We used a sub-set of participants from two ongoing prospective studies. Group 1 consisted of a cohort of ART-naïve HIV infected participants being treated with standard four drug therapy for GeneXpert positive pulmonary TB and who had ¹⁸F-FDG PET-CT imaging prior to ART initiation. Group 2 (G2) consisted of a cohort from a phase-2 randomized trial that aims to measure the efficacy of host directed therapy (HDT) who are HIV negative and had a baseline ¹⁸F-FDG PET-CT. Data were analyzed from 84 participants, 42 in each group. Active nodes were classified in six anatomical sites and their numbers compared. The maximum SUVs and the total lesion glycolysis (TLGs) were determined and compared at each site. Differences of SUVs and TLGs were measured in all sites. Considering the bulk of nodal disease as “tumor masses”, we also determined and compared their metabolic tumor volume (MTVs). **Results:** The mean age was 37 years in G1 (22–54) as well as in G2 (23–57) with a dominance in female participants in G1 (60% vs 31%) compared to G2 (p=0.009). Participants in G1 had more nodes than those in G2 in the cervical (S1), superior mediastinum (S2), aortic (S3), hilar (S4), inferior mediastinum (S5) and abdomino-pelvis (S6) sites [p=0.001; p=0.022; p=0.002; p=0.007; p=0.010 & p<0.0001 respectively]. After adjustment for sex, those with HIV infection had significantly higher SUVs, TLGs and MTVs in S1 (all with p<0.001) and S6 (all with p<0.001), suggesting that these factors are potential predictors of positive HIV status. **Conclusion:** Significantly higher number of active nodes in TB associated with HIV infection is noted. The use of ¹⁸F-FDG PET-CT may be able to distinguish the underlying cause of lymphadenopathy seen in patients affected with TB with or without HIV association. Parameters such as SUVs, TLGs and MTVs of the nodes may potentially be assessed as “molecular imaging biopsy” in a large study.

EP-0072

Tc-HMPAO labeled leucocyte scan in the diagnosis of vascular graft infection

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Introduction-Aim: Vascular graft infection (VGI) is a rare, but serious complication of vascular surgery. Diagnosis may be a challenge and delay is associated with high morbidity and mortality. The study is aiming to evaluate Tc99m-HMPAO-labeled leucocyte scan (LS) in the diagnosis of VGI. **Patients and Methods:** Fifty four patients (all males, aged 62.0±13.9 years) with clinical suspicion of VGI submitted to LS were enrolled in the study. Among them, 23 had aortic grafts, 9 aortobisiliac, 12 aortofemoral, 5 ileofemoral, 2 iliac, 1 axillofemoral and 2 popliteal artery grafts. Underlying disease was aortic aneurysm in 25, obstructive vascular disease in 13 and traumatic vascular rupture in 6 patients. Median time between graft implantation and imaging was 34.8 months (IQR 77.3 months). LS images were acquired 1, 4 and 24 hours after injection of labeled leucocytes. SPECT imaging was additionally performed in 10 patients and SPECT/CT imaging in 24 patients. Increased leucocyte uptake in the region of vascular graft, higher than the surrounding blood vessels or the contralateral site, or increasing over time, was considered positive for VGI. Final diagnosis was based on long-term clinical follow-up or surgical and microbiological findings. **Results:** Among 54 vascular grafts investigated, 16 infected and 38 non-infected grafts were finally diagnosed. Planar LS results were as follows: TP 10, TN 36, FP 1, FN 7. FN results were thought to result from slow leucocyte accumulation rate at sites of low-grade or chronic infection. Sensitivity, specificity, accuracy, positive (PPV) and negative predictive value (NPV) of planar LS for diagnosing VGI were 58.8%, 97.3%, 85.2%, 90.9% and 83.7%, respectively. SPECT/CT addition in 24 patients improved all the above values to 60.0%, 100%, 91.7%, 100% and 90.5%, respectively. Although SPECT/CT addition changed the diagnosis of planar LS in only 2 patients, it was however found helpful in 15/24 patients for accurate localization of infection and also for detection of coexisting pathology or other sites of infection in febrile patients. **Conclusion:** Tc99m-HMPAO-labeled leucocyte scan, although moderately sensitive, is a very specific imaging modality for diagnosing vascular graft infection. The addition of SPECT/CT is helpful in accurate anatomical localization of infection and also for identification of coexisting pathology potentially relevant to patient's symptoms.

EP-0073

Fab' fragments of ^{99m}Tc-labeled anti-granulocyte monoclonal antibodies in vascular graft infection

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Introduction: Vascular graft infection is an uncommon but serious complication, with a high mortality rate. Even though it can be evident early on, it is usually only diagnosed weeks to months after surgery, since signs and symptoms are often nonspecific and detection by conventional radiology (CT, ultrasound) is difficult. It is therefore pertinent to investigate the diagnostic validity of other imaging tests. **Objectives:** Deter-

mine the diagnostic value of Fab' fragments of ^{99m}Tc -labeled anti-granulocyte monoclonal antibodies (LeukoScan®) in vascular graft infection. **Subjects and Methods:** Two independent observers retrospectively analyzed Leukoscan® scintigraphies performed since March 2009 for suspected vascular graft infection. Following i.v. injection of 1110 MBq, whole body images (4 h and 24 h after injection) and SPECT-CT were acquired. Clinical records were also analyzed, with particular focus on surgical findings and clinical follow-up. Grafts were classified as infected if there were signs of infection detected during surgery or a positive microbiological culture of the graft. Grafts classified as non-infected if there were no suggestive surgical findings and negative cultures, or, in those patients whose graft was not removed, if no signs or symptoms of infection developed in the clinical follow-up. **Results:** 52 cases were analyzed. 29 patients underwent surgery to remove the vascular graft, 14 of whom had signs of infection in surgery, and 14 had positive microbiological cultures (not always coinciding), with a total of 26 patients having infected grafts. Patients who didn't undergo surgery and those without surgical signs of infection or positive cultures were evaluated as to the response to prescribed therapy and clinical follow-up. After data processing, Leukoscan® scintigraphy showed a sensitivity of 84,6% (0,72-0,93) and a specificity of 48,1% (0,34-0,62). **Conclusion:** To our knowledge, there is no other study that has validated Leukoscan® for the detection of vascular prosthetic infection. Despite its low specificity, our results place the scintigraphy with Fab' fragments of ^{99m}Tc -labeled anti-granulocyte monoclonal antibodies as a valid imaging exam in this context.

EP-0074

Comparison of ^{18}F -FDG PET-CT and ^{99m}Tc -HMPAO Labelled Leukocytes in the evaluation of fever of infectious origin

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Purpose: To compare the accuracy of positron emission tomography (PET) using ^{18}F -FDG (Fluorodeoxyglucose) PET-CT with ^{99m}Tc -HMPAO-labelled leucocytes scintigraphy (LS)/SPECT-CT in group of patients (p) with high suspicion of fever of infectious origin. **Subjects & Methods:** Retrospective review of 21 consecutive patients (15 men and 6 women; mean age 73.48, range 61-87) from January 2016 until January 2018. All of them had high morbidity: 21 cardiovascular risk factors, 15 heart diseases, 7 oncologic diseases and 3 chronic obstructive pulmonary disease (COPD). They were in hospital with high suspicion of fever of infectious origin, high persistent reactive C protein (RCP) value, leukocytosis and bad response to antibiotic therapy. Eleven patients (p) carried devices: 2 prosthetic valves, 8 endovascular prosthesis/bypass, 2 cardiovascular implantable electronic device (CIED) and 1 hip joint prosthesis. All of them underwent to (^{18}F -FDG)PET-CT and LS/SPECT-CT and microbiological tests. Furthermore, 15p had transthoracic and transesophageal echocardiography and 17p other radiological studies. We followed-up them after hospital discharge between 3 to 24 months. **Results:**

Abnormal uptake was seen in 3/21 (14.3%) and 14/21 (61.9%) patients on LS/SPECT-CT and (^{18}F -FDG)PET-CT respectively. Nine patients with abnormal uptake (^{18}F -FDG)PET-CT study, carried devices, and two of them had LS/SPECT-CT positive also. The causes of positive PET in the other patients were: abscess (n=3), pneumonia (n=1); pancolitis (n=1). Of 7p without definitive diagnosis for infection on PET-CT and LS/SPECT-CT: urinary tract infection and sepsis (n=2), bacteraemia (n=2), liver abscess identified on RMN (n=1); no specific diagnosis was reached in 2 patients. In five cases, complementary tests were positive: 1 echocardiogram (mitral valve endocarditis), 1 RMN (liver abscess), 1 soft tissue ultrasound (gluteal abscess), 2 CT (bypass infection and joint prosthesis infection), all of them demonstrated with PET except for liver abscess. Six patients died in hospital due to septic shock (n = 3) and persistent bacteraemia with no response to antibiotics (n = 3). Only one patient was admitted one month after discharge due to a new episode of infection of the vascular prosthesis that required replacement. The results thus showed an overall sensitivity of 63.2% for PET and 16.3% for LS. The overall specificity for FDG-PET was 50% as against 100% for LS. PET had a PPV of 92.3% and NPV of 12.5% whereas LS has a PPV of 66.6% and NPV of 16.7%. **Conclusion:** (^{18}F -FDG)PET-CT appears to be more valuable technique for the diagnosis of device infection with high PPV.

EP-0075

^{18}F -FDG PET/CT in the Diagnostics Of Cardiovascular Infections

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Purpose: To investigate the diagnostic performance of ^{18}F -FDG PET/CT in patients with suspected prosthetic valve endocarditis, aortic prosthesis infection and cardiovascular implantable electronic device infection. **Materials and Methods:** This prospective analysis included results of ^{18}F -FDG PET/CT examinations performed in 20 patients with fever of unknown origin and suspected cardiovascular infection after: heart valve replacement (n=18) and/or ascending aortic replacement (n=6) and/or pacemaker implantation (n=8). PET/CT results were analysed according to the areas of interest (n=32). Examinations were performed on PET/CT scanner (Biograph-64, Siemens) 90 min after ^{18}F -FDG injection (175-200Mbq). All patients were on low-carbohydrate diet for 48 hours before the PET-scan, as well as fasted for at least 15 hours before it. **Results:** Overall, PET/CT results allowed to confirm the diagnosis of infectious process in 63% (20/32) of the areas of interest: in prosthetic valve (n=12), in generator pocket and along the leads (n=3), in ascending aortic prosthesis (n=5). Including patients with negative results of echocardiography (n=11) and blood cultures (n=7). PET/CT results allowed to rule out the infectious process in 25% (8/32) of the areas of interest: in prosthetic valve (n=2), in generator pocket and along the leads (n=5), in ascending aorta prosthesis (n=1). Of these, in one case the cause of fever was identified - lung inflammation. The infectious process was verified in 13 areas of interest - by positive culture of intraoperative material (n=17) and clearly

negative dynamics of repeated PET/CT results (n=1). Negative PET/CT results (n=10) were confirmed by follow-up clinical and laboratory data during 6 ± 3 months. Sensitivity, specificity and accuracy of ^{18}F -FDG PET/CT in the diagnosis of cardiovascular infections were 95%, 80% and 90%, respectively; positive and negative predictive values - of 91% and 89%. **Conclusion:** ^{18}F -FDG PET/CT appears to be useful in the diagnosis of cardiovascular infections in patients after cardiovascular interventions. Further studies on larger groups are needed.

EP-0076

Is ^{18}F -FDG-PET/CT Able To Optimize The Treatment In Invasive Fungal Infections?

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Invasive fungal infection is a high mortality process, that requires an adequate and early treatment, however, up to 50% of the patients present a poor response to it. It is mandatory to find a useful technic able to asses the treatment response. **Objective:** To evaluate the role of ^{18}F -FDG-PET/CT monitoring treatment response as well as the impact on treatment modification in patients with invasive fungemia. **Material and Method:** We made a retrospective review of 7 patients with invasive fungal infection who underwent a staging PET/CT study and at least one monitoring study. Invasive infection risk factors, involved microorganisms and the metabolic variation on the control PET/CT were analysed. The treatment was modified according to clinical aspects and PET/CT results, in a multidisciplinary team. **Results:** All were men with a mean age of 60 years and CCI of 7. We found 43% of immunosuppressed patients, 71% had solid tumors and 14% hematological tumors. In 6/7 patients the treatment was delayed $> 48\text{h}$ and blood cultures were positive $> 48\text{h}$ post-treatment. 3/7 patients showed fever $> 72\text{h}$. 85.7% of the patients presented Candidemia [*C. albicans* (3p), *C. parapsilosis* (1p) and *C. tropicalis* (2p)]. 1 patient had invasive aspergillosis. There was a median of 2 studies per patient [2-9]. 4p (57.1%) showed progression of the primary focus or occurrence of septic metastasis and 3p (42.9%) showed decrease or absence of the FDG uptake. The management was modified in 6/7, taking into account the PET-CT and clinical aspects. Within these 6 patients, 4 showed metabolic progression, and we decided to extend the treatment (2 adding a new antifungal and 2 prolonging the treatment scheme). 3 / 4p presented fever $> 72\text{h}$ post-treatment, that was not found on patients with a favourable response. Within the remaining 3 patients with proper PET/CT evolution, one had antifungal prolongation in spite of the imaging, the treatment was reduced in one and the last one did not have any change. **Conclusions:** PET / CT has a potential use monitoring treatment response, modifying the therapeutic scheme according to the image result, added to clinical situation, thus being able to improve the morbi-mortality of the disease. The presence of positive blood cultures $> 48\text{h}$, a treatment delay $> 48\text{h}$ and fever $> 72\text{h}$ should be taken into account as a risk factor for unfavourable treatment evolution.

EP-0077

The role of ^{18}F FDG PET/CT in patients with fever of unknown origin

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Introduction: Fever of unknown origin (FUO) is defined as a temperature higher than 38.3°C than 3 weeks with a diagnosis that remains uncertain after appropriate inpatient or outpatient evaluation. Its etiology can be infectious (21-54%), noninfectious inflammation (13-24%), and neoplastic (6-31%). Despite the use of modern diagnostic techniques, underlying pathology often remains unidentified. The aim of this study was to evaluate the role of ^{18}F -FDG PET/CT in diagnosis of patients with fever of unknown origin. **Subjects and Methods:** Patients with the diagnosis of FUO who underwent ^{18}F -FDG PET/CT were evaluated retrospectively. We analyzed a total of 17 patients (9 female, 8 male), (21-80 years-old, mean: 64.7 ± 9.7). All patients except one were under antibiotic treatment and 2 were under corticosteroid therapy prior PET/CT imaging. **Results:** True positive results were obtained in ten patients, 9 of them had infection/inflammation (vasculitis (n=4), abscess (n=3) and graft infection (n=2)). One patient had the diagnosis of Hodgkin lymphoma. The cause of FUO was confirmed only ^{18}F -FDG PET/CT in 5 patients whose other conventional imaging methods were negative. True negative results were obtained in two patients, false-negative in 4 patients (Still's disease, Brucellosis, leukemia and Behçet disease). All patients with false negative results, were administered antibiotics and one patient had been treated with corticosteroids prior PET/CT imaging. In a patient, diffuse bone marrow FDG uptake was detected but bone marrow biopsy was normal and considered as false positive. Overall sensitivity and specificity of ^{18}F -FDG PET/CT in patients with FUO were 71%, and 66% respectively. **Conclusion:** Despite limited number of the cases, our results revealed that ^{18}F -FDG PET/CT is a sensitive imaging method in the diagnosis of FUO resulting both from malignancies and inflammations. It can also detect vascular infections earlier than other imaging methods. The use of PET/CT in patients with FUO can shorten the diagnostic evaluation and provides early initiation of treatment.

EP-0078

Sarcoidosis and ^{18}F -FDG-PET/CT: where to look?

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Aim: Sarcoidosis (SC) is considered a disease related to tuberculosis (TB), probably by excessive lymphatic reaction. As the treatment may have considerable side effects, assessment of the activity of disease is important. In former times SPECT with ^{67}Ga -citrate was an option. Nowadays the standard tracer for metabolic activity is ^{18}F -FDG, which in fact has been used in sarcoidosis, but papers on this issue lack structured approach with larger numbers. **Materials and Methods:** Siemens Bi-

ograph TP, 234 Patients (141 m, 93 f, age at PET 49.3 ± 13.3 y) referred for inflammation/sarcoidosis, 334 (234 first time, 100 f/u) studies between summer of 2008 and end of 2017. ^{18}F -FDG administered according to BMI, fasting - glucose level 97.7 ± 14.9 mg/dl, time from injection to imaging 54 ± 8 mins. Reading side-by side by radiologist and nuclear medical physician; additional assessment of the lung uptake (detailed for upper/mid/lower level, extent of affected tissue per level, left and right, central/peripheral and pleural, by SUV_{max} and SUV_{avg}) was done by an experienced nuclear medical physician. **Results:** With TB we found a correlation of 0.68 between SUV_{max} seen at any lesion in one patient to extent of disease. In SC this correlation was markedly poorer: 0.39. But calculating top SUV vs. SUV_{max} of lymph nodes (LN) gave $r = 0.97$, albeit LN did not always harbour the highest uptake: overall $216 = 72.2\%$ of the 299 FDG-positive individuals had their highest uptake here, $44 = 14.7\%$ in the lungs, and $39 = 13.1\%$ in other organs. Without respect to SUV details, only regarding pathological lesions, in positive cases mediastinal LN were most often involved ($252 = 84.3\%$), followed by extrathoracic LN ($145 = 48.5\%$) and pulmonary/pleural lesions ($142 = 47.5\%$). Only in 14 clinical SC cases none of these three entities were involved (4.7%). No uptake in LN was found in 29 positive cases (9.7% , albeit in three of these still elevated spleen uptake was seen), among these sole lung/pleura uptake in 15 cases (5.0%). **Conclusion:** Other than in tuberculosis we could not find a viable correlation between highest SUV and extent of disease. Imaging neck and trunk provides access to the most probable locations of disease. Frequent and significant lymph node involvement supports the assumption of sarcoidosis as a lymphatic disease, making lymph nodes the most important structure for nuclear medical appraisal of such cases.

EP-0079

Use of FDG PET/CT in Paracoccidioidomycosis: Preliminary Results

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Introduction: Paracoccidioidomycosis (PCM) is a systemic mycosis, caused by the fungus *Paracoccidioides brasiliensis*. Several infectious processes uptake ^{18}F -fluorodeoxyglucose (FDG), but rare studies have reported the use of FDG-PET/CT to detect sites of active disease in patients with PCM. The purpose of this preliminary study is to assess the possible utility of FDG-PET/CT for the evaluation of the extent of active disease in patients with PCM under antifungal treatment. **Subjects and Methods:** Thirteen patients (11 man and 2 woman, 30–73 years-old, mean age 51 ± 11 years) with clinical and serological or biopsy-proven diagnosis of PCM, under antifungal treatment, were prospectively studied. All of them performed PET/CT imaging 1 hour after administration of FDG. Conventional images were used as reference and included: chest radiography, computed tomography, ultrasonography, gallium-67 scintigraphy, bone scan and magnetic resonance imaging. **Results:** Conventional imaging identified active lesions in 7/13 patients and FDG-PET/CT in

12/13 patients. All lesions detected by conventional imaging (in lungs, adrenals, sternum and abdominal lymph node) were also detected by PET/CT. PET/CT identified additional sites of active lesions in diverse structures such as supraglottis, lung, adrenal, skin, bones, subcutaneous nodule, cecum and multiple lymph nodes. One patient did not have active lesions detected by conventional imaging or FDG-PET/CT. **Conclusion:** This preliminary study suggests that FDG-PET/CT is high sensitive for detecting active lesions in patients with PCM under anti-fungal treatment. More studies are needed to evaluate the clinical impact of FDG-PET/CT on the management of patients with PCM.

EP-0080

Role of ^{18}F -FDG PET/CT imaging in Mycobacterium Tuberculosis

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Aim: Tuberculosis has a high morbidity and mortality worldwide. *Mycobacterium tuberculosis* has a complex pathophysiology. Timely diagnosis helps in guiding appropriate treatment. Aim of this retrospective study was to assess the contribution of Fluorine-18 Fluorodeoxyglucose (^{18}F -FDG) Positron Emission Tomography /Computed Tomography (PET/CT) in the diagnosis, initial staging and treatment evaluation in tuberculosis. **Materials and Methods:** 15 consecutive patients of PUO (pyrexia of unknown origin) and suspected tuberculosis (8 men and 6 females, Age Range: 30 to 60 years) based on clinical, biochemical and microbiological evaluation were referred for FDG PET/CT between June 2017 to March 2018 were evaluated. Biopsy confirmation was available in 10 patients. All patients were followed up clinically. **Results:** FDG PET/CT identified hypermetabolic foci in all 14 patients (93%). No abnormal focal FDG uptake was seen in one patient which was previously treated with anti TB drugs for 2 yrs and after PET scan the treatment was stopped and on subsequent follow up is asymptomatic. Among the positive scans 10/15 (66.66%) scans were diagnosed with tuberculosis based on imaging features. Out of which biopsy was positive for tuberculosis in 6/10 (60%) patients. In the remaining 5 patients biopsy was not done because of classical imaging features, clinical, biochemical and microbiological evaluation. All patients were clinically followed up for duration of 3–6 months. Various pattern and organ involvement were seen as follows: tuberculous lymphadenitis, miliary tuberculosis, spondylodiskitis, genitourinary Kochs, disseminated TB with multifocal liver, spleen, bone marrow, testis and kidney involvement, pleural thickening, peritoneal, omental nodularities, pulmonary tuberculoma, procto-colitis causing fistulatus connection into the sacral spinal canal and neural foramina. In the remaining 4 patients biopsy were as follows pleural metastasis from breast carcinoma (1/15), lymphoma (1/15), chest and upper abdominal wall pyogenic abscess (1/15), chronic non-granulomatous osteomyelitis (1/15). And in remaining 1 patient (1/15) FDG PET/CT scan shows disease in the terminal ileum and was diagnosed with typhoid based on high salmonella typhi titres. **Conclusion:** FDG PET/CT has a useful role to evaluate the cause of PUO and generalized adenopathy, pleural effusion, ascites espe-

cially when other investigations like fluid adenosine deaminase levels, culture TB, gene expert for TB are inconclusive. It helps to guide biopsy from active site thus aiding in accurate histological diagnosis. It also defines extent of disease and it aids in assessing response to therapy. Negative FDG PET/CT scan reliably rules out focal etiologies for PUO. Further prospective studies are warranted for confirmation.

EP-0081

Utility of FGD PET-CT in the idiopathic retroperitoneal fibrosis

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Retroperitoneal fibrosis (RPF) encompasses a range of diseases characterized by proliferation of aberrant fibroinflammatory tissue, which surrounds the abdominal aorta, inferior vein cava, and iliac vessels. This process frequently entrapping and obstructing the ureters and eventually leading to renal failure, RPF could be idiopathic or secondary to factors such as drug use, malignancies, or infections. If promptly diagnosed and treated, idiopathic and benign forms of RPF have a good prognosis.

Aim: To assess the utility of FDG PET/CT in the diagnosis of idiopathic RPF. **Material and Methods:** We retrospective review 17 Patients (p) with clinical suspicion of iRPF who had undergone 18F-FDG PET/CT examinations at our center between December 2010-January 2018, 10 man, with mean ages 77.9 years. We evaluated in all patients the presence of acute phase reactants, antibodies, tumor markers and creatinine levels, retroperitoneal biopsies, CT and FDG PET/CT findings. The diagnosis of iRPF was made according to the Scheel criteria. **Results:** 17 patients (p) were analysed. 8p/17 with acute renal failure at the diagnosis with creatinine > 2mg/dl, 14p/17 with elevated RPC and ERS and 2p/17 IGG4+ (one of this also had elevated chromogranin, due to NE tumor found at duodenum in CT). All of them had previous CT, with the following findings: 17p had retroperitoneal soft tissue mass surrounding the infrarenal aorta (1p with retroperitoneal and mediastinal involvement), among which ureteral involvement was observed 6p/17, abdominal aortic aneurism in 2p/17 and vein cava and iliac vessels involving 8p/17. FDG uptake in lesions was visually determined as positive or negative in relation to liver uptake. The SUVmax in the retroperitoneal lesions was also calculated. 12p/17 were positive for FDG uptake SUVmax (range 2.1-11.3) and 5p/17 with retroperitoneal soft tissue masses without FDG uptake. Unsuspected findings were found, such as 1p with colorectal cancer, not seeing in other images techniques and 1p with left pelvic collection suggestive of infectious process. All positive patients in FDG- PET-CT were treated with corticosteroids, Rituximab or methotrexate, all patients with renal involving were treatment with pig-tails and aortic prostheses were placed in patients with aneurysms. Negative FDG PET-CT patients were only to clinical follow-up. **Conclusion:** 1 FDG PET/CT could be an important tool for assessing the activity with iRPF allowing to establish an early treatment. 2 FDG PET/CT also allowed detects other unsuspected lesions such as tumors or infectious process.

EP-0082

Sensitivity of the 18-FDG PET/CT for the search of infectious foci in patients with sepsis

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Aim: To evaluate the sensitività of 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) for the search of infectious foci in patients with sepsis. **Methods and Materials:** This is a single centre retrospective review on patients selectect between subjects sent to our operating unit to be undergone to FDG PET/CT between June 2016 and April 2018. Eligibility criteria of this review was an already established diagnosis of sepsis. The PET images were interpreted by a nuclear medicine physician. **Results:** 39 patients were included in this analysis [M: 27%, F: 12%, median age: 66 years (range: 19-84)]. 2 patients were subjected for 4 time for FDG-PET/CT; 1 patient was subjected to 3 time for FDG-PET/CT; 6 patients were subjected twice for examination. The total number of FDG-PET/CT was 53. The previous bacteriological research showed: 48.8% staphylococcus aureus sepsis, 17.9% methicillin-resistant staphylococcus aureus sepsis, 10.3% klebsiella sepsis, 7.7% multiple bacterial strains sepsis, 5.1% enterococcus sepsis, 5.1% candida sepsis, 5.1% escherichia coli sepsis. 7 patients could not undergone the examination for severe conditions requiring their immediate first aid. The FDG-PET/CT reports were 35.5% negatives, 33.2% identified aspecifics finds (lymphadenopathy, pulmonary thickening, outcomes fo previous known pathologies), in 12.6% we found accessories (spondylodiscitis, Paget disease, necrotic fasciitis), in 10.3% we found known findings, in 3.4% there was uptake in bone for surgery outcomes, 2.5% infection of heart device, 2.5% uptake on heart valve. **Conclusion:** Our single-center, retrospective study showed that the 18-FDG PET/CT had not a great sensitivity on the overall detection of infectious foci in patients with sepsis.

EP-0083

Transthyretin cardiac amyloidosis and aortic stenosis: when the coexistence has to be suspect

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Aim: Degenerative aortic stenosis (AS) is the most common valvular heart disease and can lead to a severe concentric remodelling, diastolic dysfunction and atrial fibrillation. These findings can be seen also in wild type transthyretin (wt-TTR) cardiac amyloidosis (TTR-CA), a restricted cardiomyopathy caused by the deposition of wt-TTR that carries a poor prognosis. TTR-CA can be accurately detected by a non-invasive technique like a bone seeking radioisotope scintigraphy, such as technetium-99m-3,3-diphosphono-1,2 propanodicarboxylic acid (99mTc-DPD) without need of myocardial biopsies. Several studies reported the coexistence of TTR-CA and low-flow-low gradient AS with normal left ventricle ejection fraction (LVEF)

and underlined the importance of screening patients in whom there is a suspicion of concomitant severe AS and TTR-CA because of the different management and prognosis between patients with only AS or with both pathologies. We decide to investigate the coexistence of AS and TTR-CA and to identify echocardiographical and laboratoristic criteria which could rise the suspect of the coexistence of the two diseases. **Material and Methods:** We retrospectively analyze 57 patients (81 ± 8 years, 86% men) that underwent ^{99m}Tc -DPD scintigraphy because of the suspect of TTR-CA with or without moderate or severe AS by the transthoracic echocardiography: 6 patients with AS were scored as positive for TTR-CA (group 1=11%), 24 without AS were positive (group 2=42%) and 27 with AS were negative (group 3=47%). **Results:** Patients with TTR-CA and AS by echocardiography, compared to patients with only AS, showed a significative higher thickness of the interventricular septum (21.17 vs. 13.64 mm, $p < 0.01$), LV posterior wall (15.60 vs. 11.15 mm, $p = 0.032$) and lower e-wave deceleration time (154.5 vs. 225.3 ms, $p = 0.060$). Patients with only TTR-CA, compared to patients with only AS, demonstrated a significant difference in the interventricular septum (19.04 vs. 13.64 mm, $p < 0.01$) and LV posterior wall thickness (17.51 vs. 11.15 mm, $p < 0.01$). Comparing the level of N-terminal probrain natriuretic peptide (NT-proBNP), patients with TTR-CA and AS expressed the highest values, significantly different from the values of the other two groups (1 vs. 2: 35471.67 vs. 9164.18 ng/dl, $p = 0.020$; 1 vs. 3: 35471.67 vs. 3969.5 ng/dl, $p = 0.012$). **Conclusion:** Transthyretin cardiac amyloidosis has low prevalence (20%) in patients with moderate or severe aortic stenosis. Both echocardiography criteria and plasma levels of NT-proBNP can alert the clinician for suspect of the coexistence of the two pathologies.

EP-0083a

Imaging Cardiac Innervation in Hereditary Transthyretin (ATTRm) Amyloidosis: a Marker for Neuropathy or Cardiomyopathy?

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Introduction: Nuclear imaging modalities using ^{123}I -metaiodobenzylguanidine (^{123}I -MIBG) and bone seeking tracers identify early cardiac involvement in hereditary transthyretin amyloidosis (ATTRm) patients. However, little is known whether results from ^{123}I -MIBG scintigraphy actually correlate to markers for either cardiac autonomic neuropathy or cardiomyopathy. The aim of this study was to gain insight whether and to which order ^{123}I -MIBG scintigraphy reflects cardiac neuropathy or cardiomyopathy. **Subjects & Methods:** All carriers of a TTR mutation and ATTRm patients who underwent both ^{123}I -MIBG and ^{99m}Tc -hydroxymethylene diphosphonate (^{99m}Tc -HDP) scintigraphy were included. Additional findings from the patient chart concerning clinical examinations, neurological function tests, echocardiography, ECG and laboratory tests, were retrieved. Cardiomyopathy was defined as NT-proBNP > 365 ng/l, and cardiac autonomic neuropathy as abnormal cardiovascular reflexes at autonomic function tests. Late ^{123}I -MIBG heart-to-mediastinum ratio (HMR) < 2.0 or wash-out > 20% were considered as abnormal. Any

cardiac ^{99m}Tc -HDP uptake was considered as abnormal. **Results:** 39 patients (13 carriers and 26 patients with proven amyloidosis) were included in this study (21 men and 18 women, mean age 51 years). Patients with cardiomyopathy, with or without cardiac autonomic neuropathy, had lower late HMR than similar patients without cardiomyopathy (median 1.1 (range 1.0–1.5) and 1.5 (1.2–2.6) versus 2.4 (1.4–3.8) and 2.4 ± 0.67 , respectively $p < 0.001$). Five patients (13%) with abnormal late HMR had no signs of cardiac bone tracer accumulation. Late HMR and wash-out were (inversely) correlated with NT-proBNP $r = -0.652$ ($p < 0.001$) and $r = 0.756$ ($p < 0.001$), respectively. Furthermore, late HMR and wash-out (inversely) correlated with cardiac ^{99m}Tc -HDP uptake $r = -0.663$ ($p < 0.001$) and $r = 0.617$ ($p < 0.001$), respectively. **Conclusion:** ^{123}I -MIBG scintigraphy reflects cardiomyopathy rather than cardiac autonomic neuropathy in ATTRm patients and carriers of a TTR mutation. ^{123}I -MIBG scintigraphy can be abnormal before any cardiac bone tracer uptake is visible.

EP-07

e-Poster Area

Other Clinical Studies: Non Oncology

EP-0087

Do additional CT information improve the characterization of incidental colonic tracer uptake in 18F-FDG PET/CT scans?

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Do additional CT information improve the characterization of incidental colonic tracer uptake in 18F-FDG PET/CT scans? To evaluate the impact of morphological information derived from contrast enhanced CT in the characterization of incidental colonic uptake in 18F-fluorodesoxyglucose positron emission tomography / computed tomography (18F-FDG PET/CT) examinations. In this retrospective study, 125 patients (female: $n = 53$, male: $n = 72$, mean age 62.9y) that underwent contrast enhanced 18F-FDG PET/CT without specific bowel preparation and colonoscopy (mean time between PET/CT and colonoscopy: 52 ± 58 d) were included. By two readers, PET/CT examinations were assessed for focal colonic tracer uptake in comparison to the background. Focal tracer uptake was correlated with morphological changes of the colonic wall such as focal thickening, polypous shape or focal contrast media uptake. Discrepancies were resolved in a consensus reading. Then, colonoscopy reports were evaluated for precancerous (oligo-tubular adenoma, serrated adenoma, sessile adenoma and tubulo-villous adenoma) and cancerous lesions verified by histopathology, serving as a reference standard. Imaging findings were then compared to the reference standard to calculate sensitivity, specificity as well as positive (PPV) and negative predictive values (NPV) for focal tracer uptake as well as focal tracer uptake and morphological changes in contrast enhanced CT. In 38.4% (48/125), focal tracer uptake was observed in 67 lesions. In the corresponding colonoscopy reports, a total of 10 cancerous and 26 precancerous lesions were found. In PET,

two cancerous lesions and 10 precancerous lesions were missed, resulting in a sensitivity, specificity, PPV and NPV of 51%, 68%, 29% and 84% for focal tracer uptake alone. By correlation focal tracer uptake with morphological changes in contrast enhanced CT, a sensitivity, specificity, PPV and NPV of 48%; 79%; 37.5%; 86% could be observed for PET/MR. Focal colonic tracer uptake has a low specificity and sensitivity for precancerous and cancerous lesions. By analyzing additional morphological changes in contrast enhanced CT imaging, the specificity can be increased without sacrificing sensitivity. Morphological changes of the colonic wall in contrast enhanced 18F-FDG-PET/CT examinations can help to decide, which patients with focal tracer uptake profit from additional colonoscopy.

EP-0088

Gastric Emptying: Establishing Normal Ranges for Most Commonly Used Practical and Simple Meals in the UK

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Aim: We found a wide variation in gastric emptying protocols in our recent UK nationwide audit (Hansrod S. 2015, 36:532 Nucl. Med. Comms.) with differences in test meals, techniques and the normal ranges used to report studies. Two relatively simple and most commonly used meals (scrambled egg sandwich and porridge) were studied to establish reliable normal ranges, in an attempt to propose a universally acceptable protocol. **Method:** 42 volunteers (20 males, 22 females, age range 22–68) with no history of GI symptoms or diabetes were studied. Each volunteer consumed two meals with similar nutritional composition on two separate days: gluten-free porridge (40g in 200ml whole milk), and scrambled eggs with 2 slices of bread. Anterior-posterior 2-minute static images were acquired with the patient standing between the detectors. Images were acquired every 5 minutes over a two-hour period, followed by a single image at 3-hours. The data was modelled using a power-exponential function that allowed measurements of gastric emptying functional parameters including lag time, half-emptying time, peak emptying rate, time-to-peak-emptying and exponential half-life. 3-hour retention was also calculated. Paired t-tests were used to compare the meals and 2-sample t-tests were used to assess any gender related differences. Regression analysis was used to assess correlation of the functional parameters with age and body habitus (BSA). **Results:** All gastric emptying functional parameters were significantly different between the two meals ($p < 0.001$). The normal range for lag time was 0–20 minutes for porridge and 4–40 minutes for scrambled egg. The normal range for half-emptying time was 19–85 minutes for porridge and 44–126 minutes for scrambled egg. The normal range for exponential half-life was 21–56 minutes for porridge and 20–80 minutes for scrambled egg. The normal range for 3-hour retention was 0–8% for porridge and 0–22% for scrambled egg. Only weak significance was found for gender related differences in gastric function for the two meals ($0.05 < p < 0.10$). Weak correlation was also observed for some functional parameters when plotted against age and BSA ($0.05 < p < 0.10$). **Conclusion:** Normal ranges for the two meals have been established. Porridge showed

significantly faster transit than scrambled egg for all measured parameters. Normal ranges are therefore meal specific and not interchangeable. Scrambled egg sandwich is the recommended meal for gastric emptying studies, although porridge would be a suitable alternative for patients who are unable to eat egg sandwiches (vegan/gluten sensitive).

EP-0089

Quantitative measurement of the ratio of bronchial arterial blood flow to pulmonary arterial blood flow

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Purpose: Lung is perfused through pulmonary and bronchial artery. The ratio of pulmonary (F_{PA}) to bronchial artery (F_{BA}) blood flow is known to be 99:1. It is reported that in some cases, such as with pulmonary artery stenosis, the contribution of bronchial artery to lung perfusion increased. However, quantitative measurement of the ratio of bronchial arterial blood flow to pulmonary arterial blood flow has not been reported. The aim of the present study was to measure the ratio quantitatively using $^{15}\text{O-H}_2\text{O}$ PET in a patient with lung cancer and to evaluate change in the ratio after the chemotherapy. **Methods:** A patient with right upper lobe lung cancer and right hilar lymph node metastasis underwent a 10 min $^{15}\text{O-H}_2\text{O}$ PET at baseline and at after one cycle of chemotherapy. We used dual blood input function model. Bronchial and pulmonary arterial input functions were derived from an ascending aorta and right ventricular time activity curves, respectively. We used nonlinear regression method to obtain pulmonary blood flow. **Results:** F_{PA} was decreased and F_{BA} increased in right upper lobe compared to those in other lung lobes. After chemotherapy, which was effective right hilar lymph node metastasis, F_{PA} increased and F_{BA} decreased in right upper lobe. F_{PA} and F_{BA} were 0.24 and 1.1 mL/min/cm³ before chemotherapy, and 0.43 and 0.82 mL/min/cm³ after one cycle of chemotherapy, respectively. **Conclusion:** In the area where F_{PA} decreased, the ratio of F_{PA} to F_{BA} decreased to 0.25 but the ratio recovered after chemotherapy.

EP-0090

In patients with pulmonary emphysema - contrary to “healthy” individuals - relative lung lobe volume and relative lobar perfusion correlate only marginally

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Introduction: Pulmonary emphysema is characterized by hyperinflation of individual lobes with simultaneous loss of alveolus structures. Clinical experience shows that perfusion and hyperinflation in patients suffering from emphysema often differ and show heterogeneous patterns. Quantitative analyses concerning this topic do not exist. Aim of the study was to analyse to what extent lobar perfusion and lobar volume are decoupled in patients with emphysema in comparison to healthy individuals. **Subjects & Methods:** 20 patients with emphysema were referred to routine lung scintigraphy before interventional proce-

dures. 12 patients without a history of lung diseases referred to routine lung scintigraphy to exclude pulmonary embolism were included as “healthy” individuals. V/Q-SPECT/CT with Technegas and about 150 MBq ^{99m}Tc -MAA was performed in all 32 patients. Quantification of relative lobar volume and relative lobar perfusion in % normalized for total perfusion and volume was done using the software “HERMES Hybrid 3D-Lung Lobe Quantification”. Finally correlation analyses of the resulting relative lobar perfusion and volume were performed to quantify dependencies. **Results:** For the 60 lobes of the 12 “healthy” individuals correlation of relative lobar perfusion and volume was excellent with $R=0.87$ and a slope of the regression line of 1.00. For the 100 lobes of the 20 patients suffering from emphysema correlation of relative lobar perfusion and volume was very weak with $R=0.36$ and a slope of the regression line of 0.49. **Conclusion:** The results of this study show that - in contrast to “healthy” individuals presenting a good correlation between relative lobar perfusion and volume - patients with pulmonary emphysema are characterized by a weak correlation. The slope of the regression line of 0.49 proves that lobar perfusion does not go along with an increasing lobar volume resulting in an increasing volume-perfusion mismatch. This mismatch is relevant above all for decisions concerning lung resection

EP-0091

Head-to-head Comparison of V/Q SPECT/CT and Multidetector CT Angiography for the Detection of Pulmonary Embolism

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Introduction: The diagnosis of pulmonary embolism (PE), an important cause of cardiovascular death, is often challenging. This is usually done by a combination of clinical findings, use of predictive scores and imaging tests, such as CT angiography (CTA) and ventilation/perfusion scintigraphy preferably using SPECT/CT images (V/Q SPECT/CT). Both imaging methods have had recent advances, and few studies have performed a direct comparison between them using state of the art equipments. The purpose of this study was to compare the sensitivity and specificity of multidetector CTA and V/Q SPECT/CT in the same group of patients. We also analyzed the percentage of positive V/Q SPECT/CT studies in patients with clinical suspicion of PE and normal CTA. **Subjects & Methods:** We prospectively studied consecutive patients under suspicion of acute PE referred for V/Q SPECT/CT or CTA, and the patients were then submitted to both procedures. Refusal and inability to perform any of the techniques were considered exclusion criteria. Data regarding age, sex, time between examinations, time elapsed since the onset of symptoms, Wells score and interpretation of each procedure by experienced specialists were obtained. The final diagnosis was decided through a consensus among the clinicians, taking into account clinical, laboratory, follow-up and all imaging procedures data. **Results:** Seventeen patients (9 male, 8 female, 21–78 years-old, mean age 42.8 years) were studied.

The mean duration of the onset of symptoms was 3.5 days (1–9 days), and the mean Wells score was 3.5 (1.5–6). Sensitivity, specificity, positive and negative predictive values and accuracy for V/Q SPECT/CT were respectively 100%, 77.78%, 75%, 100% and 86.67%, and for CTA: 50%, 100%, 100%, 72.73% and 78.57%. The overall agreement between the methods was 69.2%. Of the 10 patients with negative CTA, 4 (40%) had V/Q SPECT/CT positive, 3 of them considered as true positives and one false positive. **Conclusion:** In this preliminary study, V/Q SPECT/CT was more sensitive and had higher accuracy than multidetector CTA for detection of PE. Our results in this small sample size suggest that patients with clinical suspicion of PE and normal CTA should perform V/Q SPECT/CT.

EP-0092

Utility Of Lung Perfusion Scintigraphy to Predict Postoperative Pulmonary Function in Lung Cancer Patients Undergoing Pneumonectomy

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Purpose: To identify preoperative pulmonary perfusion scintigraphic findings that might be associated with clinical outcome after lung volume reduction surgery. **Materials and Methods:** Preoperative perfusion scintigrams in 123 patients (66 men, 57 women; age range, 41–76 years; mean age, 61 years $\pm$ 9) were reviewed and graded for emphysematous heterogeneity (from isolated areas to diffuse distribution), extent of maximally perfused lung, and lobar predominance (upper-lobe vs lower-lobe asymmetry). These findings were correlated with clinical outcome on the basis of pulmonary function, arterial blood gas levels, and exercise test results before and 6 months after surgery. **Results:** Among the 106 patients who survived surgery, there was an average improvement of 47% in the forced expiratory volume in 1 second (FEV1), of 20% in arterial oxygen tension, and of 20% in the 6-minute walking distance. Scintigraphic markers correlated best with FEV1 improvement. The strongest scintigraphic predictor of increase in FEV1 was upper-lobe predominance ($r=.38$, $P<.001$), which was followed by heterogeneity ($r=.31$, $P=.002$). The seventeen patients who died had a significantly lower percentage of maximally perfused lung than the survivors (25% vs 34%, $P=.004$). **Conclusion:** Perfusion scintigraphy can provide modest prognostic information in patients who undergo evaluation for lung volume reduction surgery.

EP-0093

Measurement of actual doses of inhaled Technegas™ and trapped ^{99m}Tc -MAA in patients' lungs with quantitative lung ventilation/perfusion SPECT/CT scans

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Introduction: Technegas™ has been used for lung ventilation studies for several decades in Europe, Asia, and Australia. Based

on the manufacturer's manual, 26–40 MBq of inhaled Technegas™ was expected in each patient. However, dose actually inhaled may vary depending on the patient's conditions. In this study, we measured the actual doses of inhaled Technegas™ and trapped ^{99m}Tc -MAA with quantitative lung ventilation/perfusion (V/P) SPECT/CT scans. **Methods:** We retrospectively reviewed lung V/P SPECT/CT scans performed from January 2017 to March 2018. All scans were performed with Siemens Symbya Intevo SPECT/CT and images were reconstructed using the xSPECT quant method. We measured the doses of ^{99m}Tc -MAA in the same syringe before and after the injection with a well counter, and we used the difference as the actually injected dose for the perfusion study. Because we also needed to input a number as the injected dose, which we could not know for the ventilation study, we measured the dose rate on the patient's right anterior chest wall, and entered 18.5, 37, or 74 MBq for the injected dose of Technegas™ based on the dose rate measured. All volumes of interest (VOIs) were drawn using MIM software®, and the integral total dose [MBq] was calculated by multiplying the volume of VOI [ml] and the concentration of radiopharmaceuticals in that volume [MBq/ml]. If the ventilation SPECT/CT scan was performed before the perfusion SPECT/CT scan, the measured dose was adjusted based on the integral total dose of the preceding scan and the time interval between the two scans. **Results:** Sixty-nine ventilation SPECT/CT scans and 66 perfusion SPECT/CT scans were analyzed. The average ratio of the actually trapped dose measured to the actually injected dose of ^{99m}Tc -MAA was $92.9 \pm 8.0\%$, the correlation coefficient was 0.904, and the following formula was obtained: Actually trapped dose measured [MBq] = $0.928 \times$ Injected dose [MBq]. The average dose of the actually inhaled Technegas™ measured was 78.4 ± 44.4 MBq. The correlation coefficient between the dose rates on the patient's right anterior chest wall and the measured dose of the actually inhaled Technegas™ was 0.926, showing excellent correlation. **Conclusion:** Quantitative SPECT/CT scans were very useful to measure the actual doses of inhaled Technegas™ and trapped ^{99m}Tc -MAA in lung V/P SPECT/CT scans with great precision, and can be used for various applications such as evaluating pre-operative lung function and disease severity.

EP-0094

Quantitative V/P SPECT in COPD from Pathophysiology to Clinical Interpretation

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Introduction: Airway obstruction and emphysema affect ventilation and perfusion of the lungs and are important for management of COPD patients and for prediction of their prognosis. Partial pressure of arterial carbon dioxide (PaCO_2) is a good indicator of lung function and related to acid-base homeostasis. We aimed to validate quantitative V/P SPECT for measurement

of lung function. **Patients and Methods:** Ninety-four Chinese patients with a stable COPD (GOLD criteria) were enrolled in an international study (age 43–86 years, smoking pack years 0–104, post-bronchodilatation FEV1 21–99 % predicted). Ventilation and perfusion tomography (V/P SPECT using Technegas and ^{99m}Tc -MAA) was performed and interpreted blindly according to European Nuclear Medicine guidelines (Bajc, M. et al. Ann Nucl Med 2015; 29: 91). Emphysema was defined as area of matched or reversed mismatched V/P defects and its extent was assessed as % of the estimated total lung volume (E%). Total preserved lung function (TPLF%) was represented as areas of matched V/P areas and was calculated as percentage of total lung volume. Single-breath diffusing capacity for carbon monoxide (DLCO) and post-bronchodilatation FVC in % of predicted value, and PaCO_2 were measured. **Results:** TPLF%, E%, DLCO, FVC and PaCO_2 ranged 15–80%, 0–80%, 17–98%, 28–125%, and 29–89 mmHg, respectively. E% and TPLF% were significantly related to DLCO ($p \leq 0.0003$). PaCO_2 remained stable when E% was below 60% and TPLF% was above 30%. PaCO_2 retention was evident when E% exceeded 60% and TPLF% fell below 30%. **Conclusion:** Results suggest that it is possible to quantify pathophysiology in COPD by V/P SPECT. E% and TPLF% measure lung function over a wide range of COPD severity. Retention of PaCO_2 occurs when matched V/P areas fall below 1/3 of the total lung volume.

EP-0095

Quantitative Assessment of Lung Ventilation-Perfusion Imbalance in Patients with Pulmonary Embolism

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Introduction: Quotient images obtained from V/Q SPECT data provide a means of quantitative assessment of the mismatch between pulmonary air ventilation and blood perfusion in 3D. The aim of this study was to investigate the distribution of ventilation-perfusion ratios and determine adequate parameters for differentiating patients with and without pulmonary emboli (PE). Threshold values derived from V/Q quotient histogram statistics may serve as additional objective criteria for diagnosing patients. **Subjects and Methods:** 72 patients underwent Tc-99m Technegas/MAA SPECT scintigraphy using a dual-head SPECT system. The clinical outcome was obtained qualitatively via visual assessment of the V/Q data. 16 scans were reported as positive and 56 as negative for PE. 4 patients were excluded due to identified COPD and poor image quality. Post-processing procedures included registration and normalization of the ventilation and perfusion images followed by semi-automated lung delineation. V/Q quotient images were calculated and distribution histograms were plotted showing the percentage of total lung volume as a function of decimal log-transformed V/Q ratios. Mean, standard deviation (SD), skewness and excess kurtosis were calculated for correlation with the clinical report. **Results:** Histograms of quotient images obtained for patients negative for PE showed a bell-shaped distribution close to normal with a

high percentage of voxels centred around unity. The mean V/Q ratios were 1.09 ± 0.09 , 0.33 ± 0.16 for the SD, 0.37 ± 0.36 for the skewness and 0.35 ± 0.64 for the excess kurtosis. Histograms for patients with PE had a flatter peak with positively skewed profile. Histogram statistics were 1.16 ± 0.11 for the mean, 0.45 ± 0.20 for the SD, 0.63 ± 0.29 for the skewness and 0.29 ± 0.65 for the excess kurtosis. Using two-tailed t-test, the mean, SD and skewness were found significantly different in two groups ($p < 0.05$). In particular, skewness showed a stronger differentiation between the groups. A threshold value of 0.60 for skewness could be used for distinguishing between the normal and pathological lung function, with a false positive rate of 19%. **Conclusion:** Quantitative assessment of distribution histograms for V/Q quotient images revealed that the mean, SD and skewness can be used for assessing the ventilation-perfusion imbalance in patients with suspected PE, and may be a useful adjunct in clinical reporting of V/Q SPECT images. This analysis was based on the clinical report; further work in a prospective setting will assess the PE status via clinical follow-up and other imaging modalities.

EP-0096

Prevalence of bile acid diarrhea as diagnosis by SeHCAT scanning and its response to treatment

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Purpose: To evaluate the prevalence of bile acid diarrhea (BAD) diagnosed by ⁷⁵Selenium-homocholyltaurine (SeHCAT) test and its response to specific therapy. **Subjectives and Methods:** During five years (march2013– march2018) the SeHCAT test was performed in 259 patients with chronic diarrhea (based on Rome Criteria). The patients were divided in 2 groups: patients with some structural pathology as inflammatory bowel disease, cholecystectomy or chronic pancreatitis among other conditions (group 1= 142 patients) and those with functional/idiopathic diarrhea (group 2= 117 patients). Seven-day abdominal retention after administration of 370 kBq of ⁷⁵Se-SeHCAT was measured and BAD (pathologic SeHCAT test) was defined if was < 15% (< 5% severe BAD; <10% moderate BAD; <15% mild BAD). Clinical response to treatment with a bile acid sequestrant (BAS) in patients diagnosed with BAD was also evaluated. We considered response when there was normalization or decrease of stool frequency. **Results:** The SeHCAT test was pathological in 164/259 patients (63.32%): 110/142 patients in group 1 (77.46%) and 54/117 in group 2 (46.15%). Additionally, 82/164 had severe BAD, 42/164 moderate BAD and 41/164 mild BAD. The specific treatment (BAS) was assessed in 61/165 patients. The response to treatment was 79.54% in severe BAD, 71.42% in moderate BAD and 100% in mild BAD (although in this last group only 3 patients were evaluated the treatment response). **Conclusion:** The prevalence of BAD was very high in our study sample. It was considered to be the cause of diarrhea in the half of the patients with functional disease and two third with the organic disease. The patients with diagnosis of BAD had a very good response to specific treatment with BAS (at least, higher than 70%).

EP-0097

Clinical Value of SeHCAT Test On The Diagnostic Of Bile Acid Malabsorption In Crohn's Disease

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Introduction: SeHCAT [tauroselcholic (selenium-75) acid] is a gold standard nuclear medicine test which diagnoses bile acid malabsorption (BAM) by measuring bile acid pool loss. Crohn's disease (CD) is a chronic inflammatory bowel disease that can be characterized by many symptoms, such as diarrhoea, which in some cases could be due to associated to BAM rather than CD itself. **Aim:** To study the correlation between Crohn's disease and bile acid malabsorption in patients with chronic diarrhoea. **Materials and Methods:** 64 patients with chronic diarrhoea, 32 with CD and 32 without any known disease, underwent the similar SeHCAT studies, with the same acquisition protocols. Retention of the taurocholic acid labeled with Selenium-75 capsule by the intestine after 7 days was calculated and compared to the first day. Normal bile salt retention is assumed when the percentage calculated is higher than 15%, when less than this, BAM can be classified as low, moderate or severe. Mann-Whitney test was used to assess the differences of percentage retention. The association coefficient Φ was used to study the correlation between CD (present/absent) and BAM (positive/negative). The p-value < 0.05 was considered to indicate statistical significance. **Results:** The patients with CD showed $13.08 \pm 21.12\%$ retention compared with $21.89 \pm 18.86\%$ from the CD absent patients and were found statistically significant differences between them ($U=280.5$, $p=0.002$). There was a significant but weak positive association between CD and BAM ($\Phi=0.252$, $p=0.044$). **Conclusion:** We have found a high incidence of bile acid malabsorption in patients with Crohn's disease. This has implications for the clinical pathway for patients with Crohn's disease.

EP-0098

⁷⁵SeHCAT scan in bile acid malabsorption in chronic diarrhea: a preliminary Italian single center experience.

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Purpose/Introduction: Bile acid malabsorption (BAM) is a common and likely under-diagnosed and under-treated cause of chronic diarrhea. Diagnosis of BAM can be confirmed using ⁷⁵Selenium homotaurocholic acid test (⁷⁵SeHCAT). However this tool is not consistently part of the diagnostic flow-chart, although regularly licensed in Italy, and remains unavailable in most centers and underutilized. The aim of this study was to present our preliminary experience with the use of ⁷⁵SeHCAT test. **Subjects & Methods:** A retrospective study on pts who routinely underwent ⁷⁵SeHCAT in our Nuclear Medicine Unit was conducted. ⁷⁵SeHCAT procedure was performed following the current standard prescribing information. According to 7 day SeHCAT retention, BAM status was reported as: normal >15% (borderline 15–20%), mild 10–15%, moderate 5–10%, severe <5%. Records detailing i.e. clinical history, ⁷⁵SeHCAT results, treatment and clinical follow-up were collected. **Results:** Overall 12 pts underwent ⁷⁵SeHCAT test in our Center (between November 2017 and April 2018): 6 F and 6 M; mean age 45 years (median 46, range 22–64); all pts were referred by local gastroenterologists with clinical suspicion of BAM because of chronic diarrhea without a known cause (3/12) or IBS-D not responder to standard medications (9/12). The length time of significant gastrointestinal symptoms varied: <12 months (1 pt), 1–3 years (3), 3–5 years (2), >5 years (5), from birth (1). Concomitant anti-diarrheal medications, potentially influencing ⁷⁵SeHCAT absorption, were assumed by 9/12 pts but in all cases interrupted at least 1 week before, until the end of the test. Overall the mean retention ⁷⁵SeHCAT score was 18% (median 10%; range 3–48). BAM was confirmed in 7/12 (58%) pts (1 mild; 4 moderate; 2 severe; mean retention 7, range 3–11) whereas excluded in 4/12 (33%) pts (mean retention 38, range 32–48). In only 1 case BAM status remained slightly borderline (19% retention). The diagnostic performance of ⁷⁵SeHCAT, in terms of differential diagnosis between BAM and other causes, led to a change in patient management in 9/12 (75%) cases, in particular 8 pts were addressed to bile acid sequestrants (BAS) therapy, with significant clinical benefit in 6/8. **Discussion/Conclusion:** In our small cohort, ⁷⁵SeHCAT scan represented a simple test able to reliably diagnose BAM and to select patients who might benefit treatment with BASs. Further analyses on larger population are warranted to establish a diagnostic algorithm of chronic diarrhea and to determine whether ⁷⁵SeHCAT represents a cost-effective option to be included earlier in the differential diagnosis.

EP-0099

Contribution of the nuclear medicine to the diagnosis of the malabsorption of bile acids. Experience in our service

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Aim: To determine the clinical usefulness of ⁷⁵SeHCAT scintigraphy in the early diagnosis of chronic diarrhea (DC) associated with bile acid malabsorption (BAM). **Material and Methods:**

We performed a prospective analysis of the patient histories who has been made ⁷⁵SeHCAT scintigraphy in our hospital, since this test was established as a health benefit in Nuclear Medicine from February 2017 to February 2018. We checked the lab test results (occult blood in feces, acute phase reactants, thyroid function, fecal calprotectin, elastase, screening of celiac disease) and pathological anatomy to exclude organic cause of DC. The isotopic study has been done obtaining images centered in abdomen at 3 hours and 7 days oral administration of a radiopharmaceutical (³⁷⁰MBq tauroselcolic acid ⁷⁵Se). We consider pathological studies with retention index below 15%. **Results:** We have performed 12 studies (11 women 1 man, mean age 38.75 years), none surgically intervened. A 58.3% (7 patients) have been pathological, 28.5% of them (2 patients) associate digestive pathology type Irritable bowel syndrome. In 85.7% the colonoscopy exclude organic cause and in all these cases was obtained positive result for BAM in the study with SeHCAT. In addition 1 patient has significant alteration of laboratory tests with elevation of fecal calprotectin, elastase and acute phase reactants. 100% of patients with SeHCAT positive for malabsorption of bile acids have significantly improved their symptomatology with very good response to treatment with cholestyramine. **Conclusions:** ⁷⁵SeHCAT scintigraphy is the gold standard method for the diagnosis of BAM, widely validated, has good correlation with the loss of bile acids in feces with very low radiation levels. According to the literature, it has high sensitivity and specificity (80–94%, 70–100% respectively), being a safe and low cost test. In our case, despite having a small sample, the test has been pathological in more than half of the patients, confirming that there is a greater probability of BAM if a basic digestive process coexists. 100% of patients with positive SeHCAT have obtained a very good response to treatment with cholestyramine, significantly improved their symptomatology and thus their quality of life.

EP-0100

Idiopathic Inflammatory Bowel Disease (IBD). The Role Of 25-Hydroxy-Vitamin D (25-OH-D) Serum Levels In Correlation With Disease Severity

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Purpose: Idiopathic bowel disease includes immune system diseases of unknown origin. The aim of this study is to evaluate the vitamin D serum levels in patients with IBD and its relation to the severity of the disease. **Materials & Materials:** 165 patients (98 men, 67 women), aged from 32 to 66 average 51 ± 9, were examined in a 4 years period. 107 had IBD in several stages and were divided into three groups. Group A (n=68, 45 men and 23 women) had ulcerative colitis, group B (n=39, 23 men and 16 women) had Crohn's disease and group C (n=58, 40 men and 18 women) had general gastrointestinal diseases.

Patients originated from clinics of University Hospital. The evaluation of vitamin D levels was made with the radioimmunoassay method with DiaSorin kits. Statistical analysis was performed by the χ^2 -test. **Results:** 82% of group A had low levels of vitamin D (deficiency), 12% showed insufficiency and 6% had sufficient levels. In group B 83% had deficiency, 15% had insufficiency and 2% had sufficient levels. It should be noted that in both groups, patients with severe diseases had very low OH-D levels. Group C patients, 57% deficiency, 32% insufficiency and 11% sufficiency ($p < 0,005$). **Conclusion:** The evaluation of serum vitamin D in patients with IBD is useful in patients' monitoring. The very low levels of OH-D are associated with disease's severity. Further studies are required to establish a possible improvement in patients' status after vitamin D substitution.

EP-0101

Altered Intestinal Permeability in Recurrent Pregnancy Loss: New Hypothesis of Endometrial Damage

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Introduction: Spontaneous pregnancy loss is the most common obstetric complication worldwide. Recurrent pregnancy loss (RPL), defined as three consecutive pregnancy losses prior to twenty-four weeks of gestational age, can be usually explained in approximately 40% of couples (i.e. parental chromosomal abnormalities, uterine anatomic defects, untreated hypothyroidism, undiagnosed or uncontrolled diabetes mellitus, antiphospholipid antibody syndrome). In all the other unexplained RPLs, causes are still debated. It was already demonstrated abnormally higher endometrial expression of pro-inflammatory cytokines in women with RPL. Recent evidences suggest that the intestinal mucosal dysfunction called "leaky gut" and characterized by an increased translocation of Gram-negative bacteria, might play a role in the inflammatory pathophysiology of the disease. Indeed, passage through a damaged epithelial barrier into the human blood of potentially antigenic molecules might induce systemic immune response and tissue inflammation. Aim of the study was to investigate intestinal permeability (IP) in RPL patients. **Subjects and Methods:** This case-control study prospectively included 60 women with history of unexplained RPL with three or more spontaneous pregnancy losses (<12 weeks of gestation) and 30 women with two or more previous uncomplicated term pregnancies (control group). None of the patients evaluated referred any gastrointestinal symptoms, as weight loss, diarrhea, abdominal distention, flatulence or abdominal pain. IP was assessed using of urinary excretion of ⁵¹Cr-ethylene diamine tetraacetate (⁵¹Cr-EDTA). After an overnight fast, patients were given to drink 0.37 MBq of ⁵¹Cr-EDTA in 10 ml of water; the standard sample (1/50 of administered dose) and a 3-ml sample of 24-hours urine collection were measured with a gamma counter. Urine sample results were expressed as percentages of the administered dose and considered indicative of

altered IP when above 3%. **Results:** ⁵¹Cr-EDTA absorption test showed higher prevalence of abnormal IP in RPL patients ($M \pm SD$: $6.4\% \pm 0.7$) compared to the control group ($M \pm SD$: $2.1\% \pm 0.4$) ($p < 0.001$). **Conclusion:** This study provided evidence of higher frequency of abnormal IP in patients with idiopathic RPL compared to controls, in absence of any gastrointestinal symptoms. As hypothesized, the abnormal gut permeability, related to disruption of bowel intercellular tight junctions, could play an important role in the pathogenesis of endometrial inflammation and reproductive disorders, in the contest of a systemic inflammatory disease. However, further investigations are required to prove the specific mechanism. Therefore, ⁵¹Cr-EDTA study to evaluate intestinal permeability should be considered in the management of unexplained RPL.

EP-0102

Altered Intestinal Permeability in Myotonic Dystrophy: A New Hypothesis of Nonalcoholic Fatty Liver Disease

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Introduction: In the context of the multisystem involvement of myotonic dystrophy (DM), a moderate increase in serum liver function indexes and hepatic steatosis are frequently detected, but their etiology is still unclear. Gut-derived endotoxin may be relevant in nonalcoholic fatty liver disease (NAFLD): previous studies suggest that increased intestinal permeability (IP), caused by the disruption of intercellular tight junctions, may play a role in the pathogenesis of hepatic fat deposition. Aim of the study was to investigate the incidence of IP in DM patients as well as the incidence of NAFLD in these patients, evaluated with multimodality investigations. **Subjects and Methods:** Forty-four patients with DM type 1 (DM1) were investigated for IP, using the urinary excretion of ⁵¹Cr-EDTA. After an overnight fast, patients were given to drink 0.37 MBq of ⁵¹Cr-EDTA in 10 ml of water; the standard sample (1/50 of administered dose) and a 3-ml sample of 24/hours urine were measured with a gamma counter. Urine sample results were expressed as percentages of the administered dose and considered indicative of altered IP when >3%. Control groups included 40 healthy volunteers and 42 non-DM patients with NAFLD (as model of hepatic fat deposition associated with intestinal hyperpermeability). Only twenty patients of them were extensively investigated for NAFLD, through liver chemistry tests, mostly γ GT, and by real-time shear wave elastography (SWE), a non-invasive method to measure liver stiffness. Results were compared with the disease severity, using the Muscular Impairment Rating Scale (MIRS) and the number of abnormal genetic expansions of polymorphic repeats. **Results:** Forty-three out of 44 (97.7%) DM1 patients showed increased IP ($M \pm SD$: $6.98\% \pm 4.80$). IP resulted signifi-

cantly higher in DM1 patients compared to healthy volunteers ($M \pm SD$: $6.98\% \pm 4.80$ vs. $2.02\% \pm 0.66$; $p < 0.001$); however, it was not different from that measured in non-DM patients with NAFLD ($M \pm SD$: $6.98\% \pm 4.80$ vs. $5.63\% \pm 2.31$; $p = 0.10$). Patients investigated extensively for NAFLD ($n = 20$) showed altered IP, similar to the whole group ($M \pm SD$: $6.26\% \pm 4.86$; $p = 0.29$). Seventeen out of 20 (85%) patients had increased γ GT, 12 (60%) steatosis and four (20%) significant fibrosis at SWE. 13/17 (76%) patients with NAFLD showed medium-high grade of MIRS and 16 (94%) more than 150 polymorphic repeats. **Conclusion:** An altered IP is almost invariably detected in DM1 patients, frequently in association with NAFLD. According to these preliminary results, NAFLD is related with more severe disease. Therefore, these data provide stronger support to the supposed pathogenic role for IP in liver dysfunction occurring in DM1 patients.

EP-0103

The Role Of 25 Hydroxy Vitamin D In Obstructive Sleep Apnoea Syndrome

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Purpose: Obstructive Sleep Apnoea Syndrome (OSAS), a disorder associated with increased cardiovascular and cerebrovascular morbidity, has been associated with lowered Vit D levels. The aim of this study is to find an association between serum 25-hydroxyvitamin D [25(OH) D] levels, in OSAS patients and controls and OSAS severity. **Patients & Methods:** 115 patients (85 men, 30 women) aged from 39 to 64 years (mean 49 ± 9 , 5 years) were included in this study. All patients came from the Pulmonary Clinic of the University Hospital of Evros. Patients were divided into controls (apnoea-hypopnea index, AHI $< 5/h$) and OSAS group (AHI $\geq 5/h$). The vitamin D status was measured by radioimmunoassay (RIA) method with kits DiaSorin at in-vitro laboratory of Nuclear Medicine Dept. **Results:** Serum 25(OH)D levels were lower (deficiency) in OSAS patients (17.8 ± 7.8 vs 23.9 ± 12.4 ng/ml, $p = 0.019$). In those patients, levels of serum 25(OH)D were negatively correlated with sleep stages transitions ($r = -0.205$, $p = 0.028$), AHI ($r = -0.187$, $p = 0.045$), oxygen desaturation index ($r = -0.234$, $p = 0.011$) and percentage of time with oxyhaemoglobin saturation $< 90\%$ ($r = -0.172$, $p = 0.041$). In contrast, they were positively correlated with average oxyhaemoglobin saturation during sleep ($r = 0.179$, $p = 0.033$), forced expiratory volume in 1 sec ($r = 0.207$, $p = 0.037$) and oxygen partial pressure ($r = 0.197$, $p = 0.029$). **Conclusions:** Vit D levels were lower (deficiency) in OSAS patients compared to non-apnoeic controls. Several indices of OSAS severity are also correlated with Vit D levels. Further studies are required to establish a possible improvement in patients' status after vitamin D substitution.

EP-0104

Oro-pharyngeal-esophageal scintigraphy (OPES) examination in patients with idiopathic inflammatory myopathies (IIM): results of an ongoing prospective study

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Purpose: OPES is a safe, well-tolerated and repeatable technique for identifying and quantifying various upper gastro-intestinal abnormalities. In IIM, dysphagia is a common manifestation, associated with severe reduction of the quality of life. Our aim is to assess prevalence and severity of dysphagia in IIM patients using OPES, and to correlate the alterations found with patient clinical status. **Methods:** Since 2014, we prospectively enrolled 51 IIM patients. Clinical evaluation included: physician and patient's disease activity assessed by a visual analogue scale (phVAS and pVAS), health quality assessment questionnaire (HAQ) and manual muscle test 8 (MMT8). To evaluate the dysphagia the "MD Anderson dysphagia inventory" (MDADI) was administered at baseline and after 6 months. OPES was conducted using both liquid (OPES-L) and semi-solid (OPES-SS) ^{99m}Tc-technetium-nanocolloid, extrapolating the following parameters: presence of pre-deglutition, multiple deglutition, aspiration, transit time (TT) and retention index (RI) at oro-pharyngeal (OP) and esophageal (E) levels. **Results:** On OPES 4 patients presented multiple deglutitions, 4 bolus aspiration, and 19 uncoordinated esophageal movement. OP-TT was altered in 44% (OPES-L) and 58% (OPES-SS) of patients; E-TT was altered in 11% (OPES-L) and 29% (OPES-SS) patients. RI resulted altered for SS bolus (OP-RI 84%, E-RI 39%), and for L bolus (OP-RI 70%, E-RI 23%) with significant difference $SS > L$ on each phase. Patients with E-RI dysfunction presented altered OP-RI (OPES-L 91%; OPES-SS 80%). According to MDADI score, 32 patients presented dysphagia at baseline (62%; 19 mild, 10 moderate, 3 severe disability) and 28/41 after 6 months (68%, 18 mild, 7 moderate, 3 severe). Patients with onset < 12 months demonstrated a higher correlation between 6-months MDADI and OP-RI OPES-SS compared to baseline MDADI. Significant correlations between disease activity parameters and MDADI were found for phVAS, pVAS, HAQ and MMT8, while on OPES-SS, P-RI correlated with phVAS, pVAS, HAQ and MMT8. **Discussion:** Upper digestive tract impairment is common in IIM, in terms of both TT and RI. OPES-SS most frequently identified alterations, probably due to the greater muscular effort required for efficient swallowing. Patients with esophageal alterations had also dysfunction during oral-pharyngeal phases, suggesting a possible esophageal involvement as secondary step in disease evolution, associated to severe disability. In early-stages, correlations between OP-RI and MDADI score evolution suggest a possible role of OPES in prediction of upper dysphagia. OPES identified patients at higher risk of aspiration and could be an effective tool at baseline and during the follow-up.

EP-0105

Building An Open Source Software Allowing Simultaneous Evaluation Of Esophageal And Gastric Dysmotility In Patients With Systemic Sclerosis And Primary Sjögren's Syndrome

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Aim: Esophageal and gastric involvements are common in systemic sclerosis (SS) and primary Sjögren's syndrome (pSS). Usually, dysmotility diagnosis is made separately with esophageal transit and gastric emptying study (GES). The aims of this study were to evaluate simultaneously intra esophageal and gastric meal distribution and to develop software to quantify gastric emptying scintigraphy. **Materials and Methods:** Twenty-five patients with pSS (8 patients) and SS (17 patients) were included in a retrospective study. Patients were studied in the morning after overnight fasting. Some medications that may have any effect on the rate of gastric emptying were stopped two days before GES. The meal consisted in liquid egg white radiolabeled with, on average, 77 MBq of ^{99m}Tc-sulfur colloid, and a high caloric breakfast. The liquid egg white was ingested by standing patients; after a swallow, and at the same time, dynamic images were recorded, with a gamma camera, at a rapid rate of 1s/frame for up to 60s to capture esophageal transit. Anterior and posterior images were acquired for 120s and were performed every 30 min until 240min. The open source software developed on Fiji/Image J (project petctviewer.org) was used to quantify gastric and esophageal emptying kinetic. Total gastric emptying was analyzed as the percentage of radioactivity retained in the whole stomach over time using the geometric mean. Gastric retention of the ^{99m}Tc-labeled solid meal up to 60% at 2h or up to 10% at 4h was considered delayed gastric emptying. Abnormal esophageal retention (up to 30 s) was considered as pathologic. **Results:** GES was delayed in 14/25 patients (56%), (6 suffering from pSS (75%) and 8 SS (47%)). Esophageal transit was abnormal in 17 patients (68%), (3 suffering from pSS (37%) and 14 for SS (82%)). Ten patients (40%) had both delayed GES and abnormal esophageal transit (2 pSS (25%) and 8 SS (47%) patients). The distal two-thirds of the esophagus were affected in all patients with abnormal esophageal transit. **Conclusion:** In patients with systemic sclerosis or primary Sjögren's syndrome, esophageal and gastric dysmotility can be analyzed during routine solid-meal GES in a single step. In our study, 10 of 25 patients (40%) had both delayed GES and abnormal esophageal transit.

EP-0106

Additional value of static images beyond dynamic oropharyngoesophageal scintigraphy in patients with neurodegenerative diseases

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Aim: to investigate the role of dynamic and static oropharyngoesophageal scintigraphy (OPES) in patients with neurological disorders, evaluated using the Dysphagia Outcome and Severity Scale (DOSS). **Methods:** We enrolled 32 neurological patients (14 women and 18 men; mean age 60 years, range: 24-87) complaining of dysphagia with diagnosis of amyotrophic lateral sclerosis (11/32 patients), bulbar onset SLA (3/32), multiple sclerosis (8/32), Parkinson's disease (4/32), spinocerebellar ataxia (2/32), neonatal brain disease (2/32) and ataxic syndrome (2/32). All patients underwent OPES using a standardized procedure (5 ml semiliquid bolus labeled with 37 MBq of ^{99m}Tc-nanocolloid; dynamic acquisition for 60 seconds). After the dynamic recording, 60-seconds static images were acquired immediately (static1), after a swallowing of a semiliquid bolus not-labeled (static2) and after a swallowing of water not-labeled (static3). Images were acquired with patients face in an 80° projection in front of gamma-camera. Region of interests on the oral cavity and pharynx were drawn to collect data about Oral and Pharyngeal Transit Time (OTT" and PTT"), Oral and Pharyngeal Retention Index (ORI% and PRI%) and Retention in oral cavity and pharynx on static images (%OralStatic1, %OralStatic2, %OralStatic3, %PharynxStatic1, %PharynxStatic2 and %PharynxStatic3 respectively). Patients were divided into 2 groups: DOSS1 (moderate, mild/moderate and mild dysphagia) which included 20/32 patients, DOSS2 (normal or slight compromised swallowing) which included 12/32 patients. T-test was applied to compare DOSS with data obtained at dynamic and static OPES. P<0.05 was considered statistically significant. **Results:** In DOSS1 mean values were: OTT"=1.75" (range 0.5"-3"), ORI%=14.32% (range 0.70%-46.50%), %OralStatic1=5.56% (range 0.28%-16.40%), %OralStatic2=1.85% (range 0.14%-4.79%), %OralStatic3=1.39% (range 0.34%-3.29%), PTT"=1.16 (range 0.5"-5"), PRI%=27.53% (range 0.80%-80.98%), %PharynxStatic1=2.42% (range 0.15%-9.27%), %PharynxStatic2=0.77% (range 0.03%-2.64%) and %PharynxStatic3=0.5% (range 0.07%-1.92%). In DOSS2 mean values were: OTT"=1.71" (range 1"-3"), ORI%=6.53% (range 1%-13.50%), %OralStatic1=2.44% (range 0.68%-5.08%), %OralStatic2=1.19% (range 0.30%-3.01%), %OralStatic3=0.92% (range 0.24%-2.32%), PTT"=1.71" (range 0.5"-11"), PRI%=16.89% (range 2.70%-73.10%), %PharynxStatic1=1.28% (range 0.28%-4.41%), %PharynxStatic2=0.49% (range 0.09%-1.30%) and %PharynxStatic3=0.31% (range 0.05%-0.78%). T-test resulted statistically significant for ORI% (t=-2.224; p=0.03) and for OralStatic1 (t=-2.454; p=0.02). **Conclusion:** Both dynamic and static OPES are well tolerated and easily performed procedures even in

patients with neurological disorders. Performing static images provides important information to complete the dynamic examination, using the unique administration of the radiopharmaceutical, in order to better assess the degree of dysphagia of patients with neurological diseases.

EP-0107

Hepatobiliary Scintigraphy After Liver Transplantation

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Introduction: One of the liver transplantations postoperative complications is the stricture of anastomosis. Hepatobiliary scintigraphy can evaluate both graft function and anastomosis patency. **Materials and Method:** During 2013-2017 289 liver transplantations were performed in our hospital (92.4% orthotopic and 7.6% related). The radionuclide method was used for the early detection of stricture of the anastomosis and the dysfunction of the transplanted organ. 38 patients aged 26 to 65 years (mean 46.3 ± 8.2) after transplantation were examined by hepatobiliary scintigraphy with a radiopharmaceutical tracer Tc-99m-bromezida (120-180 MBq, 1.8-2.0 mSv). Simultaneously evaluated clearance, absorption-biliary function and patency of the anastomosis. To assess biliary function were determined the following parameters: time of maximal accumulation and half-life the indicator of the liver, the time of maximum accumulation and half-life the indicator of the common bile duct and the area of anastomosis, the evacuation time to intestine. The delayed absorption of the indicator in the liver, violation of clearance function and changes Tmax and T1/2 were characteristic signs of the graft dysfunction. The normal indices of the absorption and biliary function were determined in the control group (20 patients without liver and gallbladder diseases under the age of 55 years). **Results:** 13 patients (34.2%) were identified with absorption and biliary liver graft dysfunction, include 5 patients (13.9%) identified with decreasing of function combined with anastomosis stricture and 4 patients (10.5%) - with anastomosis failure and appearance of minimum bile under the liver (bile leakage). The stricture of the anastomosis by hepatobiliary scintigraphy looked like as long focal delay in the distal common duct from the 15th to 60th min of the study and later was confirmed by MR-cholangiography. These cases with anastomosis stricture were required the surgical correction (4 - stent placement, 1 - Roux-en-Y reconstruction using a standard technology). **Conclusion:** Hepatobiliary scintigraphy as a screening method after liver transplantation allows simultaneously assess the changes of the liver graft function, impaired patency and anastomosis failure in the early stages of the development of complications.

EP-0108

The Importance Of Image Processing And Liver Function Analysis In Hepatobiliary Scintigraphy

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Purpose/Introduction: The use of hepatobiliary scintigraphy (HBS) is increasing exponentially for the preoperative evaluation of liver failure risk before major hepatectomy. The leading center in Europe in the application of HBS is the Academic Medical Center (AMC, Amsterdam, The Netherlands) where data are routinely processed on a Hermes Workstation (Multimodality, Hermes Medical Solutions). The cut-off for residual liver function ($2.69/\text{min}/\text{m}^2$), established by the AMC with dynamic HBS and using only the anterior projections, has been used so far. However, Geometric mean (Gmean) and SPECT/CT have been introduced for the measurement of segmental liver function. Our purpose is to calculate the functional results obtained using two different analytic methods and comparing them with Hermes data. **Subjects & Methods:** Between November 2016 and October 2017, 29 patients were submitted to major hepatectomy according to preoperative CT volumetry at Sant'Orsola-Malpighi Hospital (Bologna, Italy). Data regarding HBS were retrospectively reviewed. HBS protocol included a first dynamic acquisition (36 frames, 10 sec/frame) and a sequential SPECT (60 frames, 5 sec/frame)/low-dose CT. Images were processed using a freely downloadable image analysis software package (Image J, <https://imagej.nih.gov/ij/>). Analysis on dynamic images was done as follows: 1) drawing ROIs separately for anterior and posterior acquisitions and calculating $G_{\text{mean}}(\sqrt{\text{anterior} \times \text{posterior}})$; 2) drawing ROIs on a single Gmean image provided by our Workstation (Xeleris, GE); 3) as in point 2 but using the Hermes Hybrid Viewer via TeleHERMES™ (Hermes Solutions) uploading both the anterior and posterior images. Future liver remnant function (FLR-F) was calculated multiplying the total liver function, obtained with these three methods, by the % of counts within the ROI of the FLR on SPECT images ($^{\text{SPECT}}\text{FLR-C}$). FLR-F values, named respectively $^{\text{ROI-ROI}}\text{FLR-F}$, $^{\text{pixel-pixel}}\text{FLR-F}$ and $^{\text{Hermes}}\text{FLR-F}$ were compared by paired t test and expressed as mean values. **Results:** $^{\text{pixel-pixel}}\text{FLR-F}$ was significantly larger than $^{\text{ROI-ROI}}\text{FLR-F}$ ($3.01\%/\text{min}/\text{m}^2$ vs. $2.35\%/\text{min}/\text{m}^2$, mean difference $0.66\%/\text{min}/\text{m}^2$, $P < 0.0001$). Although $^{\text{ROI-ROI}}\text{FLR-F}$ was still significantly smaller compared to $^{\text{Hermes}}\text{FLR-F}$ (mean difference $-0.68\%/\text{min}/\text{m}^2$, $P = 0.007$), there was no statistically significant difference between $^{\text{pixel-pixel}}\text{FLR-F}$ and $^{\text{Hermes}}\text{FLR-F}$ (mean difference $-0.02\%/\text{min}/\text{m}^2$, $P = 0.930$). There was no difference also with regard to $^{\text{SPECT}}\text{FLR-C}$ (mean difference 2.6% , $P = 0.077$). **Discussion/Conclusion:** Our results showed that the major role in calculation is played by the datasets used for ROI analysis. When Gmean image datasets were made using a pixel-pixel calculation, results showed no significant differences between ImageJ and the Hermes data. Regardless of the software used, shared protocols for liver function analysis are fundamental to reduce at a minimum bias of calculations and enable comparisons across different centers.

EP-0109

The Value of Two Consecutive Post-Transplant Renal Scintigraphy Procedures. A Single-Center Retrospective analysis

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Introduction: The duration of delayed graft function (DGF) is an outcome of interest owing to the friction between improved efficiency of transplant care and an increased use of renal allografts from marginal deceased donors exhibiting DGF. Therefore, this study focused on the association between parameters of two consecutive post-transplant renal scintigraphy (RS) procedures and the duration of DGF. **Methods:** From 2011 to 2014, renal transplant recipients referred for a Tc-99m MAG3 RS procedure within 3 days after transplantation, were included in a single-center retrospective study. Primary endpoint was the duration of DGF, based on the need for dialysis or a failure of serum creatinine to decrease with $\geq 10\%$ / day during 3 consecutive days. Both the first scintigraphy, within 3 days, and the second scintigraphy, between 3–7 days after transplantation, were analyzed using a 4-grade qualitative grading scale and several quantitative indices indicating specific renal functions (*TFS*, *cTER*, *MUC10*, *Average Upslope*). The association between these values and the duration of DGF was evaluated using Kaplan Meier curves with Log-rank tests and uni- or multivariate Cox proportional hazard analysis, adjusting for the potential confounding clinical variables from the allograft donors, allograft recipients, and transplant procedures. **Results:** We evaluated 200 first and 108 (54%) consecutively performed scintigraphies. A significant association was observed between the quantitative indices, from both the first and second scintigraphy, and the duration of DGF on univariate analysis, but not on multivariate analysis. Kaplan-Meier curves for the duration of DGF and qualitative grading of the first RS, showed a significant difference in DGF duration between Grade 2, Grade 3 and Grade 4 ($p < 0.01$), and qualitative grading of the second RS showed a significant difference between Grade 3 and Grade 4 ($p < 0.01$). Multivariate analysis showed an independent significant association of the qualitative grading scale, from both the first and second RS, and the duration of DGF, HR 1.6 (1.3–2.1, $p < 0.01$) and HR 2.1 (1.4–3.1, $p < 0.01$) respectively. **Conclusions:** An independent association between a higher RS grade, from both the first and second RS, and longer duration of DGF was identified applying the 4-grade qualitative grading scale. This provides the opportunity for clinicians to identify patients with an expected longer duration of DGF.

EP-0110

Evaluation Of Renal Transplant Scintigraphy In Diagnosis Of Urinary Leakage

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Introduction: In this study, we evaluated renal transplant scintigraphies (RTSs) and the contribution of single photon emission computed tomography (SPECT)/computed tomography (CT) in the case of urinary leakage suspicion. **Subjects & Methods:** A total of 1154 RTSs with technetium-99m diethylenetriaminepentaacetic acid (Tc-99m DTPA) performed to 502 patients between October 2011 and March 2018 were analyzed retrospectively with respect to urinary leakage. Tc-99m DTPA was used for all RTSs. Late static images were obtained 1–3 hours after dynamic images in the event of urinary leakage sus-

picion. SPECT/CT was also performed when the suspicion was continuing because of unclear findings on the late static image.

Results: In 26 (mean age: 39.3 ± 16.2 ; 14 male, 12 female; 10 lived and 16 deceased donor transplants; mean performing time of RTSs after operation: 16.6 ± 13.7 days) of 502 patients, there was urinary leakage suspicion on planar images. In 15 patients, urinary leakage was clearly seen on the early dynamic or the late planar images. But SPECT/CT was needed to be performed to 11 patients. SPECT/CT confirmed the diagnosis of urinary leakage in 3 patients which were not clearly seen on the planar images. In two of them, urinoma was just anterior and adjacent to the renal graft and it was just anterior to the bladder in one patient. In 8 patients, diagnosis of urinoma was ruled out by SPECT/CT. In almost all of these patients, the suspicious extrarenal activities seen on the planar images were in the extraperitoneal area at the ipsilateral abdominal wall muscles probably due to increased blood flow and inflammation caused by recent surgery. As a result, urinary leakage was diagnosed by RTS in 18 of 502 (3.6%) patients. **Conclusion:** Renal transplant scintigraphy is the best imaging modality in the diagnosis of urinary leakage. But the diagnosis can sometimes be difficult when urinoma is small and adjacent to renal graft or bladder. It is also difficult in the case of abdominal wall inflammation due to recent surgery. We concluded that SPECT/CT is very useful in the differential diagnosis of these situations.

EP-0111

Simple Estimation of ^{99m}Tc -MAG3 Plasma Clearance in Dynamic Renal Scintigraphy

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Measurement of plasma clearance in dynamic renal scintigraphy is traditionally considered to be intrinsically unreliable and inaccurate. The aim of our study was to validate a new simple method based on plotting ^{99m}Tc -MAG3 volume of distribution against normalized time. **Methods:** we have analyzed data of ^{99m}Tc -MAG3 dynamic renal scintigraphy in 54 patients (23 men and 31 women at the age of 21–86 yrs) archived in the database www.dynamicrenalstudy.org. Reference ^{99m}Tc -MAG3 plasma clearance measured by 2 blood samples ($16\text{--}272\text{ ml/min/1.73m}^2$) was then estimated by (A) single blood sample (Bubeck et al 1992), and two methods (B, C) using the raw heart ROI curve $P(t)$ extracted from dynamic renal scintigraphy. Method (B) was based on Stewart-Hamilton principle and analogous to standard in vitro procedure estimating plasma clearance Z as the ratio of injected activity D and total area AUC under plasma concentration curve, $Z = D/AUC$. Method (C) was the new method estimating plasma clearance Z from the plot of ^{99m}Tc -MAG3 expanding volume of distribution $D/P(t)$ against normalized time $[P(t)dt/P(t)]$. Methods B and C first produced plasma clearance as fraction of total plasma volume cleared per unit time. Conventional values of Z in ml/min/1.73m^2 were obtained by multiplying fractional clearance by normal plasma volume in adults (2846ml/1.73m^2). Quality of estimation was assessed by correlation coefficient (r) and both mean absolute and rel-

active prediction errors (MAE, MRE). **Results:** Bubeck's method (A) predicted the result of the reference method with $r=0.96$, $MAE=14$ ml/min, and $MRE=24\%$. The method (B) derived from Stewart-Hamilton principle predicted the results of reference method with $r=0.94$, $MAE=20$ ml/min, and $MRE=23\%$. The new method (C) predicted the results of reference method with $r=0.94$, $MAE=19$ ml/min, and $MRE=21\%$. Diagnostic accuracy of correct classification of the patient's ^{99m}Tc -MAG3 plasma clearance below or above 50, 100, 150, and 200 ml/min/ 1.73m^2 exceeded 90% with all three validated methods (A), (B), and (C). **Conclusion:** the new method (C) based on plotting ^{99m}Tc -MAG3 volume of distribution against normalized time performs equally well as the method (B) based on Stewart-Hamilton principle and almost as well as Bubeck's one sample method (A). The new method does not require complex data processing, blood sampling, background subtraction, nor attenuation correction. Its calculation is simple and can be automated. Reasonably accurate prediction and high diagnostic accuracy of the patient's plasma clearance provided by the new method suggests that the method may become a useful tool to estimate total renal function in dynamic renal scintigraphy.

EP-0112

Assessment of the relation between pelvicalyceal dilatation in ultrasound and features of obstructive uropathy in dynamic renal scintigraphy

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Introduction: Ultrasound is the first-line imaging in the diagnostics of the urinary system. It provides valuable morphological information, but its usefulness in assessment of the function of renal parenchyma is limited. Dynamic renal scintigraphy provides much more accurate information about parenchymal function of kidneys and urinary outflow. Aim: The aim of the study was to establish morphological ultrasound criteria for high likelihood of obstructive uropathy. Material: 57 patients (37 women, 20 men, between 18 and 82 years old, average age 50) with the pelvis dilatation $\geq 10\text{mm}$ in one or both kidneys newly diagnosed in ultrasound, without earlier history of kidney and urinary tract diseases or renal surgery. A total of 77 kidneys were included in the study. **Methods:** Ultrasound and dynamic renal scintigraphy were performed on the same day. In ultrasound, maximum anteroposterior diameter of the renal pelvis (mAPD) and anteroposterior pelvic diameter at hilum (hAPD) were obtained. The ratio of total pelvicalyceal area to the whole kidney area (PCA/WKA) was also calculated. Uropathy was determined by the positive diuretic test in renal scintigraphy performed using 111 MBq of ^{99m}Tc -EC. **Results:** In dynamic renal scintigraphy, features of uropathy were found in 20 out of 77 kidneys (28%). Optimal thresholds for detection of obstructive uropathy for measured ultrasound parameters were determined based on the ROC curves: mAPD ≥ 25 mm (sensitivity 90%, specificity 77%, accuracy 81%, AUROC 0.91) hAPD ≥ 20 mm (sensitivity

85%, specificity 86%, accuracy 86%, AUROC 0.85) PCA/WKA $\geq 23\%$ (sensitivity 90%, specificity 79%, accuracy 82%, AUROC 0.87).

Conclusions: Determined thresholds of parameters measuring pelvicalyceal dilatation in ultrasound, including the easiest one to obtain in routine diagnostics - mAPD, provide satisfactory effectiveness in isolating kidneys with high likelihood of obstructive uropathy. Their application can optimize the selection of patients for further kidney diagnostic imaging (dynamic renal scintigraphy or urography).

EP-0113

Application of Normalized Values of Kidney Clearance Function in the Diagnosis of Bilateral Obstructive Nephropathy - a Preliminary Report

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Introduction: Dynamic renal scintigraphy provides effective diagnosis of obstructive uropathy and nephropathy. However, in case of a bilateral outflow impairment, relative differential renal function (DRF), which is a primary quantitative criterion for diagnosis of unilateral obstructive nephropathy (when its value is below 45%, according to EANM guidelines from 2011), becomes unreliable. In case of bilateral nephropathy with similar extent, this parameter may even be within the normal range (45% - 55%) for both kidneys. **Aim:** The aim of this study was to assess diagnostic usefulness of the original, normalized, absolute parameter proportional to the value of renal clearance function (K) in the evaluation of obstructive nephropathy in a group of patients with bilateral uropathy. **Material and Methods:** 16 healthy volunteers (32 kidneys) without history of kidney diseases were examined to determine normative value of K index. Then, 8 patients (16 kidneys) with bilateral obstructive uropathy found in standard dynamic renal scintigraphy performed using 111 MBq of ^{99m}Tc -EC (cumulative renographic curve that continued rising or dropped by less than 50% after i.v. administration of Furosemide) were examined. For each of the subjects 60 sequential 20s images were obtained, which were then assessed using an original method of post-processing scintigraphic data. It included normalization of renographic curves to the area under the heart curve. Subsequently, these normalized values from the uptake phase (between 2nd and 3rd minute) were inserted into the linear regression equation, from which K index was obtained. **Results:** In healthy volunteers the average value of K index was 0.23 ± 0.05 . The value of 0.13 (mean - 2 SD) was taken as the lower limit of the norm. Values below that limit suggest obstructive nephropathy. In patients with bilateral obstructive uropathy, 5 kidneys met the conventional criteria of nephropathy (DRF below 45%), while 11 kidneys had DRF within normal range. K index was below the norm in 9 kidneys (including 4 kidneys with low and 5 with normal DRF), while its value was normal in 7, including one kidney with reduced DRF (37%). K index changed the diagnosis in 6 kidneys out of 16 (38%). **Conclusions:** Preliminary results indicate usefulness of K index in diagnosis of obstructive nephropathy in patients with

bilateral obstructive uropathy. For further evaluation of clinical value of this method, it is planned to examine a larger group of patients with varying degrees of renal parenchymal function impairments.

EP-0114

Role of Scintigraphic Evaluation in Renal Ectopic and Fusion Anomalies

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Purpose: Renal ectopic and fusion anomalies are usually diagnosed with radiological imaging modalities such as ultrasonography (USG) and computed tomography (CT). However, functional scintigraphic studies not only recognize renal anomalies but also provide a functional evaluation of the kidneys. Tc-99m diethylenetriamine pentaacetic acid (DTPA) dynamic renal scintigraphy is used for the evaluation of perfusion, extraction, and excretion functions. In this study, we aimed to investigate the frequency and the functions of renal fusion and ectopic anomalies with dynamic renal scintigraphy, in a large group of patients.

Subjects&Methods: Between July 2013 and January 2018, we evaluated retrospectively a total of 959 patients (478 F, 481 M) who underwent Tc-99m DTPA dynamic renal scintigraphy in our department. The mean age of the patients was 43.08 years $\pm$ 15.63 (range of age: 12-86). DTPA dynamic kidney scintigraphy performed with F + 20 protocol which the images are acquired from anterior projection, and ROI's were defined for the whole kidney including the collecting system, background for each kidney and the aorta. The dose of furosemide was 0.5 mg/kg or a maximum dose of 40 mg in adult and 1.0 mg/kg or a maximum dose of 20 mg in child patients. We evaluated the functions and diuretic response of the kidneys with curves and quantitative analysis along with a visual evaluation of the three-phase dynamic scintigraphy images. **Results:** Renal ectopic or fusion anomalies were detected in 29 of 959 patients (12 F, 17 M). The mean age of the patients with renal localization or fusion anomaly was 35.62 years $\pm$ 14.18 (range of age: 12-66). We confirmed the findings of the patients with Tc-99m dimercaptosuccinic acid (DMSA) cortical kidney scintigraphy, USG and/or CT if available. We observed ectopic pelvic kidney in 16 patients (55.2%), horseshoe kidney in 11 patients (37.9%) and crossed fused renal ectopia in 2 patients (6.9%). Nevertheless, there was no crossed non-fused kidney in our patient group. The incidence of the ectopic pelvic kidney was 1.67%, horseshoe kidney was 1.15% and crossed fused renal ectopia was 0.21%. Functional evaluation of twelve (41%) of the 29 kidneys revealed an impaired extraction function, 4 (14%) of the kidneys showed delayed excretion function responded to diuretic and 5 (17%) of the kidneys exhibited delayed excretion function with no diuretic response. **Conclusion:** Dynamic renal scintigraphy is a useful imaging modality in the diagnosis and functional evaluation of the renal ectopic and fusion anomalies.

EP-0115

Role Of Renoscintigraphy With ^{99m}Tc-DTPA In Determining Renal Function In Patients With Hepatocellular Carcinoma

After Transplantation Of Liver And Immunosuppressive Therapy

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Aim: The aim of the study was to evaluate the diagnostic role of renoscintigraphy with parameters ^{99m}Tc-DTPA in assessing the renal function of patients with hepatocellular carcinoma (HCC) after transplantation of liver and immunosuppressive therapy. **Material and Method:** Retrospectively was used to study 168 patients (96 women and 72 men) aged 24 to 61 years. All patients were divided into two cohorts. The first cohort included 87 patients after immunosuppressive therapy with Tacrolimus at a rate of 0.3 mg/kg per day, the second cohort included 81 patients after taking Cyclosporin at a rate of 20 µg/kg. In studied patients, the value of glomerular renal filtration rate and the effective renal plasma flow were calculated. The radionuclide parameters of the first cohort were compared with the data of the second cohort. Renoscintigraphy was performed dynamic mode during 30 minutes after intravenous injection of ^{99m}Tc-DTPA at a rate of 2 MBq/kg. **Results:** In the patients of the first cohort the mean glomerular filtration rate of the kidneys was 91.5 $\pm$ 0.21 ml/min, in the patients of the second cohort was 62.2 $\pm$ 0.17 ml/min. The mean parameters of the effective flow of renal plasma in patients of the first cohort were 524.1 $\pm$ 0.37 ml/min, in patients of the second cohort were 449 $\pm$ 0.28 ml/min. According to the results of statistical evaluation, the average parameters of the glomerular filtration rate and the effective renal plasma flow in the second cohort of patients were significantly decreased in comparison with the calculated parameters of the first cohort of patients ($p < 0.05$). **Conclusion:** Renoscintigraphy allows to evaluate the effectiveness of treatment, as well as to carry out pathogenetic correction of immunosuppressive therapy in patients with HCC after transplantation of liver. Tacrolimus in patients with HCC after transplantation of liver was less nephrotoxic than Cyclosporin and, accordingly, is more preferable in the choice tactic of treatment.

EP-0116

Gamma-H2AX Foci In Peripheral Blood Lymphocytes To Detect And Quantify Radiation-induced DNA Damage After ^{99m}Tc MDP Bone Scintigraphy

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Purpose: Ionizing radiation-induced DNA double-strand breaks (DSBs) are considered to be the major mechanism of cell death. If unrepaired or improperly repaired, DSBs contribute to genome instability and carcinogenesis. Immunofluorescence detection of phosphorylated histone variant H2AX (γ -H2AX) is a reliable and sensitive technique to monitor ionizing radiation-induced DSBs in peripheral blood lymphocytes (PBLs). We investigated whether γ -H2AX could be used as an in vivo marker to assess the impact of DNA damage in patients undergoing bone scintigraphy (BS). **Subjects & Methods:** Eleven consecutive patients (2 women, 9 men; mean age, 47.2 years; range, 19-71 years) undergoing technetium-99m methylene

diphosphonate (^{99m}Tc MDP) bone scans were prospectively recruited. None of these patients had had any ionizing imaging procedures in the past seven days or chemotherapy/radiotherapy within the prior six months before bone scan. The average radiotracer activity injected was 922 MBq (range: 888–925 MBq). PBLs were isolated from blood samples drawn directly before the injection of the radiotracer and 2.5 hours later. After performing DNA DSBs were detected by γH2AX immunofluorescence staining and quantified (in terms of γH2AX foci/cell) with automated digital microscopy in each of the two blood samples to assess any significant differences. Statistical analysis was performed with pair t test. The study was approved by the local ethics committee, and written informed consent was obtained from each patient. **Results:** PBLs from blood taken before radiotracer injection showed a median of 0.34 γH2AX foci/cell (range 0.1–1.02) as compared with a median of 0.63 γH2AX foci/cell (range 0.28–1.41) for PBLs from blood taken 2.5 hours after injection ($P < 0.029$), consistent with evidence of DNA breaks from a single ionizing radiation study. **Conclusions:** $\gamma\text{-H2AX}$ immunofluorescence microscopy can be used to measure radiation-induced DNA double-strand breaks in the dose range of diagnostic Nuclear Medicine. ^{99m}Tc MDP = technetium-99mmethylenediphosphonate

EP-0117

Is Absolute Erythrocytosis More Frequent With Technetium-99m Or Chromium-51 Erythrocyte Labelling?

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Introduction: Absolute erythrocytosis is proved elevated total red cell mass volume beyond optimal value for more than 10 percent, using blood, plasma and red cell mass volumes measurement. It can be performed by red blood cell (RBC) labelling either with chromium-51 sodium chromate, or by technetium-99m. The aim was to compare absolute erythrocytosis frequency in patients with clinical diagnosis of absolute erythrocytosis in whom RBC labelling was performed with chromium-51 and with technetium-99m. **Subjects & Methods:** A retrospective study of the results of blood, plasma and total red cell mass volumes measurement was carried out using a database of 3616 tests performed at Center of Nuclear Medicine, Clinical Center of Serbia in Belgrade. Four hundred consecutive patients clinically diagnosed with absolute erythrocytosis were included in the investigation. Erythrocyte labelling was performed with chromium-51 in 200, and with technetium-99m in other 200. In all 400 patients optimal values of blood, plasma and red cell mass volumes were determined, too, using ICSH method. **Results:** There was no significant difference in age, gender, body mass index, optimal values of blood, plasma, and total red cell mass volumes between the examined groups. Absolute erythrocytosis was confirmed in a group of 80/200 (40 %) patients in whom RBC labelling was performed with chromium-51 and in 179/200 patients (89.5 %) in whom labelling was performed

with technetium-99m. The difference in the frequency of absolute erythrocytosis was statistically highly significant. It was 2.2 times higher in the group of patients with RBC labelling with technetium-99m compared to the group with RBC labelling with chromium-51. The suspicion of polycythemia was 3.3 times more common in the group with RBC labelling performed using technetium-99m. **Discussion:** The frequency of absolute erythrocytosis is higher when RBC labelling is performed using technetium-99m. The reason is in the fact that technetium-99m is washed-out from the labelled RBC, which yields falsely elevated values of measured blood, plasma and total red cell mass volumes. Therefore, the results of determining blood, plasma and total red cell mass volumes are more reliable and more accurate with chromium-51 compared to technetium-99m.

EP-0118

How To Differentiate IgG4-related Sialadenitis From Physiological Submandibular Accumulation Using FDG-PET/CT? - Morphological And Systemic Approach

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Aim: Sclerosing sialadenitis is one of the characteristic manifestations of IgG4-related disease (IgG4-RD), and the assessment of submandibular glands is important for accomplishing less-invasive biopsy to confirm the diagnosis of IgG4-RD. FDG-PET/CT has been considered to be helpful for the diagnosis of IgG4-RD; however, as there is substantial overlap in the FDG avidity of sclerosing sialadenitis and normal submandibular glands, simply making SUVmax cutoff levels is not so practical. Since physiological submandibular accumulation has a certain morphological and systemic pattern, our aim was to recognize the uptake distribution pattern to make more excellent differential diagnosis. **Subjects and Methods:** All the study population underwent FDG-PET/CT between 2013–2017: The cases included were 11 patients (age: 46–84, M/F: 7/4) with biopsy-proven IgG4-related sialadenitis; the controls were 23 healthy individuals under 60 years-of-age studied for cancer screening (age: 26–59, M/F: 15/8) whose submandibular glands showed SUVmax ≥ 3.0 . The shape, homogeneity, and symmetry of FDG uptake in the submandibular glands were visually compared, as well as their SUVmax. Besides, FDG accumulation in the Waldeyer's ring including palatine tonsils was measured and the superiority when compared with the submandibular gland uptake was assessed. **Results:** The cases with IgG4-related sialadenitis showed significantly higher submandibular gland SUVmax (6.2 ± 1.3 ; range 3.9–8.1) than the healthy controls (3.6 ± 0.4 ; range 3.0–4.2) ($p < 0.0001$). 7/11 of the IgG4-RD cases showed swelling, 6/11 showed deformity, and 9/11 showed heterogeneous uptake (with a fine multidirectional cleft or with a punctate feature) in the submandibular glands, whereas all the controls showed normal size, smooth margin, and homogeneous uptake (with a unidirectional linear slit). Excluding 3 cases that underwent unilateral submandibular gland resection before FDG-PET/CT, 4/8 of the IgG4-RD cases showed asymmetric submandibular uptake, whereas all the controls had symmetric uptake. In all the IgG4-RD cases except one after the unilateral gland resec-

tion, the involved submandibular glands showed higher uptake than the Waldeyer's ring including palatine tonsils ($SUV_{max} = 4.3 \pm 0.9$; range 2.4–5.6). In all the healthy controls, FDG accumulation in the palatine tonsils showed higher SUV_{max} (6.6 ± 1.6 ; range 4.4–10.1) than physiological submandibular gland accumulation. **Conclusion:** Morphological assessment about submandibular accumulation provides helpful information in the diagnosis of IgG4-RD. Moreover, the relation with palatine tonsils is important in the differential diagnosis from physiological submandibular accumulation.

EP-0119

Evaluation of the Rate of False Positive Diagnosis of Absolute Erythrocytosis / Polycythaemia Vera by Total ^{51}Cr -RBC Mass Volume Investigation

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Introduction: Autologous RBC labelling with chromium-51 is used for routine method of blood, plasma and total RBC mass volume (RBCM_V) measurement in patients with clinical diagnosis of absolute erythrocytosis (AE) and polycythaemia vera (PV). Hemoconcentration can lead to erroneous diagnosis of AE and PV. The aim was to estimate the frequency of false positive diagnosis of AE/PV and to estimate the role of haemoconcentration in it. **Subjects & Methods:** A retrospective study of the results of blood, plasma and RBCM_V measurement after autologous RBC labelling with chromium-51, was carried out using results of 1139 consecutive tests performed at Center of Nuclear Medicine, University Hospital in Belgrade, Serbia. Out of these, there were 848 patients with clinical diagnosis of either AE (369) or PV (479). Optimal values for blood, plasma and RBC mass volumes were calculated for each patient and compared with the measured values. Deviations inside the range of $\pm 10\%$ were considered physiological. RBCM_V lower than 90% of optimal meant anemia; RBCM_V higher than 110% of optimal indicated AE, RBCM_V higher than 125% suggested PV. We compared the frequency of hemoconcentration (plasma volume lower than 90% of normal value) between these four groups. **Results:** Out of 848 patients diagnosed with AE, 148 (17.4%) were anemic, 339 (40.0%) had normal RBCM_V, 138 (16.3%) had AE and 223 (26.3%) suspected PV. The initial clinical diagnosis of AE was rejected in 231/369 patients (62.6%). Clinical diagnosis of PV was rejected in 256/479 patients (53.4%). Initial clinical diagnosis was changed after blood, plasma and RBC mass volume investigation in 487/848 patients (57.4%). Hemoconcentration was present in 85.8% of anemic patients, in 59.6% patients with normal RBCM_V, in 23.1% patients with AE and in 16.1% with PV. The difference in hemoconcentration frequency was highly significant (*p* lower than 0.0001). Hemoconcentration was more frequent in anemic patients and in normal subjects than in AE and PV. Out of 848 patients 292 were subjected to phlebotomy. Prior to the RBCM_V test 84/292 (28.8%) had normal RBCM_V and 23/292 (7.9%) were anemic. After the phlebotomy however, 41/84 (48.8%) patients with previously normal RBCM_V, exhibited anemia. **Conclusion:** RBC mass volume measurement results rejected clinical diagnosis of absolute erythrocytosis/polycythaemia vera in 57.4% pa-

tients (40% had normal RBCM_V, and 17.4% were anemic). Hemoconcentration leads to erroneous conclusions in more than half of patients with clinical diagnosis of absolute erythrocytosis/PV.

EP-0120

Evaluation of red cell volume measurements by radioisotope dilution technique and venous hematocrit in the determination of plasma volume variation during hemodialysis

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Aim: During hemodialysis (HD) there is an intravascular volume depletion that can condition hemodynamic instability. The main aim was to determine the plasmatic volume changes during the HD session. In addition, secondary aims were the evaluation of the assumption of constant relationship between whole-body and venous hematocrit (*f*-cell) and the accuracy of the serial red cell volume determinations at each HD session. (it is assumed that it must be constant during the HD session in the absence of hemolysis or blood leak). **Material and Methods:** Seven patients were studied during two HD's treatment (14 HD sessions). The red cell volume (RCV) was determined by the isotopic dilution method with a single administration per patient of 1.85 MBq Chromium-51 red blood cells. Blood samples were withdrawn in duplicate at the following times during HD: 0 (before starting), 1, 2, 3 and 4 hours. It was measured the red cell volume and the venous hematocrit (Hv) at these time points. Blood volume (BV) was estimated from the measured RCV, Hv and the consensual *f*-cell ratio constant as $0.91 (BV = RCV / f_{cell}^{constant} \cdot Hv)$. Plasma volume was obtained from the difference between the blood volume and the red cell volume. Relative plasma volume (RPV) was also obtained from absolute plasma volume ($RPV_t = PV_t / PV_0$). The variable *f*-cell ratio at different times was calculated from the equation: $RPV_t = (Hv_0 \cdot f_{cell}^{constant} / Hv_t \cdot f_{cell}_t) \cdot (1 - Hv_t \cdot f_{cell}_t / 1 - Hv_0 \cdot f_{cell}^{constant})$. Statistic rAnova test was performed. **Results:** During HD, the mean hourly variation of plasma volume was -3.4% (SD = 5.7). There is a significant decrease of RPV during HD (*p* = 0.001). Means 0.98 (SD = 0.05); 0.96 (SD = 0.08); 0.87 (SD = 0.08); 0.87 (SD = 0.08) at 1, 2, 3, and 4 hours respectively. Significant differences (*p* = 0.34) were not found between the hourly *f*-cell mean of all the HD sessions. The average of *f*-cell is 0.91 (SD = 0.02) that correspond with the constant assumption at the blood volume estimation. The mean *f*-cell did not significantly change between individual subjects throughout HD (*p* = 0.760). The five measurements of the red cell volume made to each patient per HD session, provided accurate determinations, with the mean standard deviation of 36 ml. **Conclusions:** It was determined the plasma volume decrease during HD. The *f*-cell stability makes acceptable the estimation of blood and plasma volumes from red cell volume and venous hematocrit. The accuracy of the red cell measurements per patient and session confirm the high reproducibility of the methodology.

EP-0121

Lymphoscintigraphy: retrospective analysis of a case series

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Aim: To review lymphoscintigraphy referrals regarding clinical indications, main clinical history data and symptoms, lymphoscintigraphic results and follow-up. **Subjects and Methods:** Retrospective analysis of all lymphoscintigraphies performed in our department between July 2006 and December 2017, characterising: patients' age; clinical indication; location, duration and severity of lymphedema; lymphoscintigraphic results and clinical follow-up. Lymphoscintigraphies were performed using Tc-99m-labelled albumin nanocolloid. Mann-Whitney and Chi-Square tests were used for statistical analysis. **Results:** A total of 49 lymphoscintigraphies (45 first and 4 follow-up) were performed to a population of 45 patients, 41 adults with median age and interquartile range of 54[41.5;67] years; and 4 children with median age and interquartile range of 2.5[0.6;5.5] years. Clinical indications in the paediatric population were: 2 primary lymphedema, 1 secondary lymphedema and 1 chyluria; lymphatic drainage being seriously impaired bilaterally in one primary lymphedema and unilaterally in the secondary, both kept under conservative treatment. In the 41 adults, clinical indications were: primary lymphedema in 13 (31.7%), secondary lymphedema in 18 (43.9%), chylothorax in 4 (9.8%), ascites in 2 (4.9%) and other causes in the remaining 4 (9.8%). Lymphatic drainage was impaired in all primary lymphedema cases, in 66.7% of secondary lymphedema, and in 50% of the remaining indications. Within the subgroup of 31 patients with lymphedema, there was a previous diagnosis of venous insufficiency in 9 (29%); the location of the oedema was in lower limbs in 23 (74.2%) and in upper limbs in 8 (25.8%); the median and interquartile range of its duration was 10[3;60] months; and the severity of lymphedema, was moderate to severe in 9/13 (69.2%) patients with primary lymphedema and in 15/18 (83.3%) of those with secondary lymphedema. Drainage impairment and presence of collateral drainage pathways were statistically significant higher in the primary compared to the secondary lymphedema group ($p=.043$ and $p=.009$, respectively). There were no statistically significant differences between these groups regarding age ($p=.769$), duration of the oedema ($p=.324$) and presence of concurrent venous insufficiency ($p=1.00$). No statistically significant association was found between the severity of the oedema and the presence of collateral drainage pathways ($p=1.000$). On follow-up, 19/31 (61.3%) patients maintained lymphedema and underwent conservative treatment (physiotherapy and elastic compression). Complete resolution of the lymphedema was found in 4 cases: 2 slight and 2 moderate to severe. **Conclusions:** Lymphoscintigraphy is a very sensitive exam that can accurately characterize lymphatic drainage. In our population, it is clinically accepted and supports treatment planning.

EP-08

e-Poster Area

Paediatrics: Paediatrics

EP-0122

18F-DOPA PET-CT In The Different Morphological Forms Of Congenital Hyperinsulinism

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Aim: Differential diagnosis between focal and diffuse forms of congenital hyperinsulinism (CHI) plays the key role because it determines further treatment, including surgical strategy. The aim of the study was to assess 18F-DOPA-PET/CT capabilities in preoperative differentiation between morphological forms of CHI. **Methods:** We studied 13 patients (from 1 to 33 months) with clinical and laboratory signs of CHI. All patients underwent 18F-DOPA-PET/CT to identify the form of CHI. Four 10-minutes long PET/CT scans of abdomen were performed at 10, 30, 40 and 50 minutes after tracer injection (4 MBq per kilogram of body weight). The pancreatic index (PI) was calculated as a ratio between SUVmax in the most active pancreatic part to SUVmax in the next active part. PI value under 1.5 was suggested to identify the diffuse form, over 1.5 - for the focal form of CHI. All patients underwent surgical treatment with following histological study of pancreatic specimens, including immunohistochemical analysis (IGH). **Results:** According to the 18F-DOPA-PET/CT results focal form of CHI were diagnosed in 9 pts and diffuse form in 4 pts. The correlation between 18F-DOPA-PET/CT and histological results was achieved in 8 cases. In 4 cases of focal forms by PET/CT data histological study showed atypical morphological forms as combination of focal adenomatosis with the highest expression of insulin according to IGH and diffuse Langerhans islets hyperplasia, characterized by beta- cells with large hyperchromic nuclei. Maximal 18F-DOPA uptake was found in the areas of adenomatosis. In 1 case of diffuse form by PET/CT results histological study revealed multifocal adenomatosis, affecting pancreatic head, body and partially tail. **Conclusion:** 18F-DOPA-PET/CT allows with high accuracy to differentiate typical focal and diffuse forms of CHI. Atypical and multifocal morphological forms of CHI may be cause of misinterpretation of the 18F-DOPA-PET/CT results.

EP-0123

Comparison of FDG-PET/CT and Biopsy for Evaluation of Bone Marrow Involvement in Pediatric Lymphoma Patients

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Introduction: Bone marrow biopsy (BMB) is an invasive procedure for evaluation of bone marrow involvement (BMI) and

may require general anesthesia in pediatric patients. We aimed to compare the diagnostic success of 18-F-2-fluoro-2-deoxy-D-Glucose (FDG) positron emission tomography (PET) computed tomography (CT) and BMB in the initial evaluation of bone marrow involvement in pediatric lymphoma patients. **Subjects & Methods:** Seventy-seven pediatric patients (27 female, 50 male) with pathologically proven lymphoma were included in the study. 51 patients had Hodgkin Disease (HD) and 26 patients were diagnosed as Non-Hodgkin Lymphoma (NHL). All patients had bone marrow biopsy from bilateral iliac crests (2 patients had additional bone biopsy besides iliac crest biopsies) and FDG PET/CT scans within 10 days of the BM biopsy. All positive histopathological findings of BMB were regarded as true positive results. Findings of multifocal abnormally increased FDG uptakes on initial PET/CT study were regarded as true positive if the uptake site was pathologically proven or the abnormal uptake resolved on follow-up FDG PET/CT study. **Results:** Twelve (8 HD, 4 NHL) of the 77 lymphoma patients had bone marrow involvement. Among the 51 HD patients, FDG PET/CT revealed BM involvement in 8 patients, while BMB revealed bone marrow involvement in 3 patients who were also positive on FDG PET/CT scan. Among the 26 NHL patients FDG PET/CT revealed BM involvement in 3 patients, while BMB from iliac crests revealed bone marrow involvement in 2 patients. In 2 NHL patients with focal FDG uptakes at bones on PET/CT scan and negative iliac crest biopsies underwent local bone (1 femur, 1 tibia) biopsies to confirm bone marrow involvement. One NHL (T cell lymphoblastic lymphoma) patient had positive BMB and negative FDG PET/CT scan. Thirteen patients (10 HD, 3 NHL) with diffuse and mildly increased FDG uptake at bone marrow on FDG PET/CT scan had hypercellular bone marrow biopsy results without lymphoma involvement. The diffuse FDG uptake in these patients was due to the increased cellularity. The overall sensitivity of detecting bone marrow involvement was 92% and 58% ($p < 0.05$) for FDG PET/CT and BMB, respectively. **Conclusion:** Our study demonstrates that FDG PET/CT is non-invasive and highly sensitive procedure for the initial evaluation of bone marrow involvement in pediatric lymphoma patients. But it must be kept in mind that, low grade NHLs may have low FDG uptake, and thus FDG PET/CT may have lower sensitivity for certain histopathological types.

EP-0124

Role of PET-CT in staging and extent of chloroma in acute myeloid leukemia: A prospective study

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Objectives: Chloroma is a rare extramedullary tumour composed of blast cells which is a manifestation of AML. It is seen in less than 5% of AML cases. It can both predate the AML by months or can be an initial manifestation of a relapse. Bone marrow biopsy is typically used for diagnosis as well as assessment of treatment but it cannot identify extramedullary involvement. The enhancement pattern on CT & MRI are quite variable. Therefore we used hybrid imaging with PET&CT to evaluate both metabolism & structure to identify the sites of this extramedullary

involvement while simultaneously evaluating the intramedullary disease. **Material and Methods:** A total of 9 AML patients with biopsy proven chloromas were prospectively evaluated with 18F-FDG PET/CT for primary staging. Acquired Images were evaluated by two experienced nuclear medicine physicians. SUVmax of all the identified lesions was measured and compared using SUVmax of the liver as background. **Results:** A total of 9 patients (6 males, 3 females), with a mean age 9.8 yrs (6 - 19 yrs) were recruited for the study. On FDG PET/CT a total 51 lesions were identified, and divided into 3 groups as masses ($n=15$), lymph nodes ($n=9$) and soft tissue deposits ($n=25$). 8 patients presented with masses in head and neck region & one presented with a breast nodule. The mean of SUV max of mass lesions was 5.47 ($SD=2.92$). 8 patients had soft tissue deposits which included pleura, spleen, muscle, skeletal sites, prevertebral and intra-spinal deposits (mean SUVmax = 2.99; $SD = 0.95$). **Conclusion:** 18 FDG PET/CT is an excellent tool in staging and extent of chloroma.

EP-0125

Response assessment in children with lymphoma underway checkpoint inhibitor therapy using ^{18}F -PET/CT.

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Cancer immunotherapy with immune-checkpoint inhibitors is considered a promising strategy for cancer treatment. Checkpoint inhibitors, namely anti-PD1 antibodies, demonstrated efficacy across multiple types of cancer including relapsed or refractory lymphomas. Not surprisingly, flare reactions or delayed responses similar to those in patients with solid tumors have observed in patients with lymphoma. It is unclear how these reactions can be reliably identified and distinguished from the disease progression. Uniform response assessment criteria will help to make the right decision about response and it is critical for treating physicians to optimally use checkpoint inhibitor therapy in patients with lymphoma. ^{18}F -FDG PET/CT are widely used in early response evaluation conventional chemotherapy in patients with lymphoma and response assessment criteria are well established. While the response criteria applied ^{18}F -FDG PET/CT using checkpoint inhibitors continue to be studied.

Aim: To determine time points of response assessment with ^{18}F -FDG PET/CT in children with lymphoma underway checkpoint inhibitor therapy. **Materials and methods:** 10 patients with lymphoma received therapy anti-PD1 antibodies (Nivolumab). Nivolumab was administered at a dose 3 mg/kg every two weeks. 7/10 patients were with relapse of Hodgkin's lymphoma and 3/10 patients with relapse of diffuse B-cell large cell lymphoma. All patients underwent ^{18}F -FDG PET/CT before therapy with Nivolumab and for response assessment. The response was assessment in 2 patients after 3 injections, 7 patients after 4 injections and 1 patient after 5 injections of Nivolumab. The results of ^{18}F -FDG PET/CT were evaluated using LYRIC criteria. **Results:** CR was found in 2 patients after 4 injections; PR was found in 6 patients: 1 patient after 3 injections, 4 patients af-

ter 4 injections, 1 patient after 5 injections of anti-PD1; SD was found in 1 patient after 4 injections. Indeterminate response was found in 1 patient after 3 injections of Nivolumab which later was confirmed as a disease progression. **Conclusions:** Our preliminary results demonstrate the possibility to evaluate response in children with relapsed lymphoma who underway treatment with Nivolumab using ^{18}F -FDG PET/CT. However, the further studies need to be performed with more patient recruitment and analysis.

EP-0126

Necrosis evaluation at staging FDG-PET in Osteosarcoma and Ewing sarcoma: SUV prognostic value

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Osteosarcoma (OS), Ewing's Sarcoma (ES) and rhabdomyosarcoma represent 13% of pediatric malignancies. Some studies show that the 18FDG-PET parameters, including SUV max (Standardized Uptake Value) and TV (Tumor Volume) of the lesion and SUV min of necrosis correlate with the histological result and predict prognosis. We evaluated SUV max and TV of primary lesion, SUV min and TV of necrosis in 48 patients with OS (26) and ES (22), age 4-29 years (mean of 15.06 ± 5.8), underwent to 18FDG-PET staging. We have drawn ROIs on the area of hyperactivity of the lesion and on the necrotic area and measured longitudinal and transverse dimensions, and calculated the respective TV approximating them to cylindrical or ellipsoid morphology. We also measured the SUV max of the lesion and the SUV min of the necrosis. We have correlated these data to the histological outcome (Huvos for OS and Picci for ES), dividing the population studied in poor and good responders. Statistical analysis of the parameters showed a significant difference ($p < 0.05$) between the OS group and the ES group for SUV max and TV of the lesion and showed a higher average SUV max of the lesion of in the OS group (7.06 ± 0.82 OS vs 4.43 ± 2.93 ES) and a higher average TV of the lesion in the ES group ($66.5 \text{ cm}^3 \pm 100.7$ ES vs 202.7 ± 44 OS). The two groups are not different for age distribution: 15.5 ± 5.9 years for OS and 14.4 ± 5.7 years for ES. The percentage of necrosis was compared to the TV of the lesion (17% in OS and 13% in ES) and it wasn't statistically different. There is a significant statistical correlation (Spearman Rho test = 0.3 $p < 0.05$) between the histologically determined percentage of necrosis and the classification between good and poor responders and the SUV max value of the lesion. There is no significant statistical correlation with the other parameters: TV lesion, TV of necrosis, the percentage of necrosis in the lesion and SUV min of necrosis. Roc Analysis indicates a significance at the limit of the area under the 0.68 curve, $p < 0.05$ with a SUV max cut off value of 6.1 with 74% specificity and 56% sensitivity.

EP-0127

Clinical Value Of ^{11}C Methionine PET/CT In Paediatric Patients With Known Or Suspected Brain Tumours

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Introduction: In adults it is well documented the usefulness of ^{11}C -Methionine PET/CT to differentiate benign from malignant lesions, due to a low background activity in normal brain and higher uptake in tumour tissue. However, its role in the paediatric population remains uncertain. **Objective:** The aim of our study was to investigate the clinical value of ^{11}C -Methionine PET/CT in children with known or suspected brain tumours. **Material and Methods:** We retrospectively analysed all patients under 18 years old ($n=9$) who underwent ^{11}C -Methionine PET/CT scans in our Centre. 55.5% were boys ($n=5$) and the mean age was 8.9 ± 5.5 yr (range 2-18 years). Four patients had a histopathology confirmed brain tumour and 5 had suspicious lesions in MR, whose nature was to be determined. A PET/CT scan in dynamic mode for 35 minutes was performed immediately after the i.v injection of 3 MBq/Kg of ^{11}C -Methionine. The "hot spot" including the 4 pixels with higher uptake was compared with the contralateral normal cortex (index threshold: 1.4). **Results:** All patients with confirmed brain tumour ($n=4$) had been treated previous to PET scanning, and had an MR suspicious or equivocal for persistence/recurrence. In 3 of them (75%) PET was negative for the diagnosis of recurrence, being all of them currently clinically asymptomatic and/or has normal MRs. In the patient where PET/CT was positive, progression was confirmed in further MRs. Surgery confirmed recurrence of a craniopharyngioma. Of the 5 patients suspected of brain tumour, PET/CT was positive in 4 (80%), 3 of whom required further treatment (one received chemotherapy and 2 surgery that confirmed a low grade glioma). The remaining positive patient has no clinical evidence of disease, however additional MR was not performed. The last patient had a negative PET/CT, being presently asymptomatic. **Conclusions:** Although the number of patients is small, in our study ^{11}C -Methionine PET/CT has proven to be an excellent and minimally invasive technique to characterize tissue in equivocal post-treatment MRs. In patients with non-confirmed disease by structural imaging, ^{11}C -Methionine PET/CT is a helpful method to confirm malignant lesions.

EP-0128

The diagnosis of congenital focal form of hyperinsulinism in children using ^{18}F -DOPA PET/CT

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Introduction: Congenital hyperinsulinism (CHI) is a neuroendocrine disease secondary to either adenomatous hyperplasia or a diffuse abnormal pancreatic insulin secretion. While drug resistant diffuse forms of CHI required near-total pancreatectomy, focal CHI may be reversed by targeted surgical resection followed by patient's recovery. The focal condition is caused by a paternally inherited mutation. We evaluated the usefulness of ^{18}F -DOPA PET/CT to identify focal pancreatic form. **Subjects & Methods:** A total of 16 children (10 boys, 6 girls, aged between 2 -54 months, with clinical signs of neonatal CHI and positive genetic examinations (SUR1/ABCC8 or Kir6.2/KCNJ11) were en-

rolled into the study. After i.v. ^{18}F -DOPA administration (4MBq/kg) early and late dynamic thoraco-abdominal emission studies were performed. The early PET acquisition was done 5 minutes after injection - 1bed axial length 15cm, 1 frame/min, 10 frames, total time 10minutes, matrix 256x256. The late PET/CT acquisition (1bed 15cm, 1frame/min, matrix 256x256) was acquired 60 min after radiotracer injection (and immediately after i.v. 1.5 ml/kg iomeron 400) and took 20 minutes. Children were sedated using midazolam. CT parameters: Helical, 80kV, 100mA, Pitch 0.948:1 (39,47mm/rot), detector coverage 40mm. The late PET images were reconstructed using CT transmission correction for attenuation of the gamma radiation. All frames of dynamic study were evaluated visually and those of good quality (no movement, no artefacts) were summed to one static image. The evaluation was completed using comparison of maximum and mean SUV value within pancreatic regions. For focal form SUV ratio was >1.2 . **Results:** Focal forms of CHI with confirmation of SUV elevation were recorded in 8/16 children and 4 of them were operated. The diagnosis was histologically confirmed in all children with complete recovery. Another 4 patients have not been operated yet due to no optimal localization of pathological focus for surgery, child's age or other complications. Significant improvement of CHI without the necessity of further treatment were found in 2 children, which had not pathological focus in the pancreas on PET/CT. Other children remain on treatment with Octreotid or Diazoxid and are monitored regularly. **Conclusion:** In our experience ^{18}F -DOPA PET/CT is very good tool for the localization of focal CHI. Dynamic PET studies are very useful for children, because they allow to exclude the frames with motion of child during the acquisition.

EP-0129

Characterisation of neuroblastoma heterogeneity in I-123-MIBG scintigraphy and diffusion MRI

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Aim: Neuroblastoma (NB) can have a very variable clinical course, some regressing spontaneously whereas others can be highly aggressive. Despite well studied and characterised risk factors e.g. MYCN-amplification, overall survival and event-free survival specifically in stage IV disease is dismal. The aims of this study were to characterise heterogeneity in primary tumor (PT) and metastases (MT) on MRI and I-123-MIBG-scintigraphy and their impact on prognosis. **Materials:** In this retrospective study, we examined 20 patients (mean age in years 3 ± 3.8 ; 8 girls, 12 boys) managed clinically according to the NB2004 protocol. Patients were imaged with diffusion MRI and I-123-MIBG at baseline and subsequently during the treatment cycles N4 to N6 according to NB2004 protocol (interim). The following imaging parameters on diffusion MRI were analysed: ADCmean, skewness, kurtosis, centrality and eccentricity. For I-123-MIBG Curie- and SIOPEN-scoring were used. Receiver operating char-

acteristic analysis was performed to determine the best MRI parameter for differentiating between PT and MT. In addition, box plots were drawn to see the changes in individual parameters during the course of treatment. Finally, univariate analysis was performed to assess their impact on occurrence of events defined as death, relapse and/or progressive disease. **Results:** Median of ADCmean in PT at baseline/interim analyses was 0.9/1.0 as compared to 0.8/0.8 in MT. Amongst all other MRI parameters, the highest area under curve in ROC (0.564; best cut-off 0.85 $10^{-3} \text{ mm}^2/\text{s}$; sensitivity 71% specificity 54%) was observed for baseline ADCmean for differentiating PT from MT. In patients experiencing an event, the median ADCmean on PT decreased from 0.9 at baseline to 0.6 in interim MRI i.e. by 33%; in contrary in patients not experiencing any event the median ADCmean increased from 0.7 to 1.0 i.e. by 30%. However, the median ADCmean on metastatic lesions did not change at all in both the groups. On I-123-MIBG-scintigraphy, mean Marie Curie as well as SIOPEN-score in patients experiencing events was significantly higher as compared to those not having any events (Curie 11.5 ± 12.7 vs 2.7 ± 3.5 , SIOPEN 20.5 ± 23.7 vs 2.1 ± 4.8 ; $p < 0.05$). **Conclusion:** This preliminary analysis in a small patient cohort shows that the ADCmean values in PT and MT are different. Decreasing ADCmean of PT appears to be a poor prognostic factor, which has to be validated in a larger patient population. As previously reported, higher Marie Curie- and SIOPEN-scores are also associated with poor prognoses.

EP-0130

123 I-MIBG Scintigraphy in Neuroblastoma : Does the SPECT-CT Radiation is Justified ?

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Introduction: Neuroblastoma is one of the most common childhood solid tumors. iodine-123 metaiodobenzylguanidine (123 I-MIBG) remain the first-choice investigation for the diagnosis, staging and follow-up of children with neuroblastoma. The aim of this study was to investigate the utility of 123 I-MIBG SPECT-CT in the diagnosis and follow-up of children with neuroblastoma and to evaluate the additional radiation exposure due to the CT scan. **Patients and Methods:** In this retrospective study we included 40 children with known or suspected neuroblastoma: 24 males and 16 females aged 7 months to 11 years (mean age 3.76 year). All patients underwent whole-body planar imaging and hybrid SPECT/CT acquisition 18-24 hr following IV administration of 2-5 mCi (74-185 MBq) 123 I-MIBG. The patient effective dose associated with the 123 I-MIBG administration and the low-dose CT scan (25 mAs, 110 Kv and pitch =1) was calculated. **Results:** A total of 52 studies were performed in different clinical phases (40 for diagnosing and staging and 12 for monitoring response to therapy). Uptake of 123 I-MIBG by the primary tumour occurred in 36 of 40 patients (90%). In the negative whole-body scans SPECT-CT were also negative. Planar imaging showed bone and/or bone marrow involvement 14 patients with hepatic metastases in 4 of them. Among the 12 children studied for

evaluating the response to therapy 4 patients were in remission (good responders) and 8 were bad responders and they benefit of a change of treatment. Overall, SPECT-CT provided additional information (lesion localization and characterization and reader confidence) over planar imaging in 31 of the 52 studies (59%). The average Whole body effective dose from 123-MIBG was 4.95 ± 0.90 mSv and from CT scan was 0.95 ± 0.85 mSv. The average contribution of CT scans to the total effective dose from SPECT-CT studies was 20%. **Conclusion:** Our results confirmed the added value of 123 I-MIBG with SPECT-CT examination over planar imaging. The greater radiation dose inherent to the CT portion is acceptable and therefore justified on the basis of its diagnostic benefit.

EP-0131

Role of Semi quantitative I131 MIBG scores -Modified CURIE and SIOPEN score in prognostication in high risk neuroblastomas: Single Institutional Experience

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Aim: Radio iodinated metaiodobenzylguanidine (mIBG) is an established imaging modality used not only for qualitative but also for semiquantitative analysis in neuroblastoma. Semiquantitative scoring -SIOPEN [International Society of Pediatric Oncology Europe Neuroblastoma Group] and Modified Curie using radiolabelled MIBG are used for prognostication and risk stratification in high risk neuroblastomas. The present study compares both the scoring methods in Indian patient population and correlates with the progression free survival. **Materials and Methods:** A retrospective analysis of 100 MIBG scans of 84 patients with stage IV neuroblastomas at initial staging was done. The absolute scores were calculated using the standard Modified CURIE and SIOPEN method. The modified CURIE score divides the body into nine sectors for skeletal lesions and a tenth sector for soft tissue lesion with an extension scale of 0 to 3 for each region resulting in a maximum score of 30. The SIOPEN score distinguishes 12 skeletal segments with an extension scale of 0 to 6 and a maximum score of 72. The scores were done by two nuclear physicians on identical images. The interscore and inter observer variability were analysed using the Spearman's coefficient of variation. These were correlated with the progression free survival using Kaplan Meier survival analysis. **Results:** For modified Curie score correlation coefficient was $r=0.979$ for observer 2 and $r=1.000$ for observer 1 (all $P > 0.01$). By using the SIOPEN method, correlation coefficients were $r=1.000$ for both observers (all $P > 0.01$). A modified Curie score of ≤ 2 and > 2 and a SIOPEN score ≤ 4 and > 4 (best cutoff) described in previous studies was used to classify these scans into low and high risk. The mean progression free survival time for the CURIE score ≤ 2 is 35 months and 13 months for CURIE > 2 ($P=0.00$). The mean progression free survival time for the SIOPEN score ≤ 4 is 33 months and 11 months for SIOPEN score > 4 . ($P=0.00$) A modified Curie score of ≤ 2 and SIOPEN score of ≤ 4 (standard cut-off) correlates significantly to a better progression free survival. **Conclusion:** Semi quantitative MIBG scores have an excellent interobserver and interscore reliability. Higher scores

at initial diagnosis translate into unfavorable outcome and can be correlated with the disease extent and burden. Semi quantitative score thus establishes its role in risk stratification and prognostication in high risk neuroblastoma.

EP-0132

Post-therapy outcome in pediatric Neuroblastoma patients with initially concordant versus non-concordant I-131 MIBG and F-18 FDG PET coupled scans.

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Objectives: to assess the value of coupled concordant versus non-concordant I-131 MIBG and F18-FDG PET scans in predicting therapy outcome in pediatric patient with neuroblastoma. **Methods:** Comparative (mixed retro & prospective) study with 63 pathologically proved NB patients who were referred to nuclear medicine department, Children's Cancer Hospital, Egypt (CCHE), from Oct., 2009 till Jan. 2014, their age ranged from 2 to 156 months, with male to female ratio 1.4:1 & dominating high risk category (~65.1 %). They underwent F18 FDGPET and I-131 MIBG scans, with time interval not exceeding 2 weeks, using standard technique for purpose of initial assessment. Clinico-pathological, radiological and follow up data were also collected. **Results:** According to results of MIBG & FDG scans patients were classified into four categories Two concordant (positive MIBG/FDG scans & negative MIBG/FDG scans) and two non-concordant (Positive MIBG/ Negative FDG & Negative MIBG/Positive FDG). I-131 MIBG & FDG-PET concordance was evaluated and correlated with the therapy outcome "Response". Patients with "Negative concordance" (i.e. Non-MIBG & Non-FDG avid lesions) showed progression in 26 % of patients compared to 6.6% in cases with Positive concordance (i.e. MIBG & FDG avid lesions). Negative MIBG/Positive FDG Non-concordance showed progression in 28.6 % of patients. The best outcome was observed in "Positive MIBG/ Negative FDG Non-concordance" (i.e. MIBG avid/ Non-FDG avid lesions) with zero % progression. **Conclusion:** Regardless the avidity of FDG, absence of MIBG avidity seems to be associated with higher incidence of less favorable outcome.

EP-0133

Iodine-123-MIBG SPECT versus planar imaging in children with neuroblastoma

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Introduction: Neuroblastoma is the most frequent extra cranial pediatric tumor. mIBG scintigraphy is a noninvasive imaging technique who explores the whole-body tumor extension in one scanning and for the same irradiation dose. SPECT-CT increases its sensibility. The aim of our study is to demonstrate the additional value of ^{123}I -mIBG SPECT-CT compared to planar mode. **Materials and Methods:** We included in our study 23 patients with neuroblastoma for a total number of 32 exams. The scanning consisted of at least one SPECT-CT in combination

with the whole body planar imaging, 24 hours after ^{123}I -mIBG injection. The additional value of fusion images compared to planar ones was evaluated based on whether it had a better anatomic localization, detection of false positives and false negatives. **Results:** Compared to planar mode, SPECT-CT allowed a better anatomic localization: locoregional lymphatic extension (12 cases), vascular (3 cases), muscle of the wall (2 cases), root canal (4 cases), hepatic (6 cases), contiguous bone lesion (3 cases). It detected 5 new lesions (4 distant metastatic lymph nodes and a second mass in one case). It eliminated 9 false positives (digestive in one case, pyelic in 2 cases, a nonspecific inflammation of a member in one case, hepatic in 2 cases, diffuse uptake of the tumor without invasion of adjacent organs in 3 cases). In 5 cases, the results were concordant. **Conclusion:** This preliminary study shows the role of SPECT-CT in the description of locoregional tumor extension, especially lymphatic, with a better description of the lesion and by detecting false positives and false negatives. It combines functional and anatomic information which facilitates the interpretation and helps young doctors to be more confident in their conclusions.

EP-0135

Utility of “F-15” Diuretic Renogram to Clarify the Results with Equivocal Pattern of “F0” Protocol in Pediatric Patients with Suspected Pyeloureteral Junction Obstruction. Our experience

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Purpose: To assess whether diuretic renogram (MAG3) with “F-15” protocol is useful to reduce the number of equivocal patterns in the MAG3 “F0” in pediatric patients. **Subjects & Methods:** Retrospective study with 36 children (9 girls/27 boys, mean age 16,5 months/2–168 months), between July-2012 and January-2018 with suspected pyeloureteral junction obstruction: 11 right-sided, 23 left-sided and 2 bilateral, a total of 38 renal units (RU). All of them underwent a MAG3 “F0” that showed equivocal tracer washout curves, for these reason a MAG3 “F-15” was subsequently made, in an interval of no more than two months. The following parameters of the MAG3 “F0” and “F-15” were compared: differential renal function (DRF), time to peak (TTP), clearance time (T1/2), 20’/max or 30 minutes/maximum count ratio (30’/max). The anteroposterior pelvis diameter (APD) and hydronephrosis degree (DH) were evaluated at diagnosis and during the follow-up, which was on average 18 months (range 3–48 months). The cut-off points to consider the MAG3 “F-15” as obstructive or non-obstructive were an increase or decrease in the 30’/max in 10%, respectively, when compared to MAG3 “F0”. A variation in this same parameter of less than 10% classified the curve as equivocal. The patients underwent surgical or conservative management according to their clinical conditions and imaging results. For statistical analysis were used signed rank Wilcoxon and Student’s tests (p -value < 0.05). **Results:** MAG3 “F-15” showed an conclusive pattern in 28/38 RU (74%): 10 obstructive

(9 underwent pyeloplasty and one patient did not return to the hospital); 18 non-obstructive, 3 RU underwent pyeloplasty (2 crossing vessels, 1 worsening ultrasound) and 15 RUs received conservative management. In the remaining 10 RUs (26%) equivocal pattern was found, also treated with conservative management. All the patients who underwent surgery showed a 30’/max higher than 60%. Among the obstructive results, significant differences were observed between “F0”/“F15” (mean $\pm$ S-D): TTP: $10.7 \pm 8.0/20.0 \pm 23.5$ ($p=0.0074$); T1/2: $23.7 \pm 18.0/52.5 \pm 60$ ($p=0.0002$); 20’/max: $63.5 \pm 12.7/90.4 \pm 10.8$ ($p=0.0001$); 30’/max: $58.0 \pm 15.2/89.0 \pm 11.8$ ($p=0.0008$). Significant differences were also found between non-obstructive patterns: TTP: $8.8 \pm 5.3/5.3 \pm 2.8$ ($p=0.0210$); T1/2: $27.7 \pm 15.4/16.4 \pm 15.6$ ($p=0.0003$); 20’/max: $64 \pm 16.6/45 \pm 16.1$ ($p=0.00008$); 30’/max: $60.3 \pm 18.5/38.8 \pm 14.8$ ($p=0.0002$). Among the equivocal results, no significant differences were found in these parameters. The DRF did not change significantly between “F0” and “F-15”. Among the conclusive patterns (obstructive/non-obstructive), a significant improvement was observed in the ultrasound parameters (at diagnosis/follow-up): DAP pelvis: $17 \pm 5, 4/12, 5 \pm 5, 7$ ($p < 0,00001$); DH: $19 \pm 0, 73/2, 52 \pm 0, 80$ ($p=0,0005$). On the other hand, in the remaining 10 UR with equivocal patterns no significant differences were found. **Conclusion:** In pediatric patients with PUJO suspects and equivocal pattern in the MAG3 “F0”, a second MAG3 “F-15” is important to decide between a pyeloplasty or conservative management.

EP-0136

Role of diuresis renography and ultrasonography in monitoring and deciding on surgery in children with antenatally detected hydronephrosis

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Objective: Hydronephrosis (HN)-dilatation of fetal renal collecting system detected by prenatal ultrasound (US) requires post-natal follow-up. Diuresis renography plays important role in the follow-up by complementing US with the data about differential renal function (DRF) and drainage. We studied the association between US parameters and results of diuresis renography and the predictive factors of pyeloplasty in children with presumed pelvi-ureteric junction stenosis. **Patients and Methods:** The inclusion criteria were: age up to 4 years, diagnosis of prenatal HN determined by US during pregnancy based on the antero-posterior diameter (APD) of renal pelvis and at least one post-natal US which confirmed diagnosis. Exclusion criteria were: APD of pelvis < 10 mm, previous surgical treatment of HN, vesicoureteral reflux excluded by micturating cystourethrography. Sixty two patients 43 boys, 19 girls, median age 16 months were selected. They were divided into groups based on the size of pelvis, the calyceal size and thickness of parenchyma. Renography was performed for 24 minutes after the iv. application of Tc-99m mercapto-acetyl triglycine (MAG3). Furosemide was administered after 2 min. and post-void static images at 60

min. The non-commercial software developed by International Atomic Energy Agency was applied to process the studies. The criteria for pathological findings (poor or no drainage) were the renographic curve maintaining a plateau, Normalized Residual Activity (NORA) at 20. min. >1.62 , Output efficiency (OE) at 20. min. $<71\%$, post micturating NORA >0.11 . The DRF was considered normal within the range of 45%–55%. **Results:** Good drainage had 74% of children, partial drainage 11%, and poor 15%. There was a clear association between the size of pyelon, calyces, parenchyma thickness and drainage. There was also a clear association between the calyceal size, parenchyma thickness and DRF. Differential renal function was $<45\%$ in 18% of children. A relation between the type of drainage and DRF was not determined. Thus, 66.7% of those with poor drainage had preserved DRF. Seven out of nine children with poor drainage underwent pyeloplasty. The threshold for pyeloplasty was the pyelon of 18mm and calyces of 10mm. Ultrasound parameters (APD of pyelon, calyces size and parenchymal thickness), drainage and DRF were significant predictors in univariate analysis, but only drainage was an independent predictor for the need of pyeloplasty. **Conclusion:** Antero-posterior diameter of the pyelon $<15\text{mm}$ indicates a favorable course of congenital HN in most children. Pattern of drainage obtained by diuresis renography was the only independent predictor for the need of pyeloplasty.

EP-0137

Normalized Residual Activity During MAG3 Renography in Assessment of Antenatal Hydronephrosis

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Introduction: The prevalence of antenatal hydronephrosis (ANH) ranges from 1–5%. The majority of them disappears spontaneously. Diuresis renography plays important role in the follow-up of ANH by complementing morphological information obtained by Ultrasound. This study aims to investigate the value of Normalized Residual Activity (NORA) for the evaluation of renal emptying during renography in children with ANH. **Materials and Methods:** Eighty patients (49 boys and 31 girls) with 94 dilated pelvicaliceal units had undergone a $^{99\text{m}}\text{Tc}$ -MAG3 diuretic renal scintigraphy (Furosemide was injected at 20 minutes : F+20). The mean age was 15.3 ± 8.4 months. Hydronephrosis was bilateral in 14 cases. NORA30 (residual kidney counts at 30min normalized to the 1–2min counts) was calculated. In case of insufficient renal emptying, late postrect and postmicturition (PM) images were acquired 50–60 min after tracer injection and NORA PM was determined. NORA ≤ 1 is likely to correspond to a dilated unobstructed kidney. If ≥ 2 it might correspond to an obstructive phenomenon. **Results:** The PM images were acquired in 70 kidneys (NORA30 > 1). Among them 49 were reclassified into unobstructed dilated kidneys (NORA PM ≤ 1) and 12 into poor drainage (NORA PM ≥ 2). NORA allowed a reliable assessing of kidneys drainage (good or partial) in 87% of cases. After further investigations, dilated kidneys with poor drainage

were divided into two groups surgical and nonsurgical. Post-operatively the most common observation was improvement in the MAG3 emptying images in 4 of 7 cases. In nonsurgical group, 1 had improved drainage and no significant decrease in differential renal function was noted in 4 children. **Conclusion:** The overall results provided evidence that NORA is an extremely simple parameter and robust method that enhance the accuracy of diuretic nephrogram to detect obstructed kidneys in children with ANH.

EP-0138

Impact of Radioisotopic Renography in Congenital Hydronephrosis Surgery Management: a Retrospective 5 Year Experience

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Aim: We wish to share our experience and results of the collaboration between three departments (Nuclear Medicine, Pediatric Nephrology and Pediatric Surgery Department), the only ones in the North-Eastern region of Romania (with a population of 3.3 millions people), regarding congenital hydronephrosis management in children under 6 months old. **Materials and Methods:** The study has a retrospective framework with a five year pooling period (2012–2016). From 256 cases with congenital hydronephrosis in children (under 18 years old), we included 31 cases of infants (between 1 month and 6 months). The patients were classified according to sex (35.48 % were girls) and urban/rural provenance (45.16 % came from rural area). These patients were initially detected antenatally by ultrasonography (83.87 %) and then confirmed postnatally. $^{99\text{m}}\text{Tc}$ -DTPA dynamic scintigraphy with diuretic administration (according to EANM guidelines) was performed to inquire the obstructive nature of hydronephrosis and to calculate the renal split function and glomerular filtration rate. **Results:** The main clinical diagnoses were: congenital ureteropelvic junction obstruction (11 cases), vesicoureteral reflux (6 cases), megaureter (7 cases) and reno-ureteral duplication (7 cases). In the following 6 months / 1 year after the first renography, 26 patients came for follow-up. The sequential examinations provided the pediatric surgeon with a rigorous mean to appreciate the evolution in time of renal function and undertake the most appropriate therapeutical course of action. In our group of patients, the surgical timing relied heavily on the scintigraphical findings. **Conclusion:** Our experience strongly recommends the use of renography to assess the renal function in children, even at small ages, as a non-invasive imaging modality. Even if the moment of surgery is still a matter of debate, we found that the isotopic evaluation of these patients diagnosed with congenital hydronephrosis guides the moment of surgery in correlation with long term prognostics.

EP-0139

Vesicoureteral Quantification Metrics and their correlation to Kidney Damage

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Purpose/Introduction: One of the most common image modalities undertaken to detect and follow vesicoureteral-reflux(-VUR) is cystography. However, the severity of VUR, as evaluated by this imaging technique, is merely qualitative, and occasionally of difficult stratification. In this study we propose a new metric to quantify the intensity of VUR, and assess its correlation with renal damage. **Subjects&Methods:** All data from children with uncorrected VUR submitted to both cystography and ^{99m}Tc-DMSA scintigraphy between 30-9-2004 and 26-4-2018 was retrospectively reviewed. All cystographies were corrected for motion artifacts, with the *dynamic motion correction* tool of the *GEXeleris2.0 workstation*, and were divided into filling and voiding phases. Contamination areas were excluded. All frames of each phase were summed to obtain a single composite image. Automatic regions of interest (ROIs) were drawn in each composite image (threshold:0), one measuring the total urinary tract activity(T_ROI) and another limited (by a hand drawn ROI) to the renal pelvis(P_ROI). T_ROI and P_ROI were corrected for background activity. In each patient a filling and voiding percentage of VUR was calculated by dividing P_ROI by T_ROI (%VUR_F and %VUR_V).The filling and voiding VUR duration was also recorded, as well as the total length of each phase for all patients. ^{99m}Tc-DMSA scintigraphy results were categorized into group 1-normal, 2-cortical lesions with symmetric function or asymmetric function without cortical lesions, and 3-cortical lesions with asymmetric function. **Results:** A total of 161 patient were submitted to both cystography and [^{99m}Tc]Tc-DMSA scintigraphy, but 50 were excluded because function symmetry could not be assessed (69 girls, 42 boys; average age:2.9±2.9years). Sixty three patients had left VUR and 48 had right VUR. A statistically significant difference in the distribution of the %VUR_F and %VUR_V between groups 1 (0.74±1.6; 1.6±3.2) and 2 (0.72±0.77; 2.4±2.27) and group 3 (4.78±10.27; 6.07±7.42) was found (Kruskal Wallis test, p<0.05). No statistically significant difference was found for the duration of the VUR between groups. Also a statistically significant correlation was found between the differential renal function and both %VUR_F and %VUR_V (spearman, r²:0.294 and 0.350, p<0.05). Although not evaluated, these metrics seem to be highly reproducible (ROI creation based on automatic methods). **Discussion/Conclusion:** In our sample, both %VUR_F and %VUR_V were correlated, in a statistically significant manner, to renal damage, as assessed by ^{99m}Tc-DMSA scintigraphy. These results, although preliminary, seem to support the ability of these metrics to quantify VUR. Further studies, however, are warranted before their application in a clinical setting.

EP-0140

Evaluation of cyclic direct radionuclide cystography findings with DMSA scintigraphy results in children with a prior diagnosis of vesicoureteral reflux

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Purpose: Direct radionuclide cystography (DRC) with cyclic imaging is a sensitive method used for the detection of vesicoureteral reflux (VUR). Radionuclide cystography is generally recommended for follow-up evaluation of VUR. The aim of this study was to evaluate cyclic direct radionuclide cystography findings (cDRC) with DMSA scan results during the follow-up period in children with a prior diagnosis of VUR. **Methods:** Direct radionuclide cystography findings of 87 children with VUR were evaluated together with DMSA findings during follow-up. VUR grade was classified anatomically as Grades I, II and III reflux. Reflux grades of II and III were regarded as high-grade reflux. Reflux was also graded functionally as transient and continuous based on the presence of reflux on either filling or voiding phases (transient) or both phases (continuous) of at least one cycle. **Results:** Among 87 children, 33 exhibited reflux (38%). In 5 patients, reflux was observed on both sides and a total of 38 refluxing units (RU) were evaluated. According to the highest grade attained in either cycle, 32 units had Grade II (84%), 5 had Grade I and 1 had grade III reflux. Reflux was continuous in 23 (61%) and transient in 15 (39%) RUs. The incidence of an abnormal scan was higher in continous reflux group (78%) than in high-grade anatomic reflux group (58%). The addition of a second cycle resulted in the diagnosis of continuous reflux in 6 more RUs (26%). DMSA scan findings correlated significantly with functional reflux classification (p<0.05), but not with anatomic reflux classification (p>0.05). **Conclusion:** Functional classification of VUR into continuous and transient reflux resulted in higher correlation with DMSA scan findings compared to anatomic reflux grading in follow-up patients with VUR. Cyclic imaging contributed to continuous reflux diagnosis. The significance of functional information obtained from cDRC in initial diagnostic workup, management and follow-up of children with urinary tract infection needs to be determined with further studies.

EP-0141

Role of ^{99m}Tc DMSA scan as the initial investigative modality in atypical and recurrent UTI in children - "The top down approach"

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Objectives: To study the role of ^{99m}Tc DMSA scan in cases of recurrent UTI and atypical UTI as a screening modality to predict high grade VUR in pediatric age groups. **Methodology:** 51 patients between 06 months and 12 years of age detected with recurrent or atypical UTI confirmed by urine culture along with a primary VUR detected on VCUG performed 2-3 weeks after treatment (as per IAP/ISPN/AAP guidelines) were included in the study. 81 renal units with VUR were obtained from the recruited patients which was the sample size. The children recruited were subjected to a ^{99m}Tc DMSA scan 4 to 6 months after acute infection. The results of the study were tabulated in to 5 groups with 1 to 5 grades of VUR obtained on VCUG as per IRSC classification. **Key Results:** a) The scarring rate according

to the reflux of grades I, II, III IV and V were 0%, 33%, 50%, 90%, 77% and 60% respectively, with significant difference between the group of patients with VUR of grade I–III and the group with VUR IV–V ($p < 0.05$). b) In addition, the study also found an association between severity of VUR and severity of scarring. High grades of reflux (VCUG grade IV and V) were significantly associated with severe scarring (Criteria by Monsour et al.) ($P < 0.05$). c) High sensitivity (83%), high negative predictive value (78%) and relatively low likelihood ratio negative (0.26) of abnormalities on DMSA scan to detect the high-grade reflux (IV–V) were found.

Research Highlights: The present study revealed that DMSA scan with a good degree of confidence can predict the presence high grade reflux in pediatric age groups. Normal DMSA findings decreased the probability of finding the reflux of clinical significance on VCUG, supporting the strategy to perform VCUG only on patients with abnormal DMSA scans in children more than 6 months of age with recurrent UTI. This study gives further credence to the ‘top-down’ approach advocated by NICE guidelines (UK) for UTI not only in cases of first febrile UTI, but also in cases of recurrent/ atypical UTI in paediatric age groups above 6 months of age.

EP-0142

Diagnosis of Biliary Atresia using ^{99m}Tc -PMT scintigraphy versus ultrasonography of gallbladder Diagnosis of Biliary Atresia using ^{99m}Tc -PMT scintigraphy versus ultrasonography of gallbladder

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Purpose: Hepatobiliary scintigraphy plays an important role in the differentiation of biliary atresia (BA) from non-BA. The technetium-99m compounds for hepatobiliary scintigraphy are divided into two groups: ^{99m}Tc -PMT is mainly in Japan, while ^{99m}Tc -iminodiacetic acid derivatives are used in Western countries. The intravenous injection of ^{99m}Tc -PMT showed rapid blood clearance, fast hepatobiliary transit, low urinary excretion and no intestinal reabsorption. ^{99m}Tc -PMT and ^{99m}Tc -iminodiacetic acid derivatives have almost the same pharmacokinetics. Ultrasonography of gallbladder has also long played a role in screening infants with cholestasis included BA. The usefulness of BA using ^{99m}Tc -iminodiacetic acid derivatives is reported in several papers. On the other hand, there is no comprehensive report on the usefulness of differentiating BA from non-BA using ^{99m}Tc -PMT. Our objective was to evaluate the accuracy of ^{99m}Tc -PMT scintigraphy in comparison with ultrasonography of gallbladder in the diagnosis of BA. **Subjects & Methods:** 47 infants who received both ^{99m}Tc -PMT scintigraphy and ultrasonography of gallbladder due to suspected BA with neonatal jaundice were retrospectively evaluated. When no radiotracer was detected in the bowel till 24 hr, diagnosis of BA using ^{99m}Tc -PMT scintigraphy was defined as positive. When a normal-sized gallbladder could not be detected, diagnosis of BA using ultrasonography was regarded

as positive. The sensitivity, specificity and accuracy of ^{99m}Tc -PMT scintigraphy and ultrasonography were calculated with preoperative cholangiogram or follow-up as gold standard. **Results:** The final diagnoses in this group were BA (70.2%), cholestasis or neonatal hepatitis included unknown origin (23.4%), infectious diseases (4.3%) and genetic diseases (2.1%). ^{99m}Tc -PMT scintigraphy had a higher specificity (100% vs. 78.8%), a higher specificity (85.7% vs. 42.9%) and a higher accuracy (95.7% vs. 68.1%) than ultrasonography of gallbladder. **Conclusion:** Compared with ultrasonography of gallbladder, we found a higher diagnostic specificity and accuracy of ^{99m}Tc -PMT scintigraphy for detecting-BA in infants. ^{99m}Tc -PMT scintigraphy should be actively considered if BA is suspected.

EP-0143

Bone Scan and MRI in Chronic Recurrent Multifocal Osteomyelitis

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Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO) is a rare inflammatory bone disorder presenting with relapsing and remitting episodes of bone pain. MRI is the imaging modality of choice; however, long waiting lists often prevent patients to have access to MRI in a timely fashion. Aim of this study was to compare the diagnostic yield of the bone scan (BS) versus MRI in CRMO and to correlate the findings with inflammatory markers and clinical symptoms/location of pain. **Subjects and Methods:** Retrospective review of the clinical notes of children with a confirmed diagnosis of CRMO who had both bone scan and MRI between 2009 and 2014, and within 9 weeks of each other. Nine patients (7 females, 2 males, age range 7–13 years, mean 9.6) had both BS and MRI less than 9 weeks apart. We recorded for each patient: inflammatory markers at time of scans (ESR, CRP and WCC), clinical symptoms, pain location, number and location of lesions for BS and MRI. Patients were excluded if BS and MRI were done more than 9 weeks apart, or if there was any change to treatment in-between scans. BSs were acquired as a whole body sweep, with high count spot views of the areas of interest and SPECT CT when necessary. MRI scans were limited to the area of interest (only 1 patient had whole body MRI) and were acquired using T1, T2, and STIR sequences (and contrast enhanced in 6 patients). **Results:** Pain was always associated with a bone lesion on imaging. BS was always positive at the site of symptoms. MRI consistently detected more lesions than BS (45 lesions versus 31 with BS), especially in the spine. However, several lesions, mainly suggestive of bone marrow oedema, were asymptomatic, and their clinical significance was questionable. BS was better at detecting rib lesions. MRI and BS were concordant in 69% of cases. The inflammatory markers were non-specific. **Conclusion:** MRI and BS were concordant in a high number of cases. MRI detected more lesions than BS; however, several lesions were asymptomatic and of

doubtful clinical significance. BS was always positive at the site of symptoms. BS can be considered in CRMO if MRI is not readily available.

EP-0144

Osteomyelitis in children: association between analytical parameters and three-phase bone scan findings.

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Aim: To assess the correlation between the alterations in non-specific analytical parameters of infection in pediatric patients with suspicious of osteomyelitis and the findings in three phase bone scan (TPBS). **Material y Methods:** We retrospectively evaluated the results of TPBS in a series of consecutive patients referred with clinical suspicious of osteomyelitis. Data from erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cells count (WBCC) were collected, as well as the scintigraphic findings. A TPBS was carried out according to the standard procedure, focused on the suspicious area and completed with a whole body scan in the delayed phase. The results were classified as normal, cellulitis, arthritis or osteomyelitis according with the scintigraphic findings. The final diagnostic confirmation was obtained by clinical follow-up of at least one month, including the response to antibiotic treatment. Statistical analysis of the data was carried out obtaining the mean analytical values in each group (osteomyelitis and non-osteomyelitis) and comparing them with a Student's *t*-test. Afterward, we performed a ROC curve analysis. **Results:** A total of 42 children (16 girls, 26 boys, mean age 6.2 y, range 0-16 y) were included. Data about WBCC and CRP were available in all of them, and ESR in 33 of them. The scintigraphic findings were compatible with osteomyelitis in 21/42 (50%) of them, and no-compatible with osteomyelitis in the other 21/42 (50%). Statistically significant differences were observed in CRP values between the groups of osteomyelitis and non-osteomyelitis (mean group 1: 50.06, mean group 2: 22.67, $p=0.039$). The value of the area under the curve in a ROC analysis was 0.71. On the other hand, no statistically significant differences between both groups in WBCC and ESR were obtained. **Conclusion:** The scintigraphic diagnosis of osteomyelitis is associated to higher values of CRP, without apparent correlation with other analytic unspecific parameters of infection-inflammation.

EP-0145

Osteosarcoma as a second malignancy in a child, ten years after treatment for neuroblastoma

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Introduction: The risk of developing a second malignancy in children, who survived ten years after being treated for neuroblastoma, is present. The high toxicity of chemotherapy and the radiation are factors that aggravate the development of secondary tumors. **Purpose:** The presentation of an age-related incident of 15 years old boy, which was diagnosed for osteosarcoma, ten years after receiving neuroblastoma treatment.

Subjects / Methods: A 4 years old boy was diagnosed with left adrenal neuroblastoma stage IV with multiple bone metastases. Surgical removal of the left adrenal gland was performed in 2007 with subsequent chemotherapy. The histologic examination showed low-differentiation neuroblastoma. He underwent autologous bone marrow transplantation. The child completed all chemotherapy cycles and did not receive any radiotherapy. From 2008 to 2011, the I-123MIBG scintigraphy follow ups were negative for overactive adrenergic tissue. Ten years after the end of treatment, he experienced a pain located in the upper third of the left leg, especially during palpation and occasional walking lag. He was investigated by MRI and CT, which showed a large osteolytic mass, with soft tissue component in the left tibia. Secondary bone, pulmonary and hepatic metastases with bone scans and CT were excluded. PET / CT showed intense uptake of radiopharmaceutical in the intramedullary tumor in the left tibia. The diagnosis was made by tumor biopsy and histology showed high grade osteosarcoma. At the end of the diagnostic tests, treatment for osteosarcoma was initiated.

Conclusion: This incident is a rare occurrence as there are limited data on survivors with a history of free disease after neuroblastoma treatment. There is need for close monitoring of children who were diagnosed with neuroblastoma, at an early age, in order to achieve timely diagnosis and treatment in case of developing a second malignancy.

EP-0146

The role of 18F FDG PET/CT in the differentiation between benign and malignant nerve sheath lesions in an adolescent with NF-1

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Introduction: Neurofibromatosis type-1 (NF1) is characterized by the development of benign and malignant tumors that primarily affect the nervous system. Malignant peripheral nerve sheath tumors (MPNSTs) are rare in children and their incidence in patients with NF1 is 8-12%. The detection of MPNST in NF1 remains a clinical challenge especially in pediatric population. **Purpose:** The purpose of this study was to explore the role of imaging with ¹⁸F-FDG PET/CT in the discrimination between benign neurofibromas and malignant MPNSTs in NF1, which is clinically very important. **Subjects/Methods:** A sixteen-years-old boy with a history of NF1 is presented. At the age of three he was diagnosed with optic nerve glioma, plexiform neurofi-

bromas and spindle cell's malignant mesenchymal neoplasm. At the age of sixteen, new lesions were diagnosed in the MRI: multiple paravertebral lesions in the thoracic spine, the chest wall, the lower ribs, the gluteus, dorsal muscles, the anterior muscle of upper thigh, the gastrocnemius, the subcutaneous tissue of thighs and the sacroiliac joint. MRI couldn't safely differentiate benign neurofibromas from MPNSTs in this extensive disease. Therefore, patient had to undergo ^{18}F -FDG PET/CT scan at 60 min. Semi-quantitative analysis using maximum Standardized Uptake Values (SUVmax) was performed. **Results:** The largest, increased uptake was observed in the lesions of chest wall and gluteal muscles (SUVmax= 7). By studying SUV max values and bibliographic data, the above hypermetabolic lesions were consistence with MPNSTs. A surgical resection was performed and histologic evaluation confirmed the malignant nature of the lesions. A biopsy was also made in other borderline lesions with SUVmax=3,8-4,1 which correspond to benign neurofibromas. **Conclusion:** The presented pediatric case highlights the usefulness of ^{18}F FDG PET/CT as a non-invasive method for the distinction of benign neurofibroma from MPNST in NF1, especially in patients with extensive disease. ^{18}F -FDG PET/CT guided successfully surgical management and clinical planning.

EP-09

e-Poster Area

Thyroid: Treatment of Benign Thyroid Diseases

EP-0147

Influence of different glucocorticoids on intra-therapeutic effective half-life of radioiodine-131 in patients suffering from Graves' disease

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Aim: In 2010 Hautzel et.al. identified the glucocorticoid prednisolon (P) to significantly decrease intra-therapeutic intra-thyroidal effective half-life (EHL) of radioiodine-131 during radioiodine-therapy (RIT) of patients suffering from Graves' disease (GD) (1). The authors administered P to prevent the development of Graves' ophthalmopathy (GO) or an exacerbation of a pre-existing GO, which is in line with relevant international guidelines. However, P is known for a certain mineralocorticoid effect that plays a role in regulating the fluid and electrolyte balance and could therefore mediate an abbreviated EHL, causing a significant reduction of radiation dose in the target tissue. A possible way out of this dilemma is to replace P by methylprednisolone (MP) whose mineralocorticoid effect is lower. Aim of this study was therefore to evaluate the influence of MP on EHL during RIT of patients with GD. **Material and Methods:** In this retrospective analysis 211 patients with GD who underwent RIT without additional thyreostatic medication were examined. Pre-therapeutic EHL was determined without MP in a radioiodine-131 uptake test with two measured values. Patients were then subdivided into two groups. Group A: patients without GO who did not receive MP (n=176). Group B: patients who

received MP according to a fixed scheme starting one day prior to RIT due to pre-existing GO (n=35). Intra-therapeutic EHL was determined by measurement of the remaining intra-thyroidal activity twice a day during hospitalization and statistically compared to the corresponding pre-therapeutic EHL among the subgroups. **Results:** The median pre- and post-therapeutic EHL were 5.85d and 5.69d respectively in group A resulting in a median ratio of 0.98 (0.32-1.91). In group B the median pre- and post-therapeutic EHL were 5.56d and 5.96d respectively, resulting in a median ratio of 0.99 (0.41-1.58). A comparison using Wilcoxon-Mann-Whitney-test failed to show significant difference ($p=0.79$) between the subgroups. In contrast, Hautzel et. al.(1) revealed significant effects of P on EHL ($p=0.046$) in 125 patients receiving P and 190 patients without any glucocorticoid medication. **Conclusion:** The present study suggests that MP does not affect EHL of ^{131}I significantly. Therefore, MP should be preferred for patients without antithyroid medication undergoing glucocorticoid therapy, for its mineralocorticoid effect is lower compared to P. The choice of MP instead of P should be considered in relevant international guidelines. References: 1. Hautzel H et al. Qualitative and Quantitative Impact of Protective Glucocorticoid-Therapy on the Effective ^{131}I Half-Life in RIT for Graves'Disease. The Journal of Nuclear Medicine 2010; 51; 1917-1922.

EP-0148

Radiation induced stunning in patients suffering from benign thyroid diseases due to pre-therapeutic radioiodine-131 uptake test

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Aim: Existence and cause of ^{131}I thyroid-stunning (TS) are controversially discussed for decades but the fundamental physiology of this phenomenon is still not solved. As possible explanation the β -radiation is identified. Numerous studies describe TS in malignant thyroid diseases, but there are only few publications concerning TS in benign thyroid diseases (BTD) in fractionated administrations of therapeutic ^{131}I and no studies evaluating possible TS in BTD caused by ^{131}I administered in the pre-therapeutically performed radioiodine-131 test (RIUT). In this study the influence of this radiation dose on intra-therapeutic thyroidal ^{131}I -uptake is evaluated. **Methods:** A retrospective monocentric analysis of 3,425 patients suffering from BTD who were treated with ^{131}I was performed. Exclusion criteria were any thyreostatic medication, pre- and/or intra-therapeutic calculated effective half-life (EHL) beyond 8d and 24h-RIUT with an estimated EHL. Finally a total of 914 patients were included and subdivided into disease specific groups. Pre-therapeutic applied radiation dose [Gy] due to RIUT was calculated retrospectively for all patients using the Marinelli equation. Intra-therapeutic biokinetics of ^{131}I was individually calculated for each patient. The variation of pre- to intra-therapeutic maximum radioiodine-131 uptake (MRU) dependent on pre-therapeutic radiation dose [Gy] was evaluated by means of statistical methods. To evaluate potential TS caused by the pre-therapeutic administered radiation dose

[Gy], the intra-therapeutic MRU of each patient was related to the corresponding pre-therapeutic calculated MRU. **Results:** Pre-therapeutic calculated MRU ranged from 0.10 to 0.82 (median: 0.35) and intra-therapeutic MRU ranged from 0.10 to 0.74 (median: 0.33). Averaged over the whole collective intra-therapeutic MRU decreased significantly ($p<0.05$) depending on pre-therapeutic administered radiation dose (2.3% per Gray). In a subgroup evaluation a radiation dose dependent TS reaching from 1.2% per Gray (focal functional autonomy; $n=327$) to 21% per Gray (goiter; $n=135$) could be demonstrated. Only the patients suffering from multifocal functional autonomy (MFA) ($n=178$; $p=0.013$) and goiter ($p=0.00072$) showed a significant TS whereas the patients suffering from Graves' disease ($n=160$; $p=0.22$), focal functional autonomy ($p=0.16$) and disseminated autonomy ($n=114$; $p=0.18$) did not. A multivariate analysis did not show any significant correlation between TS and sex, age, thyroid target volume or administered activity [MBq]. **Conclusion:** The presented data indicate a significant dependence of TS upon pre-therapeutic administered target dose [Gy] in patients suffering from goiter and MFA. To achieve the desired intra-therapeutic radiation dose [Gy] to the thyroid, the therapeutic activity of ^{131}I for these indications should be adapted depending on pre-therapeutic applied radiation dose [Gy].

EP-10

e-Poster Area

Neuroimaging: Neuro-Oncology

EP-0149

18F-Fluorocholine PET/CT in the assessment of post-operative residual tumour in high-grade gliomas: a comparison with 5-aminolevulinic acid and post-operative MRI

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Objective: To determine the concordance between post-operative ^{18}F -Fluorocholine positron emission tomography (PETCholine), 5-Aminolevulinic Acid (5-ALA) and post-operative magnetic resonance imaging (MRI) in the assessment of post-operative residual tumour in high-grade gliomas (HGG) and to compare their diagnostic accuracy. **Methods:** Patients diagnosed with HGG were prospectively enrolled in the FuMeGA (Functional and Metabolic Glioma Analysis) study. All the subjects underwent tumour surgery. Pre and post-operative PETCholine and MRI were performed in all patients. 5-ALA-induced fluorescence was used for intra-operative assessment of post-operative residual tumour and the presence of fluorescent tissue at the end of the resection was defined as positive 5-ALA. In post-operative

studies, a moderate/intense PETCholine uptake in the primary tumour region was considered positive for residual tumour. A MRI was considered as positive if there were findings consistent with residual tumour, specially, in contrast-enhanced T1-weighted images. Additionally, a combined evaluation of post-operative PETCholine and MRI was performed, considering a positive assessment when any of them was positive. The kappa index (k) was used to measure concordance between for 5-ALA, PETCholine and MRI. The presence of residual tumour was based on a close clinical-radiological follow-up within 8 months after surgery and the diagnostic performance [sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and accuracy (Ac)] was calculated for each technique.

Results: Twenty-two studies of 18 patients with HGG were assessed. There was a weak agreement of 5-ALA with PETCholine ($k=0.2$) and with MRI ($k=0.3$). Post-operative PETCholine and MRI also had a weak agreement ($k=0.1$). Residual tumour was confirmed in 14 cases. The Se, Sp, PPV, NPV and Ac were 36%, 100%, 100%, 25% and 47% for 5-ALA; 79%, 67%, 92%, 40% and 76% for PETCholine and 57%, 100%, 100%, 33% and 64% for MRI, respectively. The combined assessment of post-operative PETCholine and MRI showed: Se=93%, Sp=67%, PPV=93%, NPV=67% and Ac= 88%. **Conclusion:** There was a weak agreement between 5-ALA, post-operative PETCholine and MRI for the assessment of residual tumour. However, PETCholine had a better accuracy in the appropriate evaluation of residual tumour, although the combined assessment with MRI improves its value. The performance of PETCholine was particularly helpful in cases of negative MRI.

EP-0150

Clinical Impact of Simultaneous ^{18}F -FDOPA PET/MRI Imaging on Brain Tumour Management: a Pilot Study

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Purpose: Brain tumour imaging relies mostly on MRI, which sometimes may be inconclusive. We sought to evaluate the contribution of simultaneous ^{18}F -DOPA PET/MRI imaging for diagnosis and treatment management of primary glial cell and metastatic brain tumours. **Methods:** We enrolled 16 consecutive patients from January to April 2018 with suspected or confirmed brain tumours. Each patient underwent simultaneous ^{18}F -DOPA PET and 3-Tesla brain MRI on a Biograph mMR (Siemens, Erlangen, Germany), with acquisition starting exactly 10 min after injection of 2 MBq/kg ^{18}F -DOPA, including a 15-min emission step and the following MRI sequences: axial T1-weighted, 3D FLAIR T2-weighted, ^1H magnetic resonance spectroscopy (^1H -MRS), dynamic susceptibility contrast, perfusion and 3D Gd T1 SE-weighted sequences). Image interpretation was based on a joint analysis by both a nuclear physician and a neuroradiologist, using SUVmax, tumour/striatum (contralateral) ratio, FLAIR hypersignal, Gd contrast enhancement, rCBV and ^1H -MRS. Gold standard for the evaluation of PET/

MRI results was pathology examination whenever surgery was indicated or follow-up in the other cases. Clinical impact on patient management was then assessed by the multidisciplinary committee. **Results:** Out of 16 patients, PET/MRI results yielded 10 relevant changes on patient management (62.5%), including 3 diagnosis changes (18.8%) and 7 treatment changes (43.8%) compared with MRI only. Diagnosis changes (group A) consisted of lesion upgrading or identification of new brain localizations; treatment changes (group B) consisted of supplementary radiation therapy, modification of the resection margins, or treatment interruption; in the remaining patients (group C), no clinical impact of PET/MRI was noted. SUV_{max} averaged 6.1 ± 2.0 in groups A+B patients vs. 5.1 ± 1.7 in group C. T/S ratio averaged 2.1 ± 0.7 vs. 1.5 ± 0.4 , respectively. rCBV revealed hyperperfusion in 5 patients and hypo/undetermined perfusion in 5 patients in groups A+B vs. 4 hyperperfusions and 2 hypo/undetermined perfusions in group C. **Conclusion:** This preliminary study shows a major clinical impact of simultaneous ^{18}F -DOPA PET/MRI imaging in glial cell and metastatic brain tumours on patient management (62.5%) compared with MRI only, procured by the synergistic work of nuclear physicians and neuroradiologists, in a one-shot examination.

EP-0151

TSPO expression and amino acid uptake in patients with high-grade glioma - a double tracer study comparing ^{18}F -GE-180 and dynamic ^{18}F -FET PET

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Background: PET using amino acid tracers such as ^{18}F -FET represents a valuable tool for glioma imaging. Besides, PET targeting the 18-kDa mitochondrial translocator-protein (TSPO) is of high interest for high-grade glioma (HGG) imaging due to its upregulation in HGG cells. ^{18}F -GE-180, a novel third-generation TSPO-ligand, has shown a high target-to-background contrast in HGG. We therefore intra-individually compared its uptake characteristics to dynamic ^{18}F -FET PET and contrast-enhanced MRI in patients with HGG. **Methods:** 20 patients with HGG (9 *IDH*-wildtype, 11 *IDH*-mutant) at initial diagnosis (n=8) or recurrence (n=12) underwent ^{18}F -GE-180 PET, dynamic ^{18}F -FET PET, contrast-enhanced MRI of the brain, and TSPO-polymorphism analysis. The maximal tumor-to-background ratios (TBR_{max}) and biological tumor volumes (BT_V; SUV threshold: background-activity x 1.8) were evaluated in the 60-80 min (^{18}F -GE-180) and 20-40 min p.i. (^{18}F -FET) summation images. Dynamic ^{18}F -FET PET analysis included the evaluation of minimal time-to-peak (TTP_{min}). In MRI, the contrast-enhancing tumor volume was assessed (VOL_{CE}). Volumes were spatially correlated using Sørensen-Dice-coefficient. **Results:** Overall, median TBR_{max} was slightly higher in ^{18}F -GE-180 PET (4.58 (2.32-8.95) vs. 3.89 (1.56-7.15); $p=0.062$) compared to ^{18}F -FET PET. Median TBR_{max} in ^{18}F -GE-180 PET was significantly higher compared to ^{18}F -FET PET in

the subgroup of *IDH*-wildtype gliomas (5.44 (2.56-8.95) vs. 4.06 (1.56-4.49); $p=0.008$); no difference was observed in *IDH*-mutant gliomas ($p>0.05$ each), whereas all 5/20 patients with higher TBR_{max} in ^{18}F -FET PET compared to ^{18}F -GE-180 PET were *IDH*-mutant gliomas. No parameter in ^{18}F -GE-180 PET correlated with TTP_{min} ($p>0.05$ each). Median $\text{BT}_{\text{V}_{\text{GE180}}}$ (32.1 ml (0.4-236.0 ml)) tended to be higher than $\text{BT}_{\text{V}_{\text{FET}}}$ (19.3 ml (0.7-150.2 ml), $p=0.062$) leading to a moderate spatial overlap of 0.55 (0.07-0.85) only. In MRI, median VOL_{CE} (9.7 ml (0.1-72.5 ml)) was significantly smaller than both $\text{BT}_{\text{V}_{\text{FET}}}$ and $\text{BT}_{\text{V}_{\text{GE180}}}$ ($p<0.001$ each), leading to a limited spatial correlation of VOL_{CE} with $\text{BT}_{\text{V}_{\text{GE180}}}$ (0.29 (0.01-0.48)) and $\text{BT}_{\text{V}_{\text{FET}}}$ (0.38 (0.01-0.68)). TSPO-polymorphism analysis revealed 12 high-, 5 medium- and 3 low-affinity-binder; no parameter in ^{18}F -GE-180 PET showed a significant dependency on the binding affinity status ($p>0.05$ each), as extraordinarily high uptake was even observed in LAB. **Conclusion:** PET with ^{18}F -GE-180 and ^{18}F -FET provides highly differing imaging information in HGG dependent on the *IDH*-mutational status, as diverging spatial overlap and extensive exceedance of contrast-enhancement in MRI was observed. Combined imaging of TSPO-expression and dynamic amino acid uptake might reveal new insights regarding non-invasive characterization of tumor heterogeneity and might influence treatment planning.

EP-0152

The Use of a New Radiopharmaceutical Based on a Technetium-99m Labeled Glucose Derivative for Visualization of Brain Tumors.

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Purpose: to study the possibility of using a new radiopharmaceutical based on technetium-99m labeled 1-thio-D-glucose to visualize brain tumors. **Subjects and Method:** 8 patients with a diagnosis of a malignant brain tumor (glioblastoma), who underwent SPECT with the radiopharmaceutical “ $^{99\text{mTc}}$ -1-thio-D-glucose”, were included in the study. SPECT was performed 240 minutes after intravenous injection of 500 MBq of “ $^{99\text{mTc}}$ -1-thio-D-glucose” into a cubital vein. In addition, the tumor / background index was calculated. **Results:** The size of the tumor in all patients was more than 1 cm according to MRI. A high-intensity accumulation of “ $^{99\text{mTc}}$ -1-thio-D-glucose” in the projection of the brain tumor was noted in all the patients examined. At the same time, the physiological accumulation of the radiopharmaceutical in the projection of the soft tissues of the aponeurotic helmet, the muscles of the head and neck, salivary glands was visualized. Mean values of the tumor / background score in this group of patients were 7.46 ± 0.8 . **Conclusion:** A pilot study demonstrated that the radiopharmaceutical “ $^{99\text{mTc}}$ -1-thio-D-glucose” is promising for imaging malignant brain tumors. In addition, it should be noted that “ $^{99\text{mTc}}$ -1-thio-D-glucose” does not accumulate in intact brain tissue. This feature of the pharmacokinetics “ $^{99\text{mTc}}$ -1-thio-D-glucose” allows obtaining more contrast scintigraphic images.

EP-0153

Static and Dynamic ^{18}F -FDOPA PET for the Characterization of Gliomas defined by IDH and 1p/19q statusT. Zaragori¹, M. Ginet¹, G. Gauchotte², L. Taillandier^{3,4}, M.Blonski^{3,4}, R. Grignon¹, V. Roch¹, P. Marie^{1,5}, L. Imbert^{1,6}, A. Verger^{1,6};¹Department of Nuclear Medicine & Nancyclotep Imaging platform, CHRU Nancy, Lorraine University, Nancy, FRANCE,²Department of Pathology, CHU-Nancy, INSERM, Nancy, FRANCE,³Department of Neuro-Oncology, CHU-Nancy, Nancy, FRANCE,⁴Centre de Recherche en Automatique de Nancy CRAN, Université de Lorraine, Nancy, FRANCE, ⁵INSERM U1116, Lorraine University, Nancy, FRANCE, ⁶IADI, INSERM U1254, Lorraine University, Nancy, FRANCE.

Purpose: The molecular features isocitrate dehydrogenase (IDH) mutation and 1p/19q co-deletion, which have major importance in gliomas typing and prognosis, have been integrated in the World Health Organization (WHO) classification in 2016. The aim of this study was to assess the diagnostic performance of the ^{18}F -FDOPA PET using static and dynamic parameters in newly-diagnosed gliomas according to this new classification. **Subjects & Methods:** Eighty-nine patients with newly diagnosed and untreated gliomas with a ^{18}F -FDOPA PET scan prior to evaluation of tumor tissue according to the 2016 WHO classification were identified retrospectively. Among them, 58 patients had available dynamic data. Mean and maximum tumor-to-brain ratios ($\text{TBR}_{\text{mean/max}}$) of ^{18}F -FDOPA uptake and Metabolic Tumor Volume (MTV) were calculated on static images. Time-to-peak (TTP) values and the slope were extracted from the dynamic data. **Results:** Twenty-six (29 %) astrocytomas (IDH mutated), 20 (22 %) astrocytomas (IDH wild type), 21 (24 %) oligodendrogliomas (IDH mutated and 1p/19q co-deleted), 16 (18 %) glioblastomas (IDH wild type) and 6 (7 %) glioblastomas (IDH mutated) were identified. TBR_{mean} , TBR_{max} and MTV discriminated between IDH mutated astrocytomas or IDH wild type astrocytomas and IDH wild type glioblastomas ($p < 0.03$), with respectively TBR_{max} (cut-off 2.15; sensitivity, 94 %; specificity, 69 %; accuracy, 79%) and MTV (cut-off 18 ml; sensitivity, 94 %; specificity, 75 %; accuracy, 83%) showing the best diagnostic performances. None of the parameters discriminated between oligodendrogliomas and glioblastomas or astrocytomas. Furthermore, both TTP and slope discriminated between IDH mutated and IDH wild type gliomas ($p < 0.05$) with the slope appearing to be the best parameter (cut-off -0.12; sensitivity, 62%; specificity, 71%; accuracy, 66%). **Conclusion:** Taken together, static and dynamic ^{18}F -FDOPA PET parameters could provide useful information for non-invasive staging of gliomas. Static ^{18}F -FDOPA PET parameters may allow discriminating astrocytomas from IDH wild type glioblastomas. Dynamic parameters are helpful to discriminate between IDH mutated and IDH wild type gliomas. **Key words:** FDOPA PET; glioma; IDH mutation; 1p/19q co-deletion

EP-0154

 ^{18}F -DOPA PET in brain tumors: which impact on Multidisciplinary Brain Tumor Board decisions ?O. Humbert¹, V. Bourg², L. Mondot², J. Gal³, P. Bondiau¹, D. Fontaine², E. Saada-Bouaid¹, M. Paquet¹, F. Almeyrac², F.Vandenbos², J. Darcourt¹; ¹Centre Antoine Lacassagne, Nice, FRANCE, ²Pasteur 2 University hospital, Nice, FRANCE, ³Centre Antoine Lacassagne, NICE, FRANCE.

This study aimed to assess the therapeutic impact and diagnostic accuracy of ^{18}F -DOPA PET/CT in patients with high-grade glioma or brain metastases. **Methods:** Patients with histologically proven grade III or IV glioma or brain metastases were prospectively included in this monocentric clinical trial (IMOTEP). Patients either had a clinical suspicion of relapse or an indication of assessment of treatment response. Multimodality brain MRI and ^{18}F -DOPA PET were performed. Patients' data were discussed during a Multidisciplinary Neuro-oncology Tumor Board (MNTB) meeting. Firstly, the discussion was based on clinical and MRI data. A first diagnosis and treatment plan were proposed. Secondly, a new discussion was conducted based on the overall imaging results, including ^{18}F -DOPA PET. A second diagnosis and therapeutic plan were proposed. A retrospective and definitive diagnosis was obtained after 3 months of follow-up and considered as the reference standard.

Results: 106 patients' cases were prospectively investigated by the MNTB. In patients with a suspicion of recurrence (N=53), the addition of ^{18}F -DOPA PET data changed the diagnosis and treatment plan in 30.2% (16/53) and 22.5% (12/53) respectively. In patients with an indication of tumor response assessment (N=53), ^{18}F -DOPA PET data had a lower impact with only 5.7% (3/53) of diagnostic changes and 3.8% (2/53) of therapeutic plan changes. The definitive reference diagnosis was available in 98/106 patients. For patients with tumor recurrence suspicion, the adjunction of ^{18}F -DOPA PET increased the Younden's index from 0.46 to 0.58, reflecting an increase in diagnostic accuracy. This was mainly due to a high increase of the Negative Predictive Value from 61.5% to 100%. **Conclusion:** ^{18}F -DOPA PET has a significant impact on the management of patients with a suspicion of brain tumor recurrence but a low impact when used to evaluate the brain tumor response to treatment.

EP-0155

Ascertaining F18 positron-emission tomography skill in glioma classification pursuant to the revised WHO classification 2016M. M. Weber¹, S. Kebir², L. Lazaridis², C. Deusch³, A. Stoppek⁴, T. Schmidt², J. Böhm⁵, M. Christoph³, B. Scheffler⁶, K. Keyvani⁷, U. Sure⁸, C. Kleinschnitz², D. Pierscanek⁸, M. Glas², K. Herrmann⁹;¹Universitätsklinikum Essen, Essen, GERMANY, ²Division of Clinical Neurooncology, Department of Neurology, University HospitalEssen, University Duisburg-Essen, Essen, GERMANY, ³Department of Neuroradiology; University Duisburg-Essen, Essen, GERMANY,⁴Division of Clinical Neurooncology, Department of Neurology, University Hospital Essen, University Duisburg-Essen, Essen,Germany, Essen, GERMANY, ⁵Division of Clinical Neurooncology, Department of Neurology, University Hospital Essen, UniversityDuisburg-Essen, Essen, Germany, Essen, GERMANY, ⁶DKFZ-Division Translational Neurooncology at the West German Cancer Center(WTZ), University Hospital Essen, University Duisburg-Essen, Essen, GERMANY, ⁷Department of Neuropathology, University Hospital

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Purpose: For the past years histopathological assessment of gliomas was mainly based on morphological features. This has changed fundamentally with the revision of the World Health Organization (WHO) classification from 2016. In light of previous trials underscoring the value of molecular markers such as isocitrate dehydrogenase (IDH) mutation and 1p19q-codeletion with reference to clinical outcome, classification of gliomas has shifted from a morphology-based to a molecular markers-based one. In this pilot study, we analyzed the potential of F18-FET with respect to non-invasive subtyping of glioma as per the revised WHO classification. **Methods:** Patients with lesions suspicious for glioma underwent FET-PET prior to surgery. Patients were then grouped according to histopathological diagnosis as follows: glioblastoma (GBM), IDH-wildtype grade II/III (GII/III-IDH^{wt}) glioma, IDH-mutant grade II/III (GII/III-IDH^{mut}1p19q^{nc}) glioma and IDH-mutant 1p19q-codeleted (GII/III-IDH^{mut}1p19q^{cod}) glioma. Maximum tumor-to-brain ratio (TBR_{max}) and mean tumor-to-brain ratio (TBR_{mean}) of FET uptake were calculated and compared among subgroups. **Results:** 27 patients met the inclusion criteria for this retrospective pilot study. Of these, 9 were later diagnosed with GBM, 7 with GII/III-IDH^{wt} glioma, 5 with GII/III-IDH^{mut}1p19q^{nc} glioma and 6 with GII/III-IDH^{mut}1p19q^{cod} glioma. TBR values were highest in the GBM group (mean TBR_{max} 2.97, mean TBR_{mean} 3.26) and slightly lower within the group of GII/III-IDH^{wt} glioma. As expected, significantly lower TBR values were observed in the GII/III-IDH^{mut}1p19q^{nc} glioma group (mean TBR_{max} 1.67 mean TBR_{mean} 1.87), while GII/III-IDH^{mut}1p19q^{cod} showed relatively high TBR values (mean TBR_{max} 2.31 mean TBR_{mean} 2.65). Statistically significant results were obtained when comparing GBM and GII/III-IDH^{mut}1p19q^{nc} glioma. **Conclusions:** Interestingly, GII/III-IDH^{mut}1p19q^{cod} gliomas, which are associated with the best prognosis among the previously defined glioma subgroups, demonstrated a relatively high FET uptake. The upshot of all this is that in patients with high TBR values, a differentiation between GBM and GII/III-IDH^{mut}1p19q^{cod} gliomas appears not feasible via FET-PET alone establishing the requirement for alternative tools for non-invasive glioma subtyping.

EP-0156

Prognostic role of pre-treatment 18F-FDG PET/CT in primary brain lymphoma

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Purpose: primary brain lymphoma is an aggressive extranodal non-Hodgkin lymphoma confined to the central nervous system at diagnosis and its prognosis is relatively poor. Many possible prognostic factors for outcome are investigated with controversial results. The role of 18fluorine-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/

CT) in this field is not well understood. Our aim was to study the metabolic behavior of brain lymphoma at 18F-FDG-PET/CT and the prognostic impact of qualitative and semiquantitative PET/CT parameters. **Subjects and Methods:** between 2006 and 2018 fifty two patients (26 female, 26 male; average age: 61 years) with histologically-confirmed diagnosis of brain lymphoma who underwent PET/CT for staging before any treatment were included. PET images were qualitatively and semi-quantitatively analyzed by measuring the maximum standardized uptake value body weight (SUV_{bw}), lean body mass (SUV_{lbm}), body surface area (SUV_{bsa}), metabolic tumor volume (MTV), total lesion glycolysis (TLG) and compared with epidemiological (age at diagnosis, gender) and morphological (max lesion diameter, number of lesions) characteristics. Progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan-Meier method. Qualitative and semiquantitative PET/CT features were correlated with OS and PFS. **Results:** thirty nine (75%) patients had positive 18F-FDG-PET/CT showing 18F-FDG uptake (average SUV_{bw} of 18.2; SUV_{lbm} of 13.9; SUV_{bsa} of 5; MTV of 14.8; TLG of 153) at the corresponding cerebral lesion; the remaining 13 (15%) were not 18F-FDG-avid. Average maximum diameter of primary cerebral lymphoma was 18.2 mm. Single focal lesion was present in 40 patients, while multiple focal lesions were present in 12 patients. Overall survival at 1st year was 62%, and 55% at 2nd year; PFS was 64% at 1st year and 48% at 2nd year. Relapse or progression of disease occurred in 22 patients with an average time of 9.7 months; death occurred in 18 patients with an average of 7.9 months. After a median follow up of 24 months, there was no difference in PFS and OS between baseline PET/CT positive and negative PET/CT groups (p=0.759 and p=0.771 respectively). PFS and OS was significantly shorter in patients with MTV>9.8 (p= 0.037 and p= 0.022 respectively) and TLG>94 (p=0.045 and p=0.0430). No other epidemiological, morphological or metabolic PET/CT features were significantly associated with survival outcomes. **Conclusions:** 18F-FDG avidity was noted in 75% confirming that brain lymphoma are usually lymphoma with 18F-FDG avidity. Metabolic tumour parameters (MTV and TLG) are useful in prognosis estimation of primary brain lymphoma, being independently associated with PFS and OS.

EP-0157

Differentiating dural metastases from meningioma in cancer patients : Role of 68Ga DOTANOC PET/CT

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Introduction: Metastases to the dura is not an uncommon occurrence in cancer patients. Radiological appearance of dural metastases seen on CT/MR imaging is often similar to that of meningioma leading to a diagnostic dilemma. Differentiating between these two entities is crucial as the clinical course and management differs significantly. Since meningiomas are known to exhibit strong somatostatin receptor (SSTR) expression we decided to explore the use of 68Ga DOTA-NOC PET/CT in differentiating them from dural metastases. **Subjects**

and Methods: Cancer patients with a dural based lesion seen on MRI/CT/FDG PET-CT considered equivocal for metastases or meningioma by a multidisciplinary team, who were referred for 68Ga DOTA-NOC PET/CT were included in the study. 68Ga DOTA-NOC was synthesized in the hospital radiopharmacy using a 68Ge/68Ga generator. 68Ga PET/CT was performed 45–60 min after intravenous injection of 74–100 MBq of the radiotracer. Scan interpretation- Visual score (VS) was defined as stated below and assigned to each lesion, VS 1: intensity of uptake < liver, VS 2: > liver < spleen, VS 3: $\geq$ spleen. SUVmax of the lesions was also noted. Final diagnosis was decided by histopathological confirmation whenever available. Stability of the lesion on imaging follow-up (1 yr) was considered diagnostic of meningioma when histopathology was unavailable.

Results: 35 patients (M:F- 21:14) with a median age of 51.5 yrs (range 35–71 yrs) were included. Lung and breast were the two most common sites of primary malignancy. Meningioma was considered as the final diagnosis in 26 patients (7-histopathological confirmation, 19- stability on radiological follow up), metastases in 6 patients (4-histopathological correlation). There was 1 patient each of pseudotumor, abscess and hemangioblastoma. Meningiomas showed intense tracer uptake in 25 patients (VS-3, $\geq$ spleen). 1 patient of atypical meningioma showed lesser uptake, VS-2 (>liver < spleen). None of the metastatic lesions showed intense uptake (VS-1,2). Hemangioblastoma was the only non- meningiomatous lesion showing intense (VS-3) tracer uptake. Meningiomas showed a significantly higher median SUVmax value compared to metastases (21.1 Vs 4.9) **Conclusion:** Meningiomas show high SSTR expression (VS>3) compared to metastases (majority VS-1). For dural based lesions in cancer patients strong 68Ga DOTA PET/CT positivity (VS-3) suggests the diagnosis of meningioma. These patients can be observed (without biopsy) with greater assurance if asymptomatic. Limitation- Atypical/anaplastic meningiomas can show lower SSTR expression (VS<3) and dural metastases from neuroendocrine primary can potentially show high SSTR expression (VS-3)

EP-0158

Role Of 18F-DOPA PET/MRI In Glioma

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Background: To characterize tumours in baseline scans and to evaluate active disease in post treatment patients and compare and evaluate differences of metabolic uptake and MRI signal characteristics on cross sectional imaging and perfusion weighted imaging, based on a voxel based assessment, in 18F-DOPA PET/MRI in children and adolescents patients with gliomas. **Patients and Methods:** 23 brain ¹⁸F-FDOPA PET/MRI studies (19 patients) were analysed for staging or follow up of brain tumours. Diagnosis of tumour was confirmed histologi-

cally by surgical resection/biopsy. Gold standard was considered biopsy when possible or imaging at follow up. Static PET acquisitions were post-reconstructed between the 10th and 15th minute after injection of 18F-FDOPA. Quantitative PET parameters (SUVmax, SUVmean, tumor/striatum ratio (T/S), and tumour/normal brain ratio (T/N) and MRI features (maximal diameters, tumour enhancement, presence of necrosis, cerebral perfusion [CBV, CBF]) were recorded. Volume of tumour was assessed based on areas of maximal visual uptake on PET or enhancement/signal change in the tumour on MRI. Separate ROIs of the specific features (enhancing, non enhancing and necrotic part) of the tumours and of the normal appearing white matter (NAWM) were drawn on MRI. Within these ROIs, SUVmax were recorded. The confidence factor i.e. the presence of viable tumour was assessed by both modalities on a 5 point scale. **Results:** Tumour lesional size varied between 15.8 mm and 62.2 mm. Thirteen lesions (56%) demonstrated contrast enhancement and 5 showed necrotic core/component. The median SUVmax was 3.1 for LGG and 3 for HGG. While a significant correlation was noted between CBF and CBV for all types of glioma ($p < 0.01$), there was no correlation between SUVmax and perfusion parameters. F-DOPA vol showed a median of 10363 cc for HGG and 5400 cc for LGG. MRI vol showed a median of 5992 cc for HGG and 4772 cc for LGG. The histogram analysis of the SUVmax within the specific features of the tumour showed that PET distinguished the enhancing and non-enhancing components from necrosis and NAWM, and demonstrated active disease in non-enhancing regions. In seventeen patients where there was concordance on both imaging modalities, the findings were categorised as definite presence of active disease. In two discordant cases, MRI was superior in identifying the presence of active disease as this was confirmed histologically. In both patients, the tumours had no gadolinium contrast enhancement. **Conclusion:** This study presents the first simultaneous comparison of a voxel based analysis of F-DOPA and MRI in glioma patients. The mismatch between F-DOPA and MRI parameters indirectly confirms the hypothesis of different biological parameters identified by F-Dopa, conventional MRI and perfusion.

EP-0159

Comparison study of ¹¹C-methionine PET/CT, ¹¹C-acetate PET/CT, and contrast enhancement on MRI for grading and prognostication in gliomas.

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Purpose: This retrospective study aimed to assess the roles of ¹¹C-methionine PET/CT (¹¹C-MET PET), ¹¹C-acetate PET/CT (¹¹C-ACE PET), and contrast-enhanced MRI for grading and predicting prognosis in patients with cerebral gliomas. **Methods:** Eighty patients (45 men, 35 women; aged 26–80 years; median age, 48 years) with glioma (Grade II, n=32; Grade III, n=16; Grade IV, n=32) underwent ¹⁸F-FDG PET, ¹¹C-MET PET, and MRI at staging. The ratio of the maximal standardized uptake value (SUV) of a glioma to the mean SUV of the contralateral cortex (G/C) on ¹¹C-MET PET (¹¹C-MET G/C) and ¹¹C-ACE PET (¹¹C-ACE G/C) was calculated. The presence of contrast enhancement

(CE) was assessed on MRI. ROC analysis and Student T-test for grading and Cox proportional hazards model and classification and regression tree (CART) models for overall survival (OS) were performed. **Results:** ^{11}C -MET G/C and ^{11}C -ACE G/C were significantly different between the Grade II, III, and IV groups ($p < 0.01$, $p < 0.01$, respectively). In multivariate analysis, ^{11}C -MET G/C and ^{11}C -MET G/C, and presence of CE on MRI were significant for OS. The CART modelling identified four risk groups for OS (group 1: without CE and ^{11}C -MET G/C ≤ 2.4 [HR=0], group 2: without CE and ^{11}C -MET G/C > 2.4 [HR=1], group 3: with CE and ^{11}C -ACE G/C ≤ 2.27 [HR=0.8], group 4: with CE and ^{11}C -ACE G/C > 2.27 [HR=2.14]. The median OS was as follows: 35.3 months (group 1), 31.4 (group 2), 28.0 (group 3), and 13.5 (group 4) (group 1 vs. group 2: $p=0.003$; group 1 vs. group 3: $p=0.013$; group 1 vs. group 4: $p < 0.001$; group 2 vs. group 3: $p=0.933$; group 2 vs. group 4: $p=0.012$; group 3 vs. group 4: $p=0.013$). CE on MRI was the first node on the decision trees in our model. As a result, in gliomas without CE, patient with ^{11}C -MET G/C > 2.4 showed poor prognosis. In gliomas with CE, patients with ^{11}C -ACE G/C > 2.27 had poor prognosis. **Conclusion:** Both ^{11}C -MET and ^{11}C -ACE uptake were significantly different between the Grade II, III, and IV gliomas. For the prediction of OS, ^{11}C -MET PET provides further prognostic information in patients with gliomas without contrast enhancement on MRI whereas ^{11}C -ACE PET is useful in prognostication in patients with gliomas with contrast enhancement on MRI.

EP-0160

Disease recurrence vs posttreatment changes: The diagnostic accuracy of O-(2-[^{18}F]-fluoro-ethyl)-L-tyrosine PET imaging in treated glioblastoma

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Aim: Discrimination between recurrent glioblastoma (GBM) and posttreatment changes with magnetic resonance imaging (MRI) is challenging. The aim was to determine the diagnostic accuracy of supplementary static O-(2-[^{18}F]-fluoro-ethyl)-L-tyrosine (FET) positron emission tomography (PET). **Methods:** In this retrospective study, 137 consecutive patients that had undergone a total of 150 FET PET scans were selected to review. Inclusion criteria were 1) histologically verified glioblastoma World Health Organization (WHO) grade IV; 2) previous tumor resection or stereotactic biopsy followed by oncological treatment consisting of first-line standard radiotherapy or radio-chemotherapy; 3) unexplained stable, or increasing contrast enhancing lesions on T1, or non-contrast enhancing lesions on T2/FLAIR on MRI later than 6 months after radiotherapy, where the distinction between posttreatment changes and disease recurrence was uncertain; 4) a static 20-minute FET PET imaging performed 20 min after tracer injection for supplementary assessment; 5) a reference standard consisting of histological evaluation following tumor re-resection or stereotactic biopsy within 3 months after FET PET scan, or clinical and/or MRI follow-up. Calculation of maximum and mean tumor-to-background ratio (TBR_{max} and TBR_{mean}) and measurement of biological tumor volume (BTv)

on FET PET scans fused to T1-weighted post-contrast MRI scans were performed blinded to the reference standard. Receiver operating characteristics (ROC) analysis was used to determine the optimal threshold of FET parameters. **Results:** One hundred twenty-six (84%) PET scans demonstrated relative FET uptake of varying intensity. Surgical intervention with pathology confirmation was performed following 88 (58.7%) PET scans, while 62 (41.3%) PET scans were evaluated by clinical and/or MRI follow-up, resulting in total 131 cases of recurrent glioblastoma and 19 of posttreatment changes. Median TBR_{max} in patients with recurrent glioblastoma and posttreatment changes were 3.2 and 1.7 ($p = 0.016$), median TBR_{mean} was 2.0 and 1.6 ($p = 0.010$), while median BTv was not significantly different ($p = 0.149$). ROC analysis yielded thresholds of 2.0 for TBR_{max} and 1.8 for TBR_{mean} for differentiation ($p < 0.0001$) between recurrent glioblastoma and posttreatment changes with sensitivities, specificities and diagnostic accuracies of 95 %, 95 % and 96 % for TBR_{max} and 89 %, 89 % and 92 % for TBR_{mean} , respectively. **Conclusion:** FET PET is a powerful noninvasive supplement to MRI for distinguishing recurrent GBM from posttreatment changes.

EP-0161

Preliminary results of activity-time curves analysis in PET/CT ^{18}F -Choline in treated cerebral tumors

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Objective: To evaluate parameters of activity-time curves in PET / CT ^{18}F -Choline in treated brain tumors and compare them with the results of the biopsy. **Material and Method:** 17 studies of ^{18}F -Choline PET/CT were performed from September'16-December'17. Exploration reason: differential diagnosis between tumor recurrence and radionecrosis. Patients without biopsy were excluded after PET/CT. Technique: Dynamic brain study (30 images, 1 minute / image) on PET/CT equipment (Philips Gemini TF). The acquisition started immediately before the radiopharmaceutical injection (296-370 MBq). Time-activity curves were obtained by drawing VOIs on the study lesion (curve 1) and on choroidal plexus (curve 2). The analysis was morphology of the curves, the relationship between curves 1 and 2, and their correlation with histological results. **Results:** A sample of 6 patients was obtained with an average age of 52.3 years (range 38-57). The initial diagnosis was of primary brain tumor in 4 patients and cerebral metastasis in 2 patients. The result of the biopsy was the presence of viable tumor in 4 patients and radionecrosis in 2 patients. Analysis of curves: The morphology and height of curve 2 was similar in all patients. Curve 1 was similar in both height and morphology in 4 patients, exceeding in all cases the height of curve 1. 3 patients had a biopsy resulting in malignancy and 1 patient resulting from radionecrosis. In the remaining 2 patients, the height of curve 1 was lower than that of curve 2. The biopsy was of malignancy in one patient and radionecrosis in the other. **Conclusions:** Although the sample is small, tumor recurrences showed a similar curve, so the analysis of activity-time curves seems promising for the differential diagnosis between radione-

crois and tumor recurrence in brain tumors. Choroidal plexus can be used as a reference area and quality control.

EP-11

e-Poster Area

Dosimetry: Dosimetry

EP-0162

Radiation induced dna damage in patients undergoing computed tomography, detection and quantification by gamma-h2ax foci measurements in peripheral blood lymphocytes

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Purpose: Double-strand breaks (DSB) are considered the most relevant radiation-induced damage to deoxyribonucleic acid (DNA). These DNA lesions are usually efficiently repaired, however, DSB misrepair can lead to chromosomal translocations and therefore initiate carcinogenesis. γ -H2AX immunofluorescence microscopy is a reliable and sensitive method for the quantification of radiation induced DNA double-strand breaks (DSB) in peripheral blood lymphocytes (PBLs). The detectable amount of these DNA damages correlates well with the dose received. However, the biological radiation damage depends not only on dose but also on other individual factors like radiation sensitivity and DNA repair capacity. We investigated whether γ -H2AX could be used as an in vivo marker to assess the impact of DNA damage in patients in the dosage range of computed tomography (CT) procedures. **Subjects & Methods:** Ten consecutive patients (5 women, 5 men; mean age, 56.9 years; range, 27-90 years) undergoing contrast enhanced CT examinations from the Thorax and/or Abdomen were prospectively recruited. None of these patients had had any ionizing imaging procedures in the past seven days or chemotherapy/radiotherapy within the prior six months before CT scans. PBLs were isolated from blood samples drawn directly before the CT procedure and 15 and 30 minutes later. DNA DSBs were detected by γ H2AX immunofluorescence staining and quantified (in terms of γ H2AX foci/cell) with automated digital microscopy in each of the three blood samples to assess any significant differences. Statistical analysis was performed with t test. The study was approved by the local ethics committee, and written informed consent was obtained from each patient. **Results:** PBLs from blood taken 15 minutes after CT scan showed a significant increase of mean DSB s rate of $37.22\% \pm 4.63$ as compared with a mean DSBs rate of $17.29\% \pm 4.35$ for PBLs taken before the scan ($P < 0.001$). The results also showed a decrease in the mean rate of DSBs in PBLs taken 30 minutes after CT scan ($29.33\% \pm 8.1$) ($P < 0.05$). **Conclusions:** γ -H2AX immunofluorescence microscopy can be used to measure radiation-induced DNA double-strand breaks, in the dose range of Diagnostic CT. CT=computed tomography

EP-0163

DNA damage investigation of Auger electron-emitters - from Bq to Gy

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Introduction: Energy deposited from Auger electrons emitted by Gallium-67 (⁶⁷Ga) and Indium-111 (¹¹¹In) occurs within a few micrometres, i.e. remains in cells in which it was released. These high LET radionuclides are thus interesting for molecular radiotherapy of micrometastases and single circulating tumour cells whilst minimizing healthy tissue toxicity. The unit of absorbed dose, Gy, is currently used for conventional radiotherapy planning and dosimetry for diagnostic tracers and radiopharmaceuticals. To develop new Auger electron-emitting radiopharmaceuticals and optimize clinical translation, we are investigating how to interpret the Gy for Auger electron-emitters, here, in terms of DNA damage. **Methods:** DNA damage was evaluated in a cell-free system by incubating supercoiled pBR322 plasmid at 1.25 or 5 ng/ μ L (20 μ L) with 0-1 MBq ⁶⁷GaCl₃ or ¹¹¹InCl₃ and loading 10 μ L on a 0.8% agarose gel. ⁶⁷Ga and ¹¹¹In was also added to DNA in a chelated form attached to p-SCN-DOTA or THP or as ⁶⁷Ga-citrate. Radioactivity was also added as an external source, i.e. physically separated from the DNA to estimate γ -induced damage contributions. Incubation was for 2, 4, 7 and 25 hours. Separately, DNA was exposed to external beam radiation (¹³⁷Cs at 5Gy/minute) from 0 to 40 Gy. The percentage of damaged DNA was calculated through measuring relaxed and linear DNA products, representing single and double strand breaks, respectively. Kinetic modelling allowed us to calculate the rate of conversion for supercoiled-to-relaxed (k_{sr}) and relaxed-to-linear (k_{rl}) DNA. **Results:** DNA damage, both single and double strand breaks, increased with radiation dose (external beam) and time when incubated with ⁶⁷Ga or ¹¹¹In, with ⁶⁷Ga seemingly more potent. Only 18% of DNA was damaged when incubated with 0.5 MBq ¹¹¹In for 2 hours at 12.5 ng DNA, compared to 74% for ⁶⁷Ga. When chelated or used as an external source, damage from both ⁶⁷Ga and ¹¹¹In was protected against. Surprisingly, for studies using 50 ng DNA irradiated by external beam, conversion rates were slower than for 12.5 ng DNA; $k_{sr} = 0.45 \pm 0.06 \text{ Gy}^{-1}$ and $k_{rl} = 0.004 \pm 0.002 \text{ Gy}^{-1}$ (50 ng) compared to $k_{sr} = 1.21 \pm 0.04 \text{ Gy}^{-1}$ and $k_{rl} = 0.017 \pm 0.001 \text{ Gy}^{-1}$ (12.5 ng). **Conclusion:** This work demonstrates how a cell-free system allows for radiobiological insight and assessments into Auger electron-emitters allowing us to confidently convert Bq to Gy and compare the basic mechanisms in causing DNA damage from radionuclides to that caused by external beam. **Acknowledgements:** Funding for the project was in part provided by the Academy of Medical Sciences.

EP-0164

Multi-cellular dosimetry of β^+ -emitting radionuclides used for cell labeling in the context of cell tracking studies with PET imaging

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Purpose: *In vitro* radiolabeling of cells combined with nuclear medicine imaging provides a potential method for *in vivo* cell trafficking analysis. Besides, the use of β^+ -emitting radionuclides is of particular interest given the good intrinsic characteristics offered by PET technology. The labeling procedure still raises concerns regarding the high amount of radioactivity typically used which induces a cell cytotoxicity. Accurate dosimetry is required to allow for a better understanding of the toxicity associated to labeling. This work aimed to develop a realistic multi-cellular dosimetry and apply the model to the analysis of 3 radionuclides used for labeling in PET: ^{18}F , ^{64}Cu and ^{68}Ga . **Methods:** A program using Python was developed to generate cell coordinates from a set of initial parameters *i.e.* cell size, cell density, bounding volume size. A cubic cell arrangement was assumed and the calculation approach was based on an analytical formula using derived-Monte Carlo S factors. Both the contribution to the dose of radioactivity located within the cells and in the culture medium were considered. The mean absorbed dose to cells was evaluated as a function of the cell density and the intra-to-extra cellular activity repartition. The results were compared with those obtained using conventional dosimetry. Dose calculations were also done under realistic conditions of leukocytes labeling with ^{18}F -FDG based on labeling parameters used in few reported studies. **Results:** The cellular-to-conventional dose ratios can vary significantly with cell density, reaching important values at low density and approaching 1 at high density. They were also influenced by the activity repartition between the cells and the medium, the highest values occurring when all activity was incorporated in the cells. A significant underestimation of mean dose to the cell by conventional model was particularly observed for ^{64}Cu up to a factor of 15 at low density, due to the emission of short-range auger electrons. ^{68}Ga and ^{18}F presented lower discrepancies between cellular and conventional doses considering the emission of larger-range β^+ . The calculations done for labeling conditions taken from literature showed that a same injected activity per cell can result in significantly different absorbed doses. **Conclusions:** The development of a realistic multi-cellular dosimetry offered a better understanding of how absorbed dose to cell is affected as a function of key labeling parameters. The establishment of the dose-effect correlation for mesenchymal stem cells is under way through functional tests *in vitro* after labeling with ^{18}F -FDG and external irradiation for comparison.

EP-0165

Patient Specific Internal Dose Estimation Based on Quantitative SPECT/CT Imaging

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Aim: Radionuclide therapy is an important clinical application for treatment of cancer and other diseases. With the development of the nuclear medicine equipment, the application of radionuclide therapy is widely increased. Accurate assessment of the organ dose and the voxelized dose distribution is critical

to increasing the accuracy and efficiency of the treatment. Compared with the organ-level dosimetry calculation, more accurate patient specific estimation of the absorbed dose to the tumor and normal tissue can be achieved by applying voxelized approach. Moreover, the voxel based estimation can display the non-uniform dose distribution within the organs and tumor. This project proposed a new method to assess the personalized dosimetry in radionuclide therapy based on SPECT/CT images.

Materials and Methods: The radiopharmaceutical is labeled with I-131 in this work. The activity distribution is obtained by the SPECT/CT images, which were scanned at different time. The activities in SPECT voxel were integrated to obtain 3D cumulated activity distribution map. It is significant to fit a time-activity curve for each voxel describe the pharmacokinetics of the radiopharmaceutical. The hybrid SPECT/CT imaging series were performed over the radionuclide therapy at multiple times. To observe the temporal process of absorb dose in one voxel, it is necessary to register the series images. The CT image set performed at day 0 were regarded as reference image, and the image sets obtained following days were adjusted to the reference image as object image. The transfer matrix was recorded and accounted for the SPECT rigid registration. In this work the Geant4 toolkit was applied to calculate the dose distribution. The SPECT imaging provided decay count in each voxel, which can be converted to radioactivity by the calibration curve. So that the activity distribution obtained from SPECT imaging served as the source item. The CT Hounsfield unit (HU) was translated into density of each voxel. The material compositions were defined furtherly. The sampling method of the complex source term and the variance reduction techniques were studied. **Results:** Monte Carlo simulation was processed to obtain voxelized dose distribution. And based on the organ segmentation the organ dose was calculated for the concerned organs in NM. **Conclusion:** The technique presented offers an efficient dosimetry method for clinical radionuclide therapy. This work will provide a useful tool for assessing the personalized dosimetry in radionuclide therapy, and then provide important reference for doctors to develop treatment plans aiming at different states of patients.

EP-0166

The MEDIRAD Multi-national I-131 Dosimetry Study for Thyroid Ablation and Adjuvant Therapy

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Purpose: The Linear-No-Threshold (LNT) model assumes that low-level dose effects (<100mSv) may be extrapolated from

known effects at higher exposure levels. This has significant implications for medical exposures. The Horizon 2020 MEDIRAD project was initiated to investigate the effects of low dose radiation. This multi-centre multi-national prospective study aims to accurately determine the absorbed doses to healthy organs and thyroid remnants from radioiodine ablation. The relation between patient biokinetics, the success of thyroid ablation and acute to mid-term toxicity will be assessed. **Methods:** Gamma cameras at four centres will be calibrated for high activity quantitative I-131 imaging, by characterising count losses due to dead-time and due to partial volume effects (PVE), for 0.79–196 cm³ volumes. Additionally dose calibrators will need to be traceable to a national standard and whole-body (WB) retention monitors will be set-up. 100 patients with histologically proven differentiated thyroid cancer (DTC) and a clinical indication for I-131 therapy post-total thyroidectomy will be recruited. Patients will follow a low iodine diet for two weeks prior to I-131 administration. A mode of thyroid stimulating hormone escalation will be performed. Three centres will recruit low-risk DTC patients, the fourth intermediate-risk patients; the activity administered will be 1.1 or 3.7 GBq I-131. A flexible patient data acquisition protocol for dosimetry has been developed to allow for inter-centre variabilities with respect to access to hybrid imaging, existing camera workloads and local national radiation protection regulations. The imaging protocol mandates a minimum of four WB planar scans (24–96 hours post-administration) plus a SPECT/CT at 48 hours encompassing normal organs and remnants between the base of skull and upper thighs. Each centre may acquire additional scans at early and late time points. Blood and urine samples and WB retention measurements may be collected for blood and bone marrow dosimetry, urinary excretion and WB dosimetry calculation. **Results:** To-date one centre has been set-up for participation in the study. Two Siemens Intevo SPECT/CT systems were characterised. Volume-dependent correction-factors for PVE count losses were measured. Count losses of 22% were observed at 3 GBq due to dead-time. **Conclusion:** This study establishes the first European network able to perform standardised quantitative radioiodine imaging for dosimetry; it is anticipated that more centres will be recruited. The dosimetric methods and tools developed will provide the means to prepare a large-scale observational epidemiological study of acute, mid- and long-term risk from absorbed doses delivered to normal organs.

EP-0167

Quantification of ¹³¹I activity in mouse kidney tissues using micro-SPECT/CT: a phantom study

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Context: Accurate quantification of radionuclide activity in mouse kidneys is needed for studying the preclinical dose-dependence of treatment-related nephrotoxicity. Discrimination of cortex and medulla activity may even be necessary, in partic-

ular for therapies based on short-range particle emitters with inhomogeneous kidney uptake. **Aim:** To investigate, by means of phantom experiments, the feasibility and accuracy of ¹³¹I activity quantification for imaging tasks representing mouse kidneys and renal cortex using micro-SPECT/CT. **Methods:** The phantom consists on several cylindrical cavities (hot rods) of different sizes ($\varnothing_{rod}$ 1–6 mm) embedded in plastic. Solid cylindrical inserts may be placed inside the largest rods (kidneys) to create two meniscus-like cavities of 1-mm maximum thickness (renal cortex). The phantom was filled with an ¹³¹I-Nal solution of known activity concentration mixed with CT radiocontrast. SPECT/CT acquisitions of the phantom without inserts (kidney and generic small tissue geometry) and with inserts (cortex geometry) were done with a VECTor/CT micro-SPECT/PET/CT (MILabs, Netherlands) equipped with a high-energy mouse collimator with 1.6-mm pinholes. SPECT images were reconstructed using manufacturer OSEM algorithm with CT-based attenuation correction and a TEW scatter correction. SPECT-image quantification of hot objects was done using different approaches for ROI segmentation: based on 3D isocontours of activity concentration data (SPECT image) and using 3D isocontours and cylindrical shapes based on CT images. Different ROI sizes were defined relative to the rod diameter (for rods without inserts) or to the renal cortex volume determined from the CT. Quantification accuracy was evaluated in terms of activity recovery coefficients. **Results:** Due to significant partial volume effects (PVE), the quantification accuracy is strongly dependent on the size of either the hot rod and the quantification ROI. ROIs matching hot rods' diameter ($\varnothing_{ROI} = \varnothing_{rod}$) always underestimate the true activity from 15% (largest rods) to >40% ($\varnothing_{rod} \leq 2$ mm). Instead, activity quantification is improved when using PVE-limiting ROIs which are oversized ($\varnothing_{ROI}/\varnothing_{rod} \geq 1.2$) or undersized ($\varnothing_{ROI}/\varnothing_{rod} = 0.75$; only if $\varnothing_{rod} \geq 3$ mm). Compared to kidney rods, PVE are dominant for the cortex: less than 40% of the activity is recovered with SPECT-based ROIs matching the cortex volume as well as with undersized ROIs, while size-equivalent CT-based ROIs are even more underestimating. **Conclusion:** The optimization of ROI segmentation strategies is key for accurate ¹³¹I activity quantification of mouse tissues with micro-SPECT. Complimentary pre-determined correction factors to compensate for PVE are nevertheless required to quantify the activity in small tissues like the renal cortex.

EP-0168

Voxel Based Multi Cycle Dosimetry for ¹⁷⁷Lu Theranostics application

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Aims: The aim is to present a comprehensive framework to compute 3D multi cycle dosimetry of radiation burden and associated uncertainty based on multi modal quantitative SPECT with ¹⁷⁷Lu. **Methods:** Siemens developed a Dosimetry Research Tool (DRT) to automate voxel based dosimetry calculation to compute both dose and its associated uncertainties based on quantitative SPECT of ¹⁷⁷Lu, or any other isotope of interest, pre-

senting it first in 2017. We now expand the method to compute the cumulative dose and associated uncertainties from a multi cycle treatment plan. We first acquire suitable data on a calibrated Siemens Intevo SPECT/CT and reconstruct all the data from the $n=4$ timepoints in $k=4$ cycles with bootstrapping of $r=10$ realizations. We then perform dosimetry calculations for each cycle, and then accumulate the dose with standard error propagation method also accumulate the uncertainty. We tested the method on simulation data, but omitting it here. We present here one example from a patient undergoing treatment with ^{177}Lu -DOTATATE for neuroendocrine tumors over a 7 month period. For demonstration purposed we only select the renal cortex and the largest tumor and liver, but in principle any organ can be selected. **Results:** We can show that the renal cortex dose accumulates to 3.67 (1st), 4.84 (2nd), 3.84 (3rd), and 3.04 Gy for the 4th cycle with associated uncertainties (95%CL) of 8.0% (1st), 5.9% (2nd), 1.8% (3rd), and 4.3% for the 4th cycle. The first tumor accumulates to 20.13 (1st), 4.82 (2nd), 2.55 (3rd), and 2.95 Gy for the 4th cycle with associated uncertainties (95%CL) of 2.9% (1st), 5.6% (2nd), 5.0% (3rd), and 6.5% for the 4th cycle. The liver accumulates to 1.79 (1st), 1.58 (2nd), 1.57 (3rd), and 1.56 Gy for the 4th cycle with associated uncertainties (95%CL) of 22.7% (1st), 7.4% (2nd), 8.0% (3rd), and 11.5% for the 4th cycle. **Conclusion:** We demonstrate the feasibility to routinely compute voxel based cumulative dose and dose uncertainty, once a calibrated quantitative SPECT/CT data series is acquired. In the next steps we will work through patient datasets, compute cumulative doses and dose uncertainties and work on a framework to link individual dose estimations to population based references and correlate with ancillary pre- and post-treatment in preparation for AI supported treatment planning.

EP-0169

Personalized Incorporation Dosimetry for Lu-177-based Radionuclide Therapy

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Purpose: The 2013/59/EURATOM guideline and the German radiation protection act (StrSchG, 27.07.2017) determine the personalized dosimetry for radionuclide therapy obligatory. Except for the radioiodine therapy, standardized procedures are not established. Therefore, the functionality and practicability of various software solutions for incorporation dosimetry are evaluated. To estimate the accuracy of the results a protocol ready to be used for day-to-day incorporation dosimetry of Lu-177-PSMA-617 and -DOTATOC including planar imaging and SPECT/CT (2,5D) that meets the above mentioned requirements is proposed. **Methods:** Measurements using an Esser-phantom filled with 50MBq Lu-177-PSMA-617-solution are performed to investigate the influence of scatter-, attenuation- and background corrections on time-activity-curves. On this basis, a dosimetry protocol requiring four planar whole body (WB) scintigrams and one SPECT/CT as input is proposed. Scatter correction is implemented as a three-window-technique and CT data is used for attenuation correction (AC). Three male patients (age: 57–76y, 65y mean, weight: 78kg mean, DD: 2x mCRPC or 1x NET)

underwent four planar WB scintigrams (2h, 24h, 48h and 72h or 166h post administration of 4GBq $\pm$ 100MBq of Lu-177-PSMA-617 or 7GBq of Lu-177-DOTATOC, respectively) and three SPECT/CTs each (24h, 48h and 72h or 166h post administration) on a GE-Millennium-VG8/8-Hawkeye gamma camera system. Critical organs (liver, kidneys, spleen, salivary glands) were delineated based on the WB conjugate views. Time-activity-curves (TAC) were calculated using QDose(v1.1.3) and Hermes-Hybrid-Dosimetry(v2.7) in hybrid mode. The cumulated activities ($\bar{A}$), derived from integrated biexponential time-activity-curve fits, were compared to results of an Excel-implementation of the proposed protocol. **Results:** The $\bar{A}$ -values as derived from the phantom measurements differ approximately 8% from activimeter $\bar{A}$ -values. Without AC, $\bar{A}$ is underestimated by more than (-)50%. Scatter- and background correction influence $\bar{A}$ in the range of about +15%. QDose and Hermes-Hybrid-Dosimetry employ neither scatter- nor suitable AC techniques and, hence, provide results for patient data $\bar{A}$ -values that are approximately 26% lower than those determined manually employing the reference protocol. Furthermore, $\bar{A}$ -values calculated with Hermes-Hybrid-Dosimetry are around 3 times higher than the QDose results. **Conclusion:** Dose results with uncertainties of 10% or less can be provided by a dosimetry protocol comprising attenuation-, scatter- and background corrections while keeping the measurement efforts on a level that is acceptable for routine operations. However, data processing with Excel or the like remains impractical. The evaluated software solutions offer an efficient workflow but still are lacking suitable attenuation correction options and, thus, sufficiently accurate dosimetry results for Lu-177 radionuclide therapy.

EP-0170

Red marrow dosimetry without whole-body measurements for patients treated with Lutathera®

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Introduction: 3D dosimetry is state of the art, however, since whole body (WB) SPECT/CT is usually not feasible, SPECT/CT acquisitions usually cover the thoraco-abdominal region only. Red marrow (RM) absorbed doses can be estimated by summing contributions of self- and cross-irradiation. Quantitative imaging of RM is feasible, however the determination of remainder of the body (RB) activity on SPECT-only acquisitions is challenging. The aim of this study is to estimate RM absorbed dose when WB measurements are not available. **Methods:** Two patients (1M, 1F) injected with approximately 7.4GBq of Lutathera® for

two cycles of treatment (ctx) were considered. SPECT/CTs at 4h, 24h, 72h and 168h were performed with the GE-Discovery NM/CT 670. Volumes of interest (VOIs) delineated were liver, spleen, kidneys, L₂-L₄ vertebrae and whole field of view (FOV). VOI segmentation was performed on the first CT image. VOI-specific rigid registration based on CT images was performed, taking the first time-point as a reference. Fitting functions were used to derive cumulated activities ($\bar{A}$). $\bar{D}(\text{RM} \leftarrow \text{RM})$ was estimated by assuming that the activity within L₂-L₄ vertebrae is proportional to total RM activity, [Shen, 2002]. $\bar{D}(\text{RM} \leftarrow \text{Liver})$, $\bar{D}(\text{RM} \leftarrow \text{Kidneys})$ and $\bar{D}(\text{RM} \leftarrow \text{Spleen})$ were estimated using S-values from OLINDA/EXM2.0. We tried to estimate the ratio FOV:WB volumes on both patients, and used the ICRP 110 models (male and female) for validation. The WB volume of patients was calculated from their mass, assuming a density of 1.01 g/cm³, whereas the FOV volume was extracted from the images. For the models, the WB volume was known, and we extracted the FOV volume by dividing each model between: upper-part (with arms), FOV and lower-part. The ratio between the volume within the FOV and the WB volume (FOV:WB) was then calculated. $\bar{A}_{\text{RB,FOV}}$ was then derived by subtracting $\bar{A}_{\text{Sources}}$ (total $\bar{A}$ from the VOIs) from $\bar{A}_{\text{FOV}}$. FOV:WB was used to estimate $\bar{A}_{\text{RB}}$, thereby allowing the calculation of $\bar{D}(\text{RM} \leftarrow \text{RB})$. **Results and Discussion:** FOV:WB was equivalent for models and patients. D_{RM} and relative contributions from RM, sources and RB respectively were: •1F-ctx: 481 mGy, 33.6%, 9.7%, 56.7%, •1F-ctx: 522 mGy, 36.1%, 5.0%, 58.9%, •1M-ctx: 325 mGy, 44.5%, 1.6%, 53.9%, •1M-ctx: 413 mGy, 48.7%, 1.5%, 49.8%. The majority of D_{RM} comes from $\bar{D}(\text{RM} \leftarrow \text{RB})$. [Forrer, 2009] reported similar results for the same radiopharmaceutical. **Conclusions:** The proposed scaling procedure can be implemented in clinical practice when WB measurements are not available. Shen *et al.* J Nucl Med, 43:1245-1253, 2002. Forrer *et al.* Eur J Nucl Med Mol Imaging, 36:1138-1146, 2009.

EP-0171

Determination of Radiation Dose in ¹⁷⁷Lu-DOTATATE Treatment with ^{99m}Tc-HYNICTATE Scintigraphy

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Purpose: ¹⁷⁷Lu-DOTATATE treatment has been applied in the treatment of neuroendocrine tumors since 2000 years. ^{99m}Tc-HYNICTATE scintigraphy is used for the diagnosis of neuroendocrine tumors. The aim of this study was to determine the radiation dose exposure of patients before treatment by investigating the relationship between radiation doses that patients will be exposed to by dosimetry with Tc-^{99m}Hynictate scintigraphy in patients who will receive ¹⁷⁷Lu-DOTATATE treatment. **Method:** The study included 11 patients with neuroendocrine cancer. The injected ^{99m}Tc-HYNICTATE activity a mean of 325.9±119.9 MBq before treatment. Whole-body images were obtained at 0.5, 1, 4, 24 h and SPECT/CT imaging at

1 hours post-injection. The injected ¹⁷⁷Lu-DOTATATE a mean of 4.94±1.4 GBq. Whole-body images were obtained at 4, 24, 48, 72 h and SPECT/CT imaging at 1 hours post-injection. The OLINDA/EXM dosimetry program was used for absorbed dose calculations. **Result:** The calculated radiation-absorbed doses for each organ showed substantial variation. Calculated radiation-absorbed doses with ^{99m}Tc-HYNICTATE were 0.03±0.04, 0.06±0.04, 0.014±0.01, 0.002±0.0006, 0.003±0.0007 mGy/MBq from kidneys, liver, spleen, red marrow and whole body. Calculated radiation-absorbed doses with ¹⁷⁷Lu-DOTATATE were 0.7±1.06, 0.21±0.21, 0.34±0.21, 0.04±0.01, 0.07±0.02 mGy/MBq from kidneys, liver, spleen, red marrow and whole body. There was a strong correlation (r = 0.981) when the exposed radiation dose exposures were compared. **Conclusion:** ^{99m}Tc-HYNICTATE showed that the maximum dose amounts of patients were determined before ¹⁷⁷Lu-DOTATATE treatment and the possible radiation toxicity could be avoided.

EP-0172

Comparison between a convolution based and a Monte Carlo based dosimetry tools for MRT

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Purpose: This work focuses on the comparison in a patient study between a voxel dosimetry tool based on S-value convolution (VoxelMed2.0, Reggio Emilia, Italy) and a voxel dosimetry tool based on Monte Carlo simulation (RAYDOSE, Cardiff University, UK). The main aim is to assess the discrepancy in absorbed dose calculation between these two modalities. **Subject and Methods:** A sample of 20 patients enrolled in a PRRT clinical trial was considered. Each patient was scanned 5 times with a SPECT/CT camera (at 1h, 4h, 24h, 40h, 70h p.i.), after a therapeutic administration of ¹⁷⁷Lu-DOTATOC. The sequential scans were registered to the reference CT using the deformable multi-pass registration algorithm of Velocity (version 3.2.0, Varian Medical Systems, Palo Alto, USA). The deformed image set was the starting point for both dosimetry tools. Both software calculated independently the TIAC (Time-Integrated Activity Curve) using a trapezoidal method until the last acquisition time and the integral of an exponential fit curve of organ activities from this time-point onwards. The percentage difference (PD) between VoxelMed2.0 and RAYDOSE was evaluated for mean absorbed dose to left kidney, right kidney, liver and spleen. Dose map and Dose Volume Histogram (DVH) were qualitatively compared. Lin's concordance coefficient was used to assess correlation between absorbed doses. **Results:** Mean PD for absorbed dose with VoxelMed and RAYDOSE were: -10.8% for left kidney, -8.6 for right kidney, -7.9 for liver, -11.2 for spleen. Dose maps obtained by the two voxel-dosimetry software showed visually similar dose distributions and DVH curves were almost overlapping. Only in a few cases (7 out of 40) PDs were larger than 20%,

but in these cases discrepancy was mainly due to the TIAC. Lin's coefficient was 0.96 considering all PDs, whereas 0.84 for left kidney, 0.92 for right kidney, 0.99 for liver and 0.90 for spleen. The Lin's coefficient showed a very good agreement between the modalities. **Conclusions:** A general slight underestimation of VoxelMed doses was observed, as compared to RAYDOSE. The concordance between VoxelMed and RAYDOSE was very good, considering both mean absorbed doses and DVHs. To use the same images set as starting point was necessary to study the pure differences between the two modalities in true clinical cases. This work was supported by the EMPIR-MRTDosimetry project.

EP-0173

Phase 0 Trial Of [^{18}F] FPEB, A PET Imaging Tracer For Quantifying Cerebral Distribution Of Metabotropic Glutamate 5 Receptors: To Study Radiochemical Safety, Biodistribution And Radiation Dosimetry In The Asian Population

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Introduction: G protein coupled metabotropic glutamate receptors type 5 (mGluRs) have been implicated in a number of neurological and psychiatric disorders. [^{18}F] FPEB is a PET radiopharmaceutical which, in preclinical studies, has shown to have high specificity and selectivity towards mGluR5. The safety and effectiveness of [^{18}F] FPEB has been previously demonstrated in small cohorts of early clinical studies performed in humans. The regional uptake pattern of [^{18}F] FPEB has been found to be consistent with known distribution of mGluR5 in the brain. The objective of this study was to evaluate radiation dosage, bio-distribution and human safety of a single injected dose of [^{18}F] FPEB in healthy subjects of the Asian population. **Subject and Methods:** Whole body dosimetry was performed in healthy Asian male adults (21–55 years old). The subjects were injected with a single intravenous dose of [^{18}F] FPEB. Sequential 4 whole-body PET/CT scans were performed at 0, 10, 30 and 60 min post injection. All scans were corrected with CT data and iteratively reconstructed. Regions of interest were drawn on PET images of the organs of interest. The radioactivity and volumes of interest were summed and residence time was calculated as area under the time-activity curve. Absorbed dose estimates for all target organs were determined using MIRD schema with OLINDA/EXM software. All adverse events were recorded until the follow-up safety visit performed one week later. **Results:** 5 healthy male subjects were injected with 168 ± 16.9 MBq of [^{18}F] FPEB. In the whole-body scan, [^{18}F] FPEB was rapidly excreted from all the organs via the biliary system and the kidneys. The whole-body mean effective dose from [^{18}F] FPEB was 0.019 mSv/MBq. The gallbladder received the largest mean absorbed dose (0.16 mGy/MBq). The results are comparable to the effective dose of [^{18}F] FDG, which is 0.019 mSv/MBq. Using [^{18}F] FDG, the urinary bladder has the highest ratio for absorbed dose per unit activity administered as 0.13 mGy/MBq. The single administration of [^{18}F] FPEB caused neither adverse events nor abnormal clinical find-

ings by physical examinations or blood tests. **Conclusion:** These data suggested that [^{18}F] FPEB is well tolerated and the radiation dose is comparable to that of [^{18}F] FDG. The findings support the use of [^{18}F] FPEB as a safe radiopharmaceutical for imaging glutamate receptors.

EP-0174

Direct Monte Carlo simulations for accurate diagnostic and therapeutic dosimetry calculations

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Aim: Following the newly transposed European Council directive 2013/59/Euratom, there is an increased interest in dosimetry-based treatment planning for patients undergoing molecular radiotherapy. Direct Monte Carlo (MC) dosimetry is perceived as resource-intensive and is not yet available on commercial systems. This study aim to assess the feasibility of using a simpler and faster convolution method for dosimetry in diagnostic and therapeutic applications. **Materials and Methods:** A patient-specific uptake distribution was obtained from an ^{18}F -NaF PET/CT scan retrieved from the Cancer Imaging Archive [1–3]. MC calculations were performed with the general purpose EGSnrc/EGS++ code [4] using the decay data from the RADTABS/MIRD software [5] for ^{18}F , ^{90}Y and ^{177}Lu . Convolution absorbed dose-kernels were generated for a uniform soft-tissue medium. Direct MC simulations were carried out using the PET uptake distribution and the CT segmented into cortical and trabecular bones, skin, soft-tissue, fat, lung and air according to the Hounsfield units. Convolution absorbed dose were also corrected by differences in tissue density. The relative difference between the convolution/corrected convolution and MC (gold standard) voxel absorbed doses was calculated, and the median value for each medium was obtained. **Results:** The convolution method underestimated the absorbed dose to all tissues but cortical bone for ^{18}F and ^{177}Lu . The trabecular bone absorbed dose was also underestimated for ^{90}Y . Correcting the convolution results by tissue density reduced the differences between convolution and MC absorbed doses for ^{18}F , ^{90}Y and ^{177}Lu by a median of 48%, 30% and 54% for trabecular bone; and 89%, 79% and 94% for cortical bone; respectively. However, these differences between convolution and MC increased for lung tissue; in particular for ^{90}Y , with a median overestimation of 145% as compared with 64% for uncorrected convolution absorbed doses. **Conclusion:** Discrepancies were observed between absorbed doses calculated with the convolution method and direct Monte Carlo despite correction by differences in tissue density. This highlights the need for Monte Carlo based dosimetry as routinely performed in other radiation treatment modalities. On-going work comprises the use of alternative uptake distributions and the assessment of the associated uncertainties. [1] Kurdziel KA *et al.* (2015). <http://doi.org/10.7937/K9/TCIA.2015.ISOQTHKO> [2]

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EP-0175

⁹⁰Y SIRT Dosimetry - a retrospective study

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Background: Accurate dosimetry following ⁹⁰Y SIRT therapy has long been problematic, and therefore is not routinely performed in most centres. However there is strong reasoning for establishing the absorbed doses delivered to tumours, as opposed to merely qualitatively reporting a treatment. **Methods:** PET/CT images following 50 ⁹⁰YSIRT therapy procedures - 22 TheraSphere and 28 SIR-Spheres - were analysed. Up to three of the largest tumour masses were outlined on the CT data, using a prior diagnostic CT for guidance, and the VOIs translated to the fused data. The activity within each tumour was determined, accounting for decay of ⁹⁰Y between administration and imaging, and the absorbed tumour doses calculated. **Results:** A large variation was found in the activity and absorbed dose given to tumours for both TheraSphere and SIR-Spheres techniques - doses from 2.7Gy to 322Gy and 26.0Gy to 234.5Gy respectively. This will be affected by tumour size - 3.2ml to 1392ml - alongside tumour uptake, effectiveness of the treatment delivery, and total activity administered. No distinct relationship was found between absorbed dose and the size of the tumour alone. 3 lesions were identified for four patients, with the 3rd being the smallest and receiving the lowest absorbed dose in all cases. The mean absorbed dose for TheraSphere treatments was 161±145Gy and SIR-Spheres 128 ±122Gy, with the error based upon the standard deviation of the mean activity concentration within the VOIs. The 4 highest absorbed tumour doses resulted from TheraSphere treatments. There were 9 cases where the distribution of ⁹⁰Y was moderately homogeneous throughout the liver lobe, and therefore absorbed doses to the tumours were determined to be low. **Discussion:** The lower average and maximum dose delivered by SIR-Spheres treatments was not unexpected based on the lower administered activities. The wide range of absorbed doses to tumours is likely related to tumour vascularity, tumour size and the poor imaging characteristics of Y-90, given the low positron fraction. This does however indicate the challenge of accurately performing post-therapy dosimetry. **Conclusion:** There is high variability of estimated absorbed doses to tumours on post treatment PET/CT. Taking into account the limitations of this imaging method and the accuracy of the results, clinically useful information may still be obtained. These quantitative findings could be utilised to identify patients with low absorbed doses in tumours which may benefit from additional SIRT administration.

EP-0176

Selective Internal Radiation Therapy (SIRT) for Liver Metastasis of Chemoresistant Breast Cancer: Overall

Survival and Dose - Response Relationship

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Purpose / Introduction: Despite combined chemotherapy, mortality rate is high in breast cancer with liver metastasis (BCLM). We retrospectively evaluated the effect of selective internal radiation therapy (SIRT) on survival and dose-response relationship in 13 women (mean age 60.2±9.7 years) treated with Y-90 microspheres for chemoresistant BCLM in our clinic between 2010 and 2017. **Subjects & Methods:** Before SIRT, absorption dose for the tumor tissue was calculated with the MIRD method on Tc99m MAA SPECT/CT images. Therapy response of targeted liver lobe was evaluated with comparison of initial and posttherapy control F18 FDG PET/CT images according to the modified PERCIST criteria. Overall survival was analyzed by the Kaplan-Meier method and dose - response relationship was evaluated using the Spearman correlation coefficient. **Results:** As five patients had bilobar liver metastases, a total of 18 SIRT procedures were performed. The median survival was 13 months (1-50 months). Tc99m MAA SPECT/CT images were available in 7 patients. The average radiation dose given to the tumor tissue was 139.9±34.2 Gy. There was no significant correlation between the absorbed radiation dose and tumor response. **Discussion / Conclusion:** Despite limited data, failed chemotherapy is associated with a poor prognosis in BCLM patients. SIRT with Y-90 microspheres may improve survival in this patient group. The lack of a significant correlation between the absorbed radiation dose and tumor response suggests the need for an increased tumor dose.

EP-0177

A PSF conversion method for comparison of ⁹⁰Y lesion absorbed doses from pre- and post- SIRT imaging

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Introduction: ^{99m}Tc-MAA SPECT is used for treatment planning of ⁹⁰Y-microsphere therapy. The quantitative prediction of ^{99m}Tc SPECT has been assessed by direct comparison with ⁹⁰Y bremsstrahlung SPECT. The aim of this study was to demonstrate that differences in partial volume effects associated with ^{99m}Tc and ⁹⁰Y preclude direct comparison of ⁹⁰Y lesion absorbed doses. As partial volume correction is challenging a resolution conversion method was developed to allow comparison of ⁹⁰Y lesion absorbed doses. **Method:** Functions were fitted to ^{99m}Tc and ⁹⁰Y SPECT point spread functions (PSF) and a PSF to convert the resolution of ^{99m}Tc SPECT to ⁹⁰Y SPECT calculated. SPECT-CT acquisitions of the NEMA IEC phantom were performed for ^{99m}Tc and

^{90}Y for four sphere-to-background ratios and converted to ^{90}Y absorbed dose maps. Volumes of interest were outlined on the CT scan and mean absorbed doses compared. Spheres less than 2.6cm^3 were excluded as mean absorbed doses were less than 2 standard deviations above background. $^{99\text{m}}\text{Tc}$ SPECT scans were convolved with the resolution conversion function and absorbed doses compared to those derived from the ^{90}Y SPECT. The method was applied to data from five patients undergoing SIRT. Lesions smaller than 2.6cm^3 and those demonstrating a location mismatch between SPECT scans were excluded from the analysis. Eleven lesions were analysed. **Results:** The best fit Phantom background absorbed dose differences derived from $^{99\text{m}}\text{Tc}$ and ^{90}Y were within 4%, $r^2=1$ ($p<0.0001$). Sphere absorbed dose differences were -4 – 16 %, $r^2=0.06$ ($p=0.4283$). Comparison after $^{99\text{m}}\text{Tc}$ resolution conversion found differences of -4 – 43 %, $r^2=0.93$ ($p<0.0001$). Analysis of clinical data found normal liver absorbed dose differences of 1 – 8 %, $r^2=0.98$ ($p=0.0012$) and lesion differences of -63 – 77 % (-27 – 40Gy), $r^2=0.69$ ($p=0.0015$). Application of the resolution conversion then gave lesion absorbed dose differences of -33 – 53 % (-11 – 23Gy), $r^2=0.77$ ($p=0.0004$). **Conclusion:** Phantom scans demonstrated that direct comparison of identical distributions resulted in large absorbed dose differences for spheres but small differences for background. A method was developed and verified to convert $^{99\text{m}}\text{Tc}$ to ^{90}Y SPECT for improved lesion comparison. It can be concluded from clinical data that $^{99\text{m}}\text{Tc}$ SPECT predicts ^{90}Y SPECT normal liver absorbed dose, and predicted lesion absorbed doses in 82% of cases.

EP-0178

Investigating the feasibility of dynamic and SPECT dual isotope imaging in Selective Internal Radiation Therapy

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Introduction: In-111 and Ga-67 isotopes have been shown to offer superior imaging performance compared to Y-90 bremsstrahlung imaging. In this work we investigate the feasibility of dual In-111/Ga-67 imaging for SIRT. This could allow the distribution of microspheres infused via different arterial networks to be separated and potentially aid in the optimisation of treatment delivery. **Method:** A 3D printed phantom comprising two concentric spheres with independently fillable hemispheres was designed to represent a lesion where arterial feeding happens through different arterial networks. The phantom was infused with 80 MBq of 111In, and 388MBq of Ga-67 at a rate of approximately 0.3 ml per second. Ga-67 infusion was started 40 seconds after the 111In infusion. Dynamic images of the phantom were acquired with a 256x256 matrix, 3.2 detector zoom, and 15 second frame duration. Three separate image datasets were acquired. Energy windows of 15% were centred at 245 keV (In-111), and 300 keV (Ga-67). A 20% energy window was centred at 176 keV for dual 111-In and 67-Ga. Time activity curves (TAC's) of the In-111 and Ga-67 energy windows were generated and compared to the 176 keV energy window acquisition data. Cross talk between energy windows was measured using the triple energy window scatter correction method on the spectra data. On completion of the infusion, a dual isotope SPECT/CT acquisition

was acquired with 72 projections, 20 seconds per projection. Reconstructions were performed using OSEM, 4 iterations 8 subsets. Image fusion was applied to the SPECT energy window datasets to allow each isotope to be viewed with different colour maps over the CT data and cross talk between phantom compartments measured. **Results:** Due to the different decay schemes of the two isotopes approximately 4 times more Ga-67 activity is required to match the image statistics of In-111. Down scatter from the higher energy Gallium photopeak contributed to approximately 12% of counts within the In-111 photopeak. Despite the additional scatter, separation of the two isotopes was possible and dynamic imaging of the infusion was successfully achieved. TAC's agreed with the delivered infusion rates of each pharmaceutical and the summed windows matched that of the dual isotope window. Multi-fusion SPECT/CT allowed simultaneous co-registration of both In-111 and Ga-67 activity distributions on the CT dataset. **Conclusion:** In-111 and Ga-67 can be successfully imaged during dual isotope administrations using both dynamic and SPECT/CT imaging protocols. Each isotope can be adequately separated and quantitative analysis performed.

EP-0179

Comparison of a simplified quantitative yttrium-90 bremsstrahlung SPECT reconstruction with yttrium-90 PET in terms of quantification for dosimetry of SIR-therapy in the liver

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Purpose: The difficulties of yttrium-90 SPECT reconstruction arise due to the continuous bremsstrahlung spectrum and the lack of a discrete photo peak. In contrast to that, yttrium-90 PET suffers from the low probability of internal pair production resulting in increased image noise. With regard to quantification for dosimetry and image quality for the detection of extra-hepatic activity, post-therapeutic yttrium-90 SPECT and yttrium-90 PET images were investigated with a phantom study and the results were applied to patient data. **Methods:** For the analysis of image quality and activity recovery, a phantom with three inserts was filled with yttrium-90 at a fore- to background ratio of 10:1 and scanned at a Siemens Symbia T2 SPECT-CT and a Siemens Biograph mCT Flow Pet-CT. The bremsstrahlung SPECT was reconstructed with an in-house rotation-based penalized one-step-late OSEM with implemented background compensation. Different parameter settings regarding iterations, subsets, matrix size and TOF were analyzed for PET reconstruction with a TrueX algorithm for clinical scan conditions. Both imaging modalities were compared by the use of recovery coefficients (RC) and signal-to-noise ratio (SNR). Additional dose images were acquired for 5 SIRT patients via convolution of the SPECT and PET activity images with a Monte-Carlo simulated dose kernel for yttrium-90 and lesion doses were determined. **Results:** The RCs of SPECT were 59% for 249ml, 41% for 52ml, 24% for 16ml and 112% for the phantom background, while the RCs for PET were determined to 98% for 249ml, 38% for 52ml, 32% for 16ml

and 77% for the phantom background. The preferred PET reconstruction for clinical scan conditions contained 3 iterations and 4 subsets in a 128x128 matrix without TOF. SNR of SPECT was between 8 and 30 whereas for PET between 8 and 31. Lesion doses were found from 23–108Gy for SPECT and 44–150Gy for PET with a deviation of on average 35% between both imaging modalities for the 5 exemplary patients. No RC corrections were applied to the images. **Conclusion:** As expected, yttrium-90 PET images show increased image noise due to the low signal. Among the analyzed reconstruction parameter settings, a reconstruction with a small number of image updates in a matrix with large voxel sizes without TOF provided the most robust result for clinical questions regarding quantification and detection of extra-hepatic activity. Our study indicates potential advantages of PET against SPECT in terms of higher activity recovery and therefore better quantification for dosimetry.

EP-12

e-Poster Area

Cardiovascular: Cardiovascular I

EP-0180

Regadenoson vs Adenosine : Evaluation of reported symptoms-adverse effects of the pharmacologic stress agents

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Purpose: To compare the frequency and duration of reported symptoms- adverse effects of regadenoson and adenosine in patients undergoing myocardial perfusion imaging (MPI). **Subjects and Methods:** 803 patients were referred to the Nuclear Medicine Department for pharmacologic stress test preceding MPI(-March 2017- February 2018). 607 underwent regadenoson stress procedure (regadenoson group-RG) and 196 adenosine stress procedure (adenosine group-AG). 110/607 in RG were patients with known COPD. RG: mean age 71,8 years, 307 men (134: known CAD, 173: suspected CAD), 300 women (61: known CAD, 239 suspected CAD). AG: mean age 70,5 years, 81 men (31: known CAD, 50: suspected CAD), 115 women (22: known CAD, 93 suspected CAD). **Results:** 47,6% of patients (36,8% of men and 51% of women) in RG experienced at least one adverse effect-symptom, versus 53,6% of patients (39,5% of men and 59,1% of women) in AG. The main reported symptom in both groups was dizziness (23,9% of the patients in RG vs 23,5% in AG), followed by discomfort (8,4% in RG vs 11,7% in AG) and chest pain (4,1% in RG vs 10,2% in AG). The frequency of other symptoms reported in RG vs AG respectively was: flushing (3,9% vs 7,1%), nausea (3,9% vs 2%), dyspnea (3,8% vs 4%), headache (3% vs 3%), weakness/fatigue (3,9% vs 4,5%), palpitations (1% vs 1,5%), stomach ache (1% vs 1%), vomiting (1% vs 0%), paresthesia (0,5% vs 1,5%). The average duration of symptoms was 2,98 min (0,16–20 min) in RG vs 3,4 min (1–18 min) in AG, whereas the median duration was 2 min

for RG vs 3 min for AG. All symptoms reversed in time with no need of remedy rescue. **Conclusion:** Regadenoson is a safe and easily usable stress agent in daily clinical practice. The frequency of the reported symptoms-adverse effects, with the exception of nausea and vomiting, was overall lower in RG vs AG.

EP-0181

Safety And Tolerability Of Regadenoson Pharmacological Stress For Pre-operative Evaluation Of Patients Scheduled To Undergo Medium To High-risk Non-cardiac Surgery: A Randomized Controlled Study With Dipyridamole / Preliminary Results

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Introduction: Regadenoson is a pharmacologic stress agent used in myocardial perfusion imaging. It is a selective A2A adenosine receptor agonist with a short half-life, high affinity for A2A receptors and low to no affinity for the other adenosine receptors (A1, A2B and A3), which are responsible for its adverse reactions. Regadenoson's main advantages are its brief protocol of administration and its ability to be administered in patients with asthma or chronic obstructive pulmonary disease (COPD) of moderate severity. A disadvantage is the higher cost of this pharmaceutical agent in comparison with the cheaper dipyridamole. The purpose of this study is the assessment of regadenoson's safety and tolerability, in comparison with dipyridamole, in a specific patient group. **Patients and Methods:** This an ongoing randomized controlled study of patients scheduled for medium- to high-risk non-cardiac surgery who have at least 1 coronary risk factor and are undergoing pre-operative evaluation with myocardial scintigraphy using pharmacological stress agents. Patients are randomized into two groups, patients receiving Regadenoson (study group) and patients stressed with Dipyridamole (control group). **Results:** 73 patients have been recruited thus far. 35 patients (aged 70.5±10.2 years, 20 males) have been randomized to pharmacologic stress with Regadenoson, and 38 patients (aged 69.5±10.1 years, 26 males) to Dipyridamole (*p* for age >0.05). Patients with known coronary artery disease were 11 (31.4%) in the Regadenoson group and 14 (36.8%) in the Dipyridamole group (*p*>0.05). Gastrointestinal discomfort (25.7% vs 5.3%, *p*=0.015) and headache (14.3% vs 23.7%, *p*>0.05) were the 2 most frequent adverse reactions in the first group, while headache (23.7% vs 14.3%, *p*>0.05) and dizziness (18.4% vs 11.4%, *p*>0.05), were the most frequent ones in the second group. Aminophylline was administered to 7 patients in each group (*p*>0.05). After injection of Regadenoson, heart rate increased by 29.4±9.0% and after Dipyridamole infusion by 15.6±8.3% (*p*<0.001). S-T depression in the ECG recording was observed in 6 (17.1%) patients in the first group (0.5–1 mm), and in 2 (5.3%, *p*>0.05) in the second group (0.5–3 mm). No patient (0%) from the Regadenoson group developed atrio-ventricular (AV) conduction abnormalities, while first degree AV block was observed in 4 (10.5%) patients from the Dipyridamole group (*p*=0.048). **Conclusion:** Regadenoson seems to be as safe

and tolerable as Dipyridamole, regarding adverse reactions, but with less AV conduction abnormalities and faster resolution of symptoms due to its shorter half-life.

EP-0182

Concordance between regadenoson stress echocardiography and myocardial perfusion study (99mTc-sestamibi) in the diagnosis of myocardial ischemia

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Introduction: Regadenoson is a intravenous pharmaceutical agent approved for the detection of myocardial ischemia used in conjunction with 99mTc-sestamibi in stress imaging. To date, few studies have appraised the utility of this drug using transthoracic echocardiography with the same purpose. We designed this prospective study to evaluate the diagnostic agreement between these two techniques used simultaneously to detect myocardial ischemia. **Methods:** In 63 patients referred to our clinic for the evaluation of chest pain, myocardial perfusion study was performed with regadenoson as a pharmacologic agent that was injected before 99mTc-sestamibi in stress imaging. Stress and rest sets of images were evaluated for relative uptake of Tc99m-sestamibi in order to detect and characterize perfusion defects. The echocardiogram was performed 60–90 seconds after the administration of the drug using a standardized technique. Two independent observers (one cardiologist and one nuclear physician) interpreted the images, both unaware of the result of the complementary technique. **Results:** Sixty-three patients were included, 32 (51%) of them males. Median age was 72 years (IQR 61–78). Twenty-two (35%) patients had had a diagnosis of ischemic heart disease before the study (either a myocardial infarction or a coronary revascularization). The prevalence of cardiovascular risk factors was very high in this sample, being 23 (37%) current or former smokers, 47 (75%) had arterial hypertension, 23 (37%) had diabetes, 47 (75%) had dyslipidemia. The median pre-test probability of coronary artery disease in those without a true previous diagnosis was 25% (13–52), being 44% in the intermediate risk and 54% in the low risk stratum. A non-significant reduction in systolic blood pressure was detected with the drug: 134.9 (21.4) mmHg Vs 132.1 (24.6) mmHg, $p=0.07$. However, a slight reduction in diastolic blood pressure was noted: 77.4 (11.0) mmHg Vs 74.1 (13.1) mmHg, $p=0.007$, with a striking increase in heart rate: 68.4 (13.9) bpm Vs 92.1 (17.0) bpm, $p<0.001$. More patients had a SPECT test showing myocardial ischemia (27% Vs 17%; $p<0.001$). The kappa index obtained from this sample was 0.55 (CI95% 0.31–0.79). In the group of patients without a history of coronary artery disease ($n=41$), kappa index was even lower: 0.37 (CI95% 0.0–0.74). **Conclusions:** Myocardial perfusion study provides more positive tests than stress echocardiography when regadenoson is used as the stressor agent. The concordance between both test modalities is at best modest.

EP-0183

Regadenoson myocardial perfusion imaging: Correlation between stress evidence and scintigraphic results

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Purpose / Introduction: Regadenoson is a selective A2A adenosine receptor agonist used as a stress agent for myocardial perfusion imaging (MPI). Similarly to other stress agents, regadenoson may cause several side-effects. We investigated the correlation between symptoms and/or ST segment changes during regadenoson administration with myocardial perfusion imaging (MPI) results (positive/negative studies). **Subjects & Methods:** We enrolled 133 consecutive patients (82 males, 51 females, mean age 69.6 y.o) referred to our department for a clinically indicated pharmacological stress MPI. Data on the symptoms and ST segment changes, observed during regadenoson administration, were recorded. As a criterion of positive electrocardiographic findings, we considered >1 mm horizontal or downsloping ST segment depression 80 ms after the J point, or >1 mm of additional ST segment rise in leads without pathologic Q waves. All participants underwent both stress and rest MPI. Two experienced observers evaluated the scintigraphic images; studies with evidence of myocardial ischemia or scar were classified as positive studies (PS). Seven patients were excluded from the study due to non-diagnostic MPI results. The investigation of the association between MPI and categorical variables of interest was performed by chi-squared statistics; One Way Analysis of Variance was used to assess possible differences between MPI and continuous variables. All tests were 2-sided and level of significance was set at 5%. **Results:** Eighty patients had MPI PS. Regadenoson-related symptoms were observed in 72 patients. No symptoms were reported in 54 patients; thirty-six patients had PS. One symptom was observed in 36 patients, while two or more different symptoms were reported in 36 patients; PS were interpreted in 23 and 21 patients, respectively ($p=0.107$). The three most common symptoms were dyspnea (36/126), discomfort (18/126), and dizziness (15/126). Twenty-one patients with dyspnea, 11 patients with discomfort, and 8 patients with dizziness had PS (patients with PS but without the above-mentioned symptoms were 59, 70, 72, respectively). Furthermore, positive ST segment changes were recorded in 9 patients; 6 had positive ST segment changes and PS (patients without ST changes and PS were 74). MPI results were not significantly associated with the presence of either regadenoson-induced symptoms or electrocardiographic changes during pharmacological stress. **Discussion / Conclusion:** Our findings indicate that the presence of symptoms and/or ST segment changes during regadenoson administration does not significantly correlate with the visual interpretation of MPI studies.

EP-0184

Myocardial Perfusion Imaging (MPI) with Regadenoson (Rapiscan®) in patients with first A-V degree block: Our experience

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Purpose: To evaluate the security of Regadenoson (Rapiscan®) during MPI test with pharmacologic stress, in patients who had showed a first degree A-V block in the baseline ECG. **Subjects and Methods:** 34 patients (men:17 and women:17) with first degree A-V block at baseline ECG and previous suspected/confirmed coronary artery disease (CAD) were evaluated between April 2017-April 2018. The average age was 72±8,3 years-old. At the moment of the test, 9 patients were being treated with β-blockers, 14 patients had stopped taking the potentially interfering medication and 7 of them had no treatment. Previously, 3 patients had history of mild/moderate asthma and 1 patient had a chronic obstructive pulmonary disease (COPD) GOLD II. Posology and method of administration: Regadenoson (Rapiscan®) was administered as protocolized in a single injection of 400 micrograms (5 ml), 10-second injection, into a peripheral vein, after the radiopharmaceutical injection. Baseline blood pressures, oxygen saturation (SO₂) at minutes 1, 3 and 6 postinjection, increases in heart rate, appearance of side effects and alterations in the ECG during stress were registered. Subsequently, obtaining and interpretation of images were performed. **Results:** Maximum baseline systolic/diastolic blood pressure registered was 193/98mmHg, respectively. Minimum baseline heart rate was 43bpm and the maximum taquicardization was 133bpm (two minutes postinjection), minimum SO₂ was 94% and maximum was 99%. The side effects registered were fatigue 5/34 (14,7%), 2/34 hypotension 95/63mmHg (5,8%), headache 2/34 (5,8%), 1/34 dyspnea (2,9%) and 1/34 increase intestinal peristalsis (2,9%). 13 patients (38,2%) needed administration of euphiline between minutes 6-8 (80mg) to reverse the side effects and 1 patient at minute 3 for an intense dyspnea. 1 patient showed a 2mm ST-segment depression in precordials V3-V4, without ischemia imaging. 4 patients had inducible mild/moderate ischemia and another patient showed residual damage after heart attack. **Conclusion:** In our experience, the pharmacologic stress with Regadenoson allows the evaluation of coronary ischemia in a safe way, avoiding the complications secondary to adenosine interacting and activating the A1 cell surface receptors, in patients with first degree block at baseline ECG.

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Purpose: This study aimed to validate the accuracy of a major-event risk model that was created in the multicenter J-ACCESS prognostic study using a new independent multi-center cohort of patients with chronic kidney disease (CKD). **Methods:** Based on J-ACCESS multicenter study in Japan three risk models have been created using multivariable logistic analysis and currently utilized for clinical practice. Three-year major cardiac event risk (%) comprising cardiac death, non-fatal acute coronary syndrome, and severe heart failure requiring hospitalization. Model 1 derived from 4031 patients and used 4 variables of age, summed stress score (SSS), left ventricular ejection fraction and diabetes. Models 2 and 3 derived from 2,395 patients and included an additional variable of estimated glomerular filtration rate (eGFR, continuous variable) for Model 2, and five variables with four SSS classes and categorical variable of eGFR for Model 3. The validation data were multicenter prognostic cohort of CKD patients without hemodialysis (n = 526), and three-year follow-up was completed. The Kaplan-Meier survival analysis was performed for three groups of low (< 3%/3 y), intermediate (3 - 9% /3 y), and high (>9%/3 y) risk, and receiver operating characteristic (ROC) analysis to predict major cardiac events was also performed with area under the curve (AUC). **Results:** During the follow-up time of 3 years, 59 (11.2%) major cardiac events occurred. Survival analysis showed that risk stratification was effective using any of the three risk groups, and ROC-AUC was 0.66, 0.67, and 0.66 for Models 1, 2, and 3, respectively (n. s. among groups). Risk stratification was good for patients with eGFR < 15 mL/min/1.73m² (n = 427), showing comparable prediction and actual event rates (prediction/outcome: < 3%/3.1%, 3-9%/9.9%, and > 9%/15.9 % for patients with low, intermediate and high risk groups (p = 0.0087, Model 2). However, actual event rates were equally high across all risk groups for patients with eGFR < 15 mL/min/1.73 m². Frequency of high C-reactive protein was high in groups with high event rate. **Conclusion:** The J-ACCESS major event risk models can stratify patients with CKD and eGFR < 15 mL/min/1.73m². Although the risk model including eGFR works better to predict their event rate in CKD patients, patients with low eGFR (< 15 mL/min/1.73m²) are potentially at high risk patients across all estimated risk values.

EP-13

e-Poster Area

Cardiovascular: Cardiovascular II

EP-0185

J-access Risk Model For Major Cardiac Events: Comparison Between Prediction And Outcome In Patients With Chronic Kidney Disease

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EP-0186

Myocardial perfusion imaging in women with suspected coronary artery disease

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Aim: The specific attributes of coronary artery disease (CAD) in women are drawing particular attention. This work investigates the clinical characteristics and imaging results of women with suspected CAD, referred for myocardial perfusion scintigraphy (MPS). **Method:** The demographic and clinical features of 538 consecutive women with suspected CAD, aged 65±10 years,

were analyzed. Patients were submitted to stress-rest MPS (92% dipyridamole, 2% adenosine, 6% exercise). The clinical probability of CAD was determined according to both the Diamond-Forrester criteria (age, symptoms) and the Morise scoring system (age, symptoms, estrogen status, diabetes, hypertension, dyslipidemia, smoking, obesity) as "low", "intermediate" and "high". Based on a 17-segment model, scans were graded as normal ($SSS < 4$) or abnormal ($SSS \geq 4$), whereas clinically significant ischemia was defined as stress abnormality in ≥ 3 segments. **Results:** Kappa statistics showed: In determining MPS results according to the clinical probability of CAD based on the Diamond-Forrester and Morise criteria: A history of heart failure was found an independent predictor of an abnormal MPS result, but no variable could determine clinical significant ischemia. **Conclusion:** In women with suspected CAD: (1) the Diamond-Forrester criteria overestimate the clinical probability of CAD in comparison to the Morise grading system, which incorporates cardiovascular risk factors together with age and symptoms. (2) Abnormal MPS results and clinically significant ischemia were noted in few cases, regardless the clinical probability of CAD. (3) No variable was related with clinically significant ischemia.

EP-0187

Comparison of two commercial software packages for the calculation of transient ischemic dilation (TID) index in patients who underwent gated SPECT myocardial perfusion imaging

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Purpose/Introduction: The introduction of quantitative parameters, such as the transient ischemic dilation (TID) index, from gated single photon emission computed tomography (SPECT) enhanced the clinical (particularly, the prognostic) value of myocardial perfusion imaging. We aimed to compare the obtained values of TID using two commercial software packages (Emory Cardiac Toolbox, Myovation). **Subjects & Methods:** The study sample consisted of 954 patients (502 males) mean age 63.5 years ($SD=10.9$ years), who were referred to our departments for the assessment of known or suspected coronary artery disease, as clinically indicated. The participants underwent either treadmill test (Bruce protocol) or pharmacological stress (adenosine or regadenoson, with low-level exercise according to the European Association of Nuclear Medicine Procedural Guidelines), combined with ^{99m}Tc-tetrofosmin gated SPECT (stress/rest, one-day protocol). The concordance of the two software packages was evaluated with the computation of intra-class correlation coefficients (ICCs). Paired t-tests were also used to investigate differences in mean values among the two packages. Patients were divided into subgroups according to heart size (rest end-systolic volume, ESV cut-off value: 25 mL) and perfusion imaging (summed stress score, $SSS \geq 3$). Repeated measurements analysis of variance (ANOVA) was ad-

opted to evaluate the differences observed in the two software packages among the subgroups defined based on ESV and SSS.

Results: The ICC for TID values was 0.71 in total sample indicating a good correlation ($p < 0.001$) between the two packages. Similar results were obtained for patients with rest $ESV \leq 25$ mL and for those with rest $ESV > 25$ mL. Moreover, the ICC was 0.64 ($p < 0.001$) for patients with $SSS < 3$ and 0.77 ($p < 0.001$) for patients with $SSS \geq 3$. Mean TID values obtained using Myovation were significantly lower compared to those obtained using Emory Cardiac Toolbox (0.97 ± 0.11 vs. 1.00 ± 0.12 , $p < 0.001$). The difference in TID mean values between the two packages was similar and still significant in patients with $ESV \leq 25$ mL and in those with $ESV > 25$ mL ($p = 0.270$). In addition, the aforementioned difference was similar in patients with $SSS < 3$ and in those with $SSS \geq 3$ ($p = 0.292$). **Discussion/Conclusion:** According to our results, Myovation provided lower TID mean values compared to Emory Cardiac Toolbox. Despite the observed good correlation, the difference in mean TID values calculated from the two packages was statistically significant.

EP-0188

Impact Of Filtering On Single Photon Emission Tomography Reconstruction For Quantitative & Qualitative Improvement Of Intermediate Coronary Artery Disease - Comparison With Angiography And Computerised Tomography Angio

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Purpose/Introduction: Filtering has great impact on the processing and quantitative/qualitative assessment of SPECT images, with more effect on intermediate clinical cases. Much discrepancy in selection of proper filter and its parameters for individual cases are exist. The authors investigated the impact of most common available filters on NM images of patients with CAD, and compared the results with the CT- Angio and invasive angiography for accuracy evaluation. **Subjects/Methods:** The investigation initiated by performing the various SPECT / CT scan of Jaszcak & NEMA chest phantoms having hot and cold inserts (9.5-37 mm). Data acquired on **GE 670 PRO SPECT/CT; 360°, 64 frames, 60s, 128, LEGP** with CT attenuation (120 kV & 170 mA). The images reconstructed with FBP and ITERATIVE OSEM utilizing filters; Hann, Butterworth, Metz, Hamming and Wiener. The Image contrast measured to assess absolute nearness of the inserts. Scans of 20 patients with CAD, 17 males and 3 females, age 41-77 year old who had been reported earlier reprocessed with the nominated filter and were reported by 2 NM consultants. The results compared to the earlier reports and to the CT-Angio and Angiography. **Results:** The optimization suggested 3 filters; Wiener (Wi), Metz and Butterworth (But) provide highest contrast (99% to 3%) and (81% to 32%) for the cold and hot inserts respectively, with the (Wi) filter to be the best option. The reprocessed patients scan with the (Wi) presented an elevated improvement in diagnostic accuracy, correlated well with the CT-Angio and Angiography results ($p = 9.36E-7$ & $r = 0.910$ for

Wi vs $p=0.047$ & $r=0.501$ for But). Four out of five cases that reported normal, appeared to have moderate to severe Ischemia, and one remained normal when reprocessed with the Wiener filter ($r=1$ for Wi vs $r=0.577$ for But). **Discussion/Conclusion:** It appears the Wiener filters could produce results with highest contrast for both cold and hot spheres (99.5%–36.4%), and for the patient data it is more consistent with angiography results, with much elevated accuracy in intermediate cases ($r=0.910$ for Wiener and $r=0.501$ for Butterworth vs angiography). However, the optimum parameters obtained for the filters have no relation with the resolution of the imaging system but the details of the objects could be improved.

EP-0189

Correlation between ST changes during stress test and summed stress score in female patients who underwent myocardial perfusion imaging

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Purpose/Introduction: In women, ischemic changes recorded during stress test tend to be of lower clinical value in comparison to men. We aimed to investigate the correlation between ST segment changes during stress test and myocardial perfusion, as evaluated based on summed stress score (SSS), in female patients. **Subjects & Methods:** The study sample consisted of 317 patients with mean age 64.7 years ($SD=10.2$ years), who were referred to our department for the assessment of known or suspected coronary artery disease, as clinically indicated. The participants underwent either treadmill test (Bruce protocol) or pharmacological stress (adenosine or regadenoson, with low-level exercise according to the European Association of Nuclear Medicine Procedural Guidelines), combined with ^{99m}Tc -tetrofosmin gated single photon emission computed tomography - SPECT (stress/rest, one-day protocol). As a criterion of positive (ischemic type) ST segment changes, we considered >1 mm horizontal or downsloping ST segment depression 80 ms after the J point, or >1 mm of additional ST segment rise in leads without pathologic Q waves. Studies with $SSS<3$ were classified as normal, studies with SSS 3–8 were considered as mildly abnormal, and those with $SSS>8$ were considered as moderately - severely abnormal. **Results:** In the study sample, 155 patients underwent a Bruce treadmill test and 162 pharmacological stress. Positive ST segment changes were found in 47.4% of the patients who underwent treadmill test, and 21.1% after pharmacological stress. Among the participants who underwent treadmill test, the proportion of patients who had SSS 3–8 was 24.7% in cases without positive ST segment changes and 16.2% in cases with ischemic type changes. Moreover, the proportion of women who had $SSS>8$ was 6.8% in cases with ST segment changes, whereas no patient without ST change had $SSS>8$. Among the participants who underwent pharmacological stress, the proportion of patients who had SSS 3–8 was 37.8% in cases without positive ST segment changes and 38.2% in cases with ischemic type changes. Further, the proportion of

women who had $SSS>8$ was 6.3% in cases without ST changes and 8.8% in cases with ischemic type changes. **Discussion/Conclusion:** A significant number of female patients with ischemic type ST changes during stress test exhibit a normal myocardial perfusion imaging study. However, in participants with a moderately - severely abnormal study who underwent treadmill test, positive ST changes were recorded more frequently.

EP-0190

Comparison Of Diagnostic Accuracy Of Scoring Systems Using Myocardial Perfusion Imaging With Single Photon Emission Computer Tomography And Invasive Coronary Angiography For Coronary Artery Disease Severity Evaluation

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Aim: To evaluate prognostic value of myocardial perfusion imaging (MPI) with single-photon emission computer tomography (SPECT) of hemodynamically significant coronary artery (CA) stenosis on basis of comparative analysis with angiographically observed Gensini score (GS). **Material and Methods:** Overall 232 patients (mean age 57.21 ± 5.6 y.) with coronary artery disease (CAD) were included in this study. Risk factors (DM, AH, smoking, hyperlipidemia, BMI, smoking) of adverse cardiac events (ACE) were analyzed in patients. All of them underwent to stress/rest MPI/SPECT using two-detector rotating gamma-camera, followed by coronary angiography (CAG). During SPECT 20-segment model of left ventricle was applied. Summed stress score (SSS) was used for estimation of intensity of perfusion defects in stress. Normal MPI was considered if $SSS<4$; slightly abnormal: $SSS=4-7$; moderate and significantly abnormal: $SSS=8-13$ and $SSS>13$, respectively. The degree of ischemia was also assessed on basis of summed difference score (SDS) analysis: $SDS<2$ - no ischemia, $SDS=2-7$ moderate ischemia and $SDS>7$ - significant ischemia. Severity of CAD was evaluated angiographically with Gensini scoring (GS) system. In GS the degree of stenosis in CA are 0 for no stenosis, 1 for 1%–25% stenosis, 2 for 26%–50% stenosis, 16 for 91%–99% stenosis and 32 for 100% stenosis. The score then was multiplied by a factor corresponding to importance of location CA lesion. According to GS patients were divided into 3 groups with score: 1) 0; 2) 1–34, and 3) over 35. **Results:** In 66 (28.4%) patients GS was 0 (group 1). In this group there was significantly lower patients with ACE risk factors in comparison with those with GS 1–34 and more than 35 (33.1% vs 46.7% and 78.1%, respectively, $p<0.05$). In group 1 extension of perfusion defects in stress (SSS) and severity of ischemia (SDS) were lower than in other 2 subgroups. For the group 1 SSS was 3 [0; 5]; and SDS - 1 [0; 3]; 95% CI $p<0.001$. For GS=1–34 (group 2) SSS - 7 [5; 10] and SDS - 4 [2; 6]; 95% CI, $p<0.05$. For GS>35 (group 3) SSS - 15 [7; 21]; SDS - 7 [5; 9]; 95% CI, $p<0.001$. **Conclusions:** SPECT-MPI and CAG have good diagnostic performance for CAD extent and severity, and they provide different and complementary information for diagnosis and evaluation of CAD (ischemia and atherosclerotic plaque detection). A good relationship was achieved scintigraphic score of ischemia (SSS and SDS) and angiographic score (GS) of CAD.

EP-0191**The Hibernating Myocardium In Prediction Of Outcome After Coronary Bypass Surgery In Patients With Postinfarction Left Ventricular Aneurysm: A Gated Myocardial Perfusion Spect Study***M. Vakhromeeva, A. Vakhrameeva; Pirogov National Medical Surgical Center, Moscow, RUSSIAN FEDERATION.*

Background: Myocardial perfusion imaging has emerged as an increasingly emerged valuable tool to identify and risk-stratify patients with CAD (and CAD with postinfarction left ventricle aneurysms - LVA) to develop an acceptable revascularization strategy. **Aim:** To investigate restoration of regional function and blood flow after revascularization in patients with postinfarction LVA. **Methods:** In our study we included 52 patients with postinfarction LVA (47 men, 90,4% and 5 women, 9,6%), mean age $51,1 \pm 11,1$ years. All patients were performed "stress/rest" or "rest" gSPECT with ^{99m}Tc -Technetium using two-detector rotating gamma-camera ("Discovery NM/CT 670", GE) before operation (for assessment viable myocardium) and after surgical treatment (for assessment hibernating myocardium recovery). In all patients before and after revascularization we determined perfusion and regional wall thickening on unified 20-segment polar maps. Perfusion polar plots were compared with functional ones on which the zones of systolic wall thickening were assessed. **Results:** After the operation we identified perfusion improvement of varying severity in all 52 (100%) patients. On average, perfusion defects decreased throughout the group from $28,8 \pm 6,6\%$ to $18,7\% \pm 7,1\%$ ($P < 0,01$). However, in patients with a baseline volume of hypoperfused zones (HZ) of no more than 30-35%, perfusion defects decreased on average by 46,5% (from 21,3 to 70,1%), but in patients with HZ volume of more than 35%, the decrease in defects was on average 14,3% (9,8 - 28,2). The total ejection fraction of LV for the whole group increased by 5,8% (from $43,3 \pm 7,7\%$ to $49,1 \pm 8,3\%$, $P < 0,01$). However, as the segmental analysis showed, contractility significantly improved only in 30,1% of initially dysfunctional segments (91 of 302) - only in segments with accumulation of the tracer in excess of 50% (with initially hibernated myocardium). **Conclusions:** Myocardial perfusion gSPECT yields excellent predictive accuracy for recovery of function after revascularization. The likelihood of recovery of function after revascularization is related to the extent of myocyte injury and the amount of HZ. Improvement in regional contractile function is seen in approximately one third of dysfunctional segments. Improvement of perfusion in patients with postinfarction LVA after the surgical treatment depends on the volume of viable (hibernating) myocardium in postinfarction zone.

EP-0192**Improvement of left ventricular asynchrony after revascularization predicted from phase and mechanical indices in gated-myocardial perfusion SPECT***T. Niimi¹, M. Sugimoto¹, S. Yoshida¹, H. Miyazawa¹, M. Nanasato¹, H. Maeda²; ¹Nagoya Daini Red Cross Hospital, Nagoya, JAPAN, ²Nagoya University School of Health Sciences, Nagoya, JAPAN.*

Purpose: Assessment of contraction synchronicity is considered important for the diagnosis of coronary artery disease (CAD). We evaluated the synchronicity in contraction and assessed the recovery following contraction insufficiency after revascularization. **Methods and Materials:** We assessed 16 patients with CAD (mean age: 66.8 ± 10.7 years, 13 male) by using resting electrocardiographic-gated ^{99m}Tc agents single-photon emission computed tomography (SPECT), which was performed in all the patients before and after revascularization. To differentiate between abnormal contractions of the cardiac wall, the phase analysis with phase bandwidth, standard deviation (SD), and entropy were analyzed using cardio REPO (EXINI Diagnostics, Lund, Sweden/ FUJIFILM RI Pharma, Co. Ltd., Tokyo, Japan), and contraction amplitude, synchronous contraction index (SCI), contraction work and ejection fraction (EF) were evaluated by using quantification of segmental function by solving the Poisson equation (QSFP) analysis. Additionally, 16 normal participants (mean age: 73.3 ± 10.8 years, 7 male) were analyzed using the same methods as comparative indicators. Participants at low risk for CAD, had normal left ventricular (LV) function, and showed normal perfusion on imaging were classified as normal. Statistical analyses were performed with $p < 0.05$ considered as statistically significant. **Results:** Improvement of LV asynchrony after revascularization was confirmed in all indicators of phase analysis and QSFP analysis (SCI: $p < 0.05$, otherwise $p < 0.005$). Average contraction amplitude improved from 24.3% to 28.2% (normal average $35.5\% \pm 4.3\%$), SCI increased from 73% to 81% (normal average $96.2\% \pm 1.6\%$), contraction work increased from $4.8 \text{ mJ}\cdot\text{cm}^{-2}/\text{beat}$ to $5.9 \text{ mJ}\cdot\text{cm}^{-2}/\text{beat}$ (normal average $7.3 \pm 1.2 \text{ mJ}\cdot\text{cm}^{-2}/\text{beat}$), and the EF improved from 44.6% to 50.6% (normal average $77.4\% \pm 6.2\%$). A correlation between the phase SD of the phase analysis and the contraction work of the QSFP analysis was confirmed for the relationship of each indicator calculated as per a normal case ($p < 0.05$). In addition, correlation was confirmed between contraction work and EF ($p < 0.05$). **Conclusion:** SCI and contraction work were numerical indices which analyzed cardiac function mechanically, and the relation with the indices of phase analysis was also clarified. Along with phase analysis, they may prove useful for the prediction of recovery from contraction insufficiency after revascularization.

EP-0193**SPECT guidance for revascularization of Coronary Chronic Total Occlusion (CTO)***W. M. Schaefer, D. Knollmann; Kliniken Mariahilf, Mönchengladbach, GERMANY.*

Purpose/Introduction: In patients with Coronary Chronic Total Occlusion (CTO) therapeutic decisions on revascularization often diversify, sometimes even nihilism occurs. Assuming that a CTO must induce a severe ischemia, an interventional procedure should reduce ischemic burden. Since collaterals can supply the CTO-dependent region, it is often impossible to predict the extent of ischemia when only morphological data are available. Aim of our study was to investigate how heterogeneous the ischemic burden in CTO can be and therefrom discuss, whether a noninvasive stress test should always be done beforehand of

revascularization of CTOs. **Subjects & Methods:** In 13 patients with CTO (9*RCA, 2*RCX, 2*LAD) and predominantly preserved left ventricular function gated perfusion adenosine stress/rest SPECT-studies (MPS) were performed using ^{99m}Tc -MIBI and a cardiac camera (CardioMD, Philips). Using gender specific institutional normal databases for comparison, extent of ischemia in % was calculated for stress and rest and the resulting difference. Considering standard vessel territories reversible ischemic burden was calculated in % for the different territories. Variability of ischemic burden was calculated for the complete data sets as well as for the different territories, here under consideration how much of the reversible ischemia was within the CTO and how much in the adjacent territory. **Results:** Total ischemic burden ranged from 3 to 32% (mean 20.6 ± 8.7) for stress, from 0 to 26% (mean 8.5 ± 8.3) for rest and from 0 to 29% (mean 12.2 ± 8.6) for difference. For the region supplied by the CTO artery reversible ischemic burden within the territory ranged from 0 to 66% (mean 25.9 ± 19.5), in the most affected adjacent territory ischemic burden ranged from 0 to 74% (mean 16.6 ± 21.6). **Discussion/Conclusion:** In patients with CTO MPS show extreme heterogeneous ischemic burden - even no reversible ischemia was found - which should be incorporated in the decision tree whether a revascularization should be performed. The ischemic burden in the adjacent territory was unexpectedly high to us, which can be due to technical reasons - like misallocation - or due to real ischemia in territories from which collaterals supply the CTO region (steal phenomenon).

EP-0194

Tc-99m MIBI gated SPECT: myocardial perfusion and diastolic function findings in patients with typical chest pain and normal coronary arteries

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Aim: The aim of this study was to assess myocardial perfusion and diastolic left ventricular function in patients with typical anginal chest pain, positive exercise test and angiographically normal or near-normal coronary arteries. **Material and Methods:** 39 patients (17 male, 22 female, mean age 61.5 ± 8.1 years) were included in this study. All the patients had typical angina chest pain, positive exercise test, and angiographically normal or near-normal coronary arteries. The patients with established CAD, history of myocardial infarction, heart failure, stage 2 and 3 hypertension, LVH, and other diseases and conditions influencing myocardial perfusion or diastolic function, were excluded from the study. After initial assessment, the patients were divided into two groups: patients without history of hypertension (group 1: 17 pts, LVMMI 128 ± 27 g/m²), and patients with the history of borderline or mild hypertension, well-controlled with standard medical therapy (group 2: 22 pts, LVMMI 132 ± 21 g/m²). All the patients discontinued antinanginal medical treatment before the imaging study. Both rest and stress GSPET were performed in all patients one hour after the intravenous injection of 740 MBq of ^{99m}Tc -MIBI. The 17-segment model of MPI images was used for scoring. Summed stress score (SSS), summed rest score (SRS), summed difference score (SDS), and

total perfusion deficit (TPD) were calculated for myocardial perfusion assessment. Peak filling rate (PFR), mean filling rate during the first third of diastolic time (MFR/3), and time to peak filling (TTPF) were calculated to assess diastolic function. **Results:** Significant differences were found between group 1 and group 2, regarding: SRS (1.8 ± 0.8 vs. 3.6 ± 1.6 ; $p < .05$), SSS (5.7 ± 1.4 vs. 7.6 ± 2.3 ; $p < .05$), stress TPD (8.4 ± 1.3 vs. 10.4 ± 2.5 ; $p < .05$), rest TPD (3.7 ± 0.9 vs. 5.0 ± 1.6 ; $p < .05$), stress PFR (2.0 ± 0.3 vs. 1.7 ± 0.3 ; $p < .05$), stress TTPF (173 ± 32 vs. 215 ± 39 ; $p < .05$), and rest TTPF (156 ± 13 vs. 182 ± 28 ; $p < .05$). Both in group 1 and group 2 significant correlation were revealed between SSS and stress TTPF ($r = 0.54$ and $r = 0.64$, respectively, both $p < .05$) and between SSS and sMFR/3 ($r = -0.68$ and $r = -0.58$, respectively, both $p < .05$). In group 1 significant correlations were found between sTPD and sTTPF ($r = 0.72$; $p < .05$) and SRS and rTTPF ($r = 0.51$; $p < .05$). **Conclusions:** Our results suggested relationship between stress-induced worsening of diastolic function and myocardial perfusion abnormalities in patients with typical angina, positive exercise test and angiographically normal or near-normal coronary arteries. Therefore, gated-SPECT might give, at the same time, incremental information about perfusion and diastolic function, and provide objective findings to assess patients with suspected myocardial ischemia.

EP-0195

Prediction of future adverse cardiac events by stress myocardial perfusion imaging in the patients with procedural failure for chronic total occlusions

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The success rate of chronic total occlusion (CTO) by coronary intervention procedure have been disappointing. However, it's unclear if this prognostic benefit may apply to patients with residual CTO, where related myocardial ischemia might be prevented by a well developed collateral circulation. The aim of this study was to evaluate prognostic value of stress myocardial scintigraphy (MPS) in patients with residual CTO left by procedural failure. Between April 2002 and December 2007, 22 patients with procedural failure in recanalization of CTO were prospectively registered. This study focuses on patients with at least one CTO in main coronary artery left after procedural failure. In all patients, adenosine stress Tc-99m tetrofosmin scintigraphy was prospectively performed 4 to 6 months after procedural failure in the recanalization of CTO. The left ventricle was divided into 17 segments on three short axes and one vertical long axis slices, and each segment was graded according to perfusion using a semiquantitative 4-point system. MPS were evaluated calculating the summed stress score (SSS), summed rest score (SRS), and summed difference score (SDS) indexes (SDS less than 4 was considered minimal ischemia, between 4 and 8 was considered mild ischemia, and greater than 8 was considered severe ischemia). All patients were followed-up for cardiac events. Hard events defined as cardiac death and myocardial infarction, soft events defined as incidence of unstable angina and revascularization procedures. Follow-up lasted more than

120 months. Hard events were observed in 15 pts. None of them had minimal ischemia detected by MPS. Soft events occurred with in 0 (0%), 10 (15%), and 9 (16%) patients with minimal, mildly abnormal, and severely abnormal findings. During follow-up period, patients with minimal ischemia were at low risk of hard cardiac events compared with patients with mildly and severely abnormal findings. A significant difference was observed in hard, soft, and composite event-free survival among patients with minimal, mildly abnormal, and severely abnormal findings. When multiple Cox regression analysis was implied, the factors that remained significant in final model for soft events were SSS, SDS, and angina during stress testing. However, SDS was the only independent predictors for both hard and soft events. MPS provides independent prognostic information for the risk stratification of patients with a residual chronic total occlusion left by procedural failure. The event rate is directly related to the scintigraphic extent of residual ischemic area. Patients with normal perfusion have an excellent event-free survival rate.

EP-0196

Myocardial Perfusion Imaging in Liver Transplantation Candidates - The Prognostic Influence of Different Risk Factors

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Introduction: Patients undergoing liver transplantation (LT) are at higher risk of cardiac events, thus careful preoperative cardiac risk assessment is imperative. However, data regarding the role of non-invasive stress testing in LT candidates are scarce. The aim of this study was to assess prognostic implications of cardiovascular risk factors in LT candidates submitted to myocardial perfusion imaging (MPI). **Methods:** All patients who underwent SPECT technetium-99m tetrofosmin imaging before LT from July 2009 to December 2017 were selected. LT candidates were submitted to 1-day stress/rest protocol, with the stress test being performed under adenosine or regadenoson. Perfusion distribution abnormalities were quantified by a segmental model score and the endpoint, defined as all causes of death or cardiovascular complications after MPI was recorded. Statistical analyses were carried out using SPSS version-23. **Results:** A total of 144 LT candidates were included, 121 men (84%) and 23 women (16%), with a mean age of 63±8 years old. The most frequent cause of end-stage liver disease was alcoholic disease (68.1%). Thirty four patients (23.6%) had an abnormal MPI study with median perfusion abnormality at stress and rest of 11.1±8.6% and 9.6±8%, respectively. Thirteen (9%) of them were high-risk patients (ischemia area >10%). Of the 144 LT candidates, 85 (59.0%) patients underwent LT, four (2.8%) had cardiovascular complications and 42 (29.2%) died. The median follow-up was 43.3±28.3 months. Using Kaplan-Meier analysis, cardiovascular complications had statistical significant relation with necrosis (p=0.017) and left ventricular ejection fraction (LVEF) (p=0.000).

No other relation was found with cardiovascular complications (arterial hypertension p=0.747, diabetes p=0.502, dyslipidemia p=0.516, smoking p=0.491, ischemia p=0.659). The death didn't show any significant relation with any of the studied variables.

Conclusion: In our sample, abnormal MPI was common in LT candidates. Necrosis, as well as LVEF seem to be related with development of cardiovascular complications. No relation was found between the study variables and the occurrence of death.

EP-0197

Exercise-induced Left Bundle Branch Block in Gated Myocardial Perfusion SPECT: Significance and prognostic value

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Introduction: The appearance of exercise-induced left bundle branch block (EI-LBBB) throughout the performance of a stress test is an unusual finding and its significance, uncertain. The aim of the current work was to determine the prevalence of this phenomenon amongst the studied population in our centre, as well as to describe the clinical and scintigraphic features of these patients in order to find out the prognostic value of this event. **Subjects and Methods:** Clinical features of 1886 patients that attended our centre to have a gated-SPECT stress test to diagnose coronary artery disease were reviewed. Eight of them presented EI-LBBB during the exercise and were monitored for an average period of 27±8 months, whilst they were searched for the appearance of any major cardiovascular events. A coronary catheterization was performed on the four patients that showed perfusion defects. **Results:** EI-LBBB prevalence was 0.42%. Six out of eight patients were women. All patients obtained a clinically negative stress test result. Electrocardiographic results could not be evaluated due to the appearance of EI-LBBB. The average heart rate at which EI-LBBB occurred was 97±8bpm. Perfusion and function results were non-altered in 4 patients. Two patients showed moderate-severe ejection fraction depression. The coronary catheterization obtained negative results in all 4 patients presenting perfusion defects. None of the included patients presented any major cardiovascular events during the follow-up period. **Conclusions:** The prevalence of EI-LBBB amongst the patients that had a gated-SPECT stress test at our institution was very low and its presence did not correlate with a greater risk of suffering any major cardiovascular events. Finding an EI-LBBB was significantly more frequent in women. Two patients presented non-ischemic structural myocardial pathology but none of them were diagnosed with coronary artery disease. The gated -SPECT perfusion test obtained a high negative predictive value for coronary artery disease. In our patients EI-LBBB could be more frequently associated with heart failure and low ejection fraction rather than with coronary artery disease.

EP-0198

Incremental Value of a Combination of Coronary Artery Calcium Score and MPI SPECT in Patients with High Risk of Multi Vessel Disease

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Introduction: The severity of perfusion defect on myocardial perfusion imaging (MPI) SPECT can be underestimated in the case of multi vessel disease (MVD). This pathological state is common in diabetes mellitus, chronic kidney disease (CKD) or left ventricular (LV) dysfunction. Aim of our study was to assess the added value of combination MPI SPECT with coronary artery calcium score (CACS) in such patients with higher risk of MVD. **Subjects and Methods:** We analysed results of stress MPI SPECT and CACS retrospectively in 408 consecutive patients - 241 were with DM, 145 with CKD and 111 had LV dysfunction. The severe cardiac events (CE) defined as cardiac death or myocardial infarction (MI) were observed. **Results:** During the mean follow-up period of 21±17 months we recorded 18 cardiac deaths and 10 MI. These CE were significantly less frequent in patients with normal MPI SPECT ($P < 0.0001$). There was significantly higher rate of CE in patients with CACS > 1000 in both subgroups of patients with normal and abnormal MPI SPECT ($P = 0.005$, $P = 0.048$). **Conclusion:** CACS brings additional value to MPI SPECT in risk stratification of patients with higher probability of MVD.

EP-0199

Gender-based Clinical Outcomes In Diabetics With Hba1c Greater Than 7.3% And Normal And Abnormal Gated Myocardial Perfusion Imaging

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Aim: To find out gender based clinical outcomes in diabetics having normal and abnormal stress gated myocardial perfusion imaging (GMPI) and glycosylated hemoglobin (HbA1c) > 7.3%.

Material and Method: This prospective study was conducted at Nuclear Cardiology Department of Karachi Institute of Heart Diseases (KIHD), Karachi, Pakistan. Total 523 diabetics who had stress GMPI with HbA1c > 7.3% from June 2014 till December 2015 were included. This cut-off for HbA1c was taken from our previously published study performed upon early cohort. These patients were followed for 02 years (till December 2017) for fatal, non-fatal myocardial infarction (FMI and NFMI) and overall events. Follow-up was not available in 37 patients, who were excluded and leaving a cohort of 486. **Results:** The mean age of total cohort was 58 ± 10 years having a body mass index (BMI) 26.95 ± 5.48, mean HbA1c of 9.09 ± 1.68 and mean duration of diabetes was 145 ± 88 months. Mean incidence of hypertension, dyslipidemia, family history and smoking was 78%, 43%, 37% and 15% respectively. Stress GMPI was normal in 62% while 16%

had fixed defects and 22% had reversible ischemic defects with mean left ventricular ejection fraction (LVEF%) of 56 ± 16%. Out of 486 total patients, 266 were male and 220 were female without significant difference in age, BMI, HbA1c, duration of diabetes, family history. Male cohort had significantly higher incidence of smoking and dyslipidemia while hypertension was more prevalent in female cohort ($p < 0.05$). Normal GMPI and LVEF were significant higher in females while males had more reversible defects and no difference was found for fixed defect between two groups. Annualized event in total cohort for both normal and abnormal GMPIs was 3.70%, 1.23% and 2.47% for overall, FMI, and NFMI events without significant gender difference. No significant difference in event rate was seen for normal GMPIs in both groups. However, significantly higher overall, FMI and NFMI were seen in female cohort with abnormal GMPI. **Conclusion:** We conclude that female diabetics having HbA1c > 7.3% despite of having significantly lower abnormal GMPI and ischemic burden had significantly higher overall, fatal and non-fatal MI events compared to male counterpart. Higher incidence of hypertension and menopause could be the confounding factors for poor outcome in diabetic women. For normal GMPI similar outcome was seen in both genders.

EP-14

e-Poster Area

Cardiovascular: Cardiovascular III

EP-0200

Comparison of ECG-synchronized myocardial perfusion imaging and cardiac coronary computed tomography angiography in calculations of LV mass and hemodynamic parameters

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Aim: To estimate the accuracy of the values of end-diastolic (EDV), end-systolic (ESV) volumes, ejection fraction (EF) and left ventricular (LV) myocardial mass obtained from gated myocardial perfusion imaging (gSPECT-MPI) on CZT-camera calculating in comparison with cardiac coronary computed tomography angiography (CCTA). **Methods:** A total of 34 patients (mean age of 62±5 years) with suspected or known coronary artery disease (CAD) were examined. All patients underwent CCTA and gSPECT-MPI using GE Discovery NM/CT 570C (GE Healthcare, USA) with cadmium-zinc-telluride (CZT) detectors. For the comparative analysis, the values of rest EDV, ESV, EF and myocardial mass LV according to gSPECT-MPI were used. **Results:** Statistically significant differences in the values of EDV (CCTA: 168(145-210); gSPECT-MPI: 112(94-141); $p < 0.05$), ESV (CCTA: 72(49-83); gSPECT-MPI: 44(32-66); $p < 0.05$) and myocardial mass (CCTA: 123(107-143); gSPECT-MPI: 140(124-168); $p < 0.05$) were found out. The values of LV EF did not differ significantly (CCTA: 64 (54-69), ECG-PSM: 61 (50-66), $p > 0.05$) for the both methods. Statistically significant correlation for EDV, ESV and LV mass ($r = 0.81$, $r = 0.78$, $r = 0.82$, respectively, $p < 0.05$) and mean correla-

tion of LV EF ($r = 0,66$, $p < 0,05$) were found. The Bland-Altman analysis showed statistically significant differences for EDV, ESV and LV mass. Limits of agreement for hemodynamic parameters were as follows: EDV 9 - 105 ml; ESV -9 - 55 ml; LV mass -51,6 - 20,7 g. The agreement between both methods was found only for EF LV (limits of agreement: -16,9% - 18,4%; $p < 0,05$). The linear regression equations for accurate calculation of volumetric parameters and LV mass according gSPECT-MPI data were calculated. **Conclusion:** gSPECT-MPI significantly underestimates the values of EDV and ESV, and overestimates LV myocardial mass values. The values of EDV, ESV, EF and LV myocardium mass, calculated by gSPECT-MPI have a statistically significant correlation with CCTA data. The LV EF according to gSPECT-MPI on CZT-camera shows excellent agreement with CCTA.

EP-0201

Comparison of conventional and cadmium-zinc-telluride SPECT camera in women with suspected coronary artery disease

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Aim: Breast attenuation may impact the diagnostic accuracy of myocardial perfusion imaging (MPI). No data are available comparing conventional and cadmium-zinc-telluride (CZT) SPECT cameras for detection of coronary artery disease (CAD) in women. We directly compared the results of conventional and CZT SPECT camera in women with suspected CAD. **Materials and Methods:** A total of 109 consecutive women with suspected CAD referred to stress MPI were underwent cardiac imaging by both conventional and CZT camera. Visual analysis was performed by two observers using four-point score system in a 17-segments model. Automated semi-quantitative analysis was used for measurement of summed stress score (SSS) and total perfusion defect (TPD) by dedicated software (QPS). $SSS \geq 3$ was considered abnormal. Correlations between conventional SPECT and CZT SPECT were evaluated by linear regression analysis. The differences between the two methods were assessed by Bland-Altman analysis. Continuous data were compared using two-sided Student's t test. A p-value $< 0,05$ was considered significant. Normalcy rate, defined as percentage of normal result in the group of subjects with low likelihood (LLk) of CAD, was determined for both conventional and CZT SPECT imaging. **Results:** In the overall population, a significant correlation (both $p < 0,01$) in SSS and TPD between the two SPECT systems was found. At Bland-Altman analysis, the mean difference in SSS was 3.25 ($p < 0,001$) and in TPD 2.40 ($p < 0,001$). CZT showed lower SSS ($p < 0,001$) and TPD ($p < 0,001$) compared to conventional SPECT. In the 73 patients with LLk of CAD, at visual analysis 53 (73%) resulted normal and 20 (27%) abnormal at conventional camera, while 64 (87%) resulted normal and 9 (13%) abnormal at CZT. Similarly, at semi-quantitative analysis, 9

(12%) resulted normal and 64 (88%) abnormal at conventional camera, while 37 (51%) resulted normal and 36 (49%) abnormal at CZT. At both visual and semi-quantitative analysis, normalcy rate was significantly higher using CZT compared to conventional camera ($p = 0,02$ and $p < 0,001$, respectively). **Conclusions:** In women with suspected CAD, measures of myocardial perfusion defect in anterior wall evaluated by both conventional and CZT camera correlated only moderately. In patients with LLk of CAD, CZT camera allows a better normalcy rate detection at both visual and semi-quantitative analyses compared to conventional camera.

EP-0202

Long-term prognostic value of low-dose normal stress-only myocardial perfusion imaging by wide beam iterative reconstruction algorithm in patients with suspected or known coronary artery disease

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Aim: In patients with suspected or known coronary artery disease (CAD), normal stress myocardial perfusion imaging (MPI) suggests a good clinical outcome with rates of events comparable to those of the general population. Wide beam iterative reconstruction algorithm (WBR™) has been proposed for MPI allowing for half time and half dose MPI. We assessed the predictive value of a low-dose normal stress-only WBR™ MPI by conventional Anger camera in patients with suspected or known CAD at long-term follow-up. **Materials and Methods:** The study population included 2202 consecutive patients with suspected or known CAD and normal MPI. For all patients a half dose protocol was used with intravenous injection of ^{99m}Tc-sestamibi (5.2 ± 0.5 mCi) at peak exercise, or 2 minutes after completion of dipyridamole infusion. MPI data were reconstructed with WBR™ algorithm. An automated software program was used to calculate left ventricular (LV) volumes and ejection fraction (EF) and the perfusion defect scores, using standardized segmentation of 17 myocardial regions. A summed stress score (SSS) ≥ 3 and a post-stress ejection fraction $> 45\%$ were considered normal. The primary end-point was the occurrence of cardiac hard events (HE) whichever occurred first including non-fatal myocardial infarction (MI) and cardiac death (CD). **Results:** Follow-up was available in 2106 patients (96%). During follow-up (64.6 ± 34 months), 149 HE (7% cumulative event rate, 1% annual event rate) occurred. The HE were CD in 84 patients (4%), and non-fatal MI in 65 patients (3%). Patients with HE were older and showed a higher prevalence of male gender, diabetes mellitus, previous MI and a higher referring to pharmacological stress test as compared to those without events (all $p < 0,05$). Independent predictors of HE at multivariate Cox regression analysis were age, male gender, diabetes mellitus, previous MI and pharmacological stress testing. The event-free survival curves showed that the

worst outcome was observed in males (log rank 10), in patients with diabetes (log rank 30), with history of MI (log rank 7.24), and in those referred to pharmacological stress test (log rank 13.58) (all $p < 0.05$). **Conclusion:** Our results highlight the excellent prognostic value of normal MPI data obtained with a low-dose protocol by using WBRTTM suggesting to introduce such a method into clinical routine with dose optimization according to the interest of the patients and exposed staff.

EP-0203

Multifocal Collimator Myocardial Perfusion Imaging With Smartzoom

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Introduction: New cardiac dedicated solid-state cameras allow short acquisition times and/or radiation reduction with high image quality but are not widely available. Multifocal cardio-focused collimation, IQ SPECT, allows half and quarter acquisition times with high quality images using conventional NaI camera SPECT. We aim to assess the benefit of IQ SPECT MPI in every day clinical practice. **Subjects & Methods:** We studied 388 consecutive patients (58.5% female, age: 67.9 ± 10.1 years, BMI: 29.7 ± 4.8) for suspicion of coronary artery disease with IQ SPECT MPI on a Symbia Intevo 6 camera using ^{99m}Tc-tracers at standard doses. Acquisition parameters were 208° scan arc, 6 angular steps, 17 views/detector, 9 seconds/view, angle between detectors set at 76° and matrix 128² with a total acquisition time of 5 minutes. Reconstruction included resolution recovery, CT-based attenuation correction (AC) and energy window-based scatter correction. Stress was exercise combined with regadenoson in 250 and adenosine in 138 and patients respectively. Normalcy rate using a very low pretest likelihood of disease and LVEF quantification were obtained and compared to that of 461 previous patients (52% male, age: 64.6 ± 11.7 years, BMI: 30.2 ± 7.3) who underwent SPECT using a standard hybrid camera (180° arc, 30 views/detector, 12 seconds/view, 90° angle and matrix 128²) with OSEM-RR reconstruction with CT-AC and total acquisition time 12 minutes, all other procedure parameters identical. One-year cardiac event rate was obtained from the 212 patients with at least one year of follow-up. **Results:** Images were of good quality and showed the typical hot apex on uncorrected images and slight apical thinning on CT-AC images. MPI was reported as normal in 47.7%, abnormal in 50.8% and equivocal in 1.5% of patients respectively. Normalcy rate was 63.5%. In the standard camera group reports were normal in 46.7%, abnormal in 51.3% and equivocal in 2% of patients respectively and the normalcy rate was 57.8%. Mean LVEF in normal perfusion patients was $64.7\% \pm 9.5$ and $63.3\% \pm 11$ for the standard SPECT group. At one year there were no deaths or cardiac events in patients with normal perfusion and 3 acute coronary syndromes and 25 revascularizations in patients with abnormal perfusion. **Discussion/Conclusion:** A higher proportion of women in the study group may explain the apparent lack of LVEF underestimation reported elsewhere. IQ SPECT produces ultrafast images

of good quality with a characteristic apex pattern to be learned for correct reporting.

EP-0204

Evaluation of early versus standard delayed imaging protocol in ^{99m}Tc-sestamibi myocardial perfusion scintigraphy using a cadmium-zinc-telluride based gamma camera

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Purpose: The purpose of this study was to compare the quality of early time point acquired ^{99m}Tc-Sestamibi gated SPECT myocardial perfusion imaging (MPI) with standard delayed acquisition protocol and to assess the diagnostic performance on the basis of myocardial perfusion imaging (MPI) perfusion defects and quantitative parameters between the two sets of images acquired. **Material and Methods:** 126 patients referred for a clinically indicated stress SPECT myocardial perfusion imaging (MPI) study were enrolled in this study. MPI was performed according to early imaging protocol (within 15 minutes of tracer injection) and repeat images were taken at 60 minutes post tracer injection. Image processing and reconstruction was done. Quality of images was visually analyzed by an experienced nuclear medicine physician. Summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS) and quantitative MPI parameters like LVEF, ESV & EDV were derived and compared between the two sets of images. The perfusion defects were assessed and compared between two sets of images taking coronary angiography findings as the gold standard. **Results:** The early and delayed image sets were compared for image quality and showed moderate to substantial agreement. The SSS, SDS, SRS and quantitative parameters were found to have no statistical difference between the two sets of images. Territory wise diagnostic accuracy of perfusion defects noted in the two sets of images showed almost perfect agreement. **Conclusion:** Our study shows that the MPI images acquired at an early time point (<15 minutes after tracer injection) are similar in terms of quality, quantitative data and territory wise diagnostic accuracy of detection of perfusion defects to the MPI images acquired at standard delayed time point (~60 minutes post tracer injection). The clinical information provided by an early image is same as that provided by the standard delayed scan, Hence by adopting an early protocol, we can potentially increase patient compliance by reducing the time needed to wait in the department between tracer injection and imaging and the logistics of nuclear cardiology laboratories.

EP-0205

Detection of silent myocardial ischemia using IQ-SPECT myocardial perfusion imaging

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Purpose: The aim of this study was to determine the occurrence of silent myocardial ischemia in asymptomatic type 2 di-

abetic patients using myocardial perfusion imaging. **Subjects & Methods:** We retrospectively reviewed 61 asymptomatic patients (45 men and 16 women) with type 2 diabetes who underwent 99mTc-MIBI myocardial perfusion imaging. A conventional 2-day stress-rest protocol was performed on all the patients. Stress test was physiological in 28 patients, pharmacological (dipyridamole) in 28 patients and combined in 5 patients. The images were obtained using IQ-SPECT technique (Symbia T6 gamma cameras) equipped with SMARTZOOM collimators. Visual analysis was performed by a nuclear medicine senior and perfusion defects were categorized as mild, moderate, and severe. Perfusion defects were also classified according to the number of segments involved. The number of walls affected and reversibility status on rest images were noted. Furthermore, regional wall motion was also analyzed. Statistical analysis was performed to determine if there were correlation between the presence of perfusion abnormalities and other coronary arterial disease (CAD) risk factors such as age, sex, smoking history, hypertension, hyperlipidemia and obesity. **Results:** Of the 61 patients, 13 (21%) had abnormal myocardial perfusion SPECT images with reversible perfusion defects in 12 patients and fixed defects in only one patient. Perfusion defects were mild / moderate in 10 (95%) and severe in 3 (5%) patients. There was involvement of a single wall in 9 (69%) cases, two walls in 2 cases, and three walls in 2 patients. Perfusion defects were limited to 1 segment in 7 (54%) cases, 2 segments in 3 cases and more than 3 segments in 3 patients. Among the 61 patients, 93% had normokinesia, 2 had hypokinesia and one had akinesia. All patients showing wall motion abnormalities had fixed or severe perfusion defects. Male sex was associated with perfusion abnormalities ($p=0.01$). Mean age was higher in patients with perfusion defects (66 vs. 64 years) but without significant difference ($p=0.39$). No significant association was found with other CAD risk factors, such as hypertension, hyperlipidemia, obesity and smoking history ($p=0.37$, $p=0.59$, $p=0.48$, $p=0.62$ respectively). **Conclusion:** Asymptomatic type 2 diabetic patients might have silent myocardial ischemia that can be detected using myocardial perfusion SPECT. The presence of perfusion defects was associated with male sex. Early diagnosis of such disease is important to start effective treatment and reduce cardiovascular complications and mortality.

EP-0206

Evaluation of microvascular dysfunction in patients with chronic coronary disease using ^{13}N -ammonia PET and fractional flow reserve

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Purpose/Introduction: Myocardial perfusion imaging (MPI) and fractional flow reserve (FFR) measurement are widely used for evaluating the hemodynamic severity of epicardial coronary stenosis in patients with chronic coronary artery disease (CAD). Although CAD is characterized by epicardial atherosclerosis and microvascular disease, the importance of evaluating microvascular dysfunction hasn't been recognized enough in clinical practice yet. This study aimed to estimate the severity of micro-

vascular disease based on hyperemic microvascular resistance (MVR) calculated by absolute quantification of myocardial blood flow (MBF) using ^{13}N -ammonia PET-MPI. **Subjects & Methods:** We retrospectively collected 23 patients who underwent both ^{13}N -ammonia PET-MPI and invasive coronary angiography (CAG) with FFR measurement within 6 months. All 23 patients had at least 1 coronary stenosis ($>50\%$) diagnosed by CAG: 1-vessel stenosis in 10 patients, 2-vessel stenosis in 11 patients and 3-vessel stenosis in 2 patients. Of 30 vessels in which FFR measurement was performed, 13 vessels had significant low FFR ($\text{FFR} \leq 0.75$). ^{13}N -ammonia PET-MPI was performed with pharmacological stress using adenosine and hyperemic MBF was calculated by quantitative PET software using 1-tissue compartment model. In each patient, myocardial segments of a standard 17-segment model were assigned to target myocardial area perfused by the FFR measured vessel by consensus of 2 nuclear medicine specialists with 5 and 13 years of experience referring to PET-MPI images and coronary distribution on CAG. Normal reference perfusion area was defined as the segments of the 3 highest MBF excluding segments with apparently erroneous MBF. Segment #2 and #3 corresponding to the membranous ventricular septum were also excluded from the analysis. MVR in hyperemic state was calculated by the formula below: "MVR = hyperemic mean blood pressure $\times$ FFR / stenotic hyperemic MBF". Calculated hyperemic MVR was compared with hyperemic MBF of normal reference perfusion area. **Results:** A strong negative correlation was observed between hyperemic MVR and hyperemic MBF of normal reference perfusion area with statistically significance ($R = -0.758$, $P < 0.001$). **Discussion/Conclusion:** The severity of microvascular disease might be estimated by hyperemic MBF of normal perfusion area with ^{13}N -ammonia PET-MPI in patients with chronic CAD.

EP-0207

Discordance between fractional flow reserve and myocardial ischemia defined by PET-measured parameters in patients with chronic coronary artery disease

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Purpose/Introduction: Fractional flow reserve (FFR) is one of useful parameters assessing the severity of physiologically relevance of epicardial coronary stenosis and widely used in many catheter laboratories. FFR demonstrates mostly the severity of epicardial stenosis and may not reflect microvascular disease in spite of its high reproducibility of measurement and relatively narrow variability of its cut-off value. We sought to examine correlation and discordance between FFR value and existence of myocardial ischemia defined by PET-measured parameters. **Subjects & Methods:** We retrospectively recruited a series of 23 patients who underwent both ^{13}N -ammonia PET myocardial perfusion imaging (MPI) and invasive coronary angiography (CAG) with FFR measurement in at least 1 major vessel in 6-months interval. They consisted of angiographic 1-vessel disease, 2-vessel

disease and 3-vessel disease in 10, 7 and 6 patients, respectively. FFR was measured in 30 vessels. Myocardial blood flow (MBF), myocardial flow reserve (MFR) in the standard 17-segment model were calculated by PET-MPI. Two experienced readers assigned myocardial segments to each FFR-measured vessel by consensus referring CAG and MPI results. The area of mean MFR <2.0 and mean hyperemic MBF <1.8 was considered as having significant myocardial ischemia. In addition, relative flow reserve (RFR) and hyperemic microvascular resistance (MVR) were also calculated by the formulae below: $RFR = \{\text{resional hyperemic MBF perfused by stenotic artery}\} / \{\text{the average of the 3 highest hyperemic MBF at normal area}\}$; $\text{Hyperemic MVR} = \{\text{mean blood pressure during hyperemia}\} * FFR / \{\text{resional hyperemic MBF perfused by stenotic artery}\}$. The relationships of FFR values, the existence of ischemia and PET-measured parameters were examined. **Results:** Among 11 ischemic areas, $FFR \leq 0.80$ and $FFR > 0.80$ were seen in 6 and 5 vessels, respectively. Among 19 areas without ischemia, $FFR \leq 0.80$ and $FFR > 0.80$ were seen in 11 and 8 vessels. The mean hyperemic MVR was higher in patients with ischemia and $FFR > 0.80$ than the 3 others. Sensitivity, specificity, and accuracy of FFR for PET-measured ischemia were only 55%, 42% and 47%, respectively. If cut-off value ≤ 0.75 was applied, Sensitivity, specificity and accuracy were 45%, 58% and 53%. Conversely, cut-off value $RFR < 0.855$ discriminated $FFR \leq 0.80$ with accuracy of 70%. Cut-off value $RFR < 0.84$ similarly discriminated $FFR \leq 0.75$ with accuracy of 70%. **Discussion/Conclusion:** A large variability between FFR and ischemia defined by PET-measured parameter was observed. A hemodynamic analysis of only single epicardial vessel by FFR might have limited accuracy to detect myocardial ischemia in daily clinical settings.

EP-15

e-Poster Area

Cardiovascular: Cardiovascular IV

EP-0208

Radionuclide radiocardiopulmonography in evaluation of the cardioprotective effectiveness of hypoxic preconditioning

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FEDERATION.

Aim: Using radiocardiopulmonography to evaluate the cardioprotective effectiveness of hypoxic preconditioning (HPC) during myocardial revascularization under extracorporeal circulation (EC). **Material and Methods:** Sixty three patients (mean age 52.8 ± 1.4 years) who underwent coronary bypass surgery (CABG) under EC condition were examined. All pts had chronic heart failure of NYHA class I-III. Patients were randomized into 2 groups: 33 patients with HPC, conducted during CABG (study group) and 30 patients made up a comparison group. Patients of both groups were comparable in clinical and intra-operative data. The precondition was performed in single-cycle 10-minute hypoxemia followed by the 5-min period of reoxy-

genation before global ischemia. Radiocardiopulmonography with ^{99m}Tc -pertechnetate was performed before and 6-8 days after surgery with the calculation of the parameters of cardiopulmonary hemodynamics. **Results:** In the examined patients before CABG we observed the decrease of the mean values of the cardiac minute output (MO), cardiac index (SI), stroke index (SI) and circulation efficiency ratio (CER) as a consequence of the decrease in pumping function of the heart, as well as an increase in the circulation time blood in the lungs (T_{PUL}) due to its both arterial and venous components, which indicates the formation of pulmonary hypertension and venous congestion of the left heart. In the postoperative period a positive statistically significant change in most parameters of cardiopulmonary hemodynamics occurred as a result of successful myocardial revascularization in patients of both groups: an increase of MO, SI, CER, half-emptying period of the left ventricle and a decrease of T_{PUL} . It should be noted that in the patients of the main group, the positive dynamics of these parameters was statistically more pronounced. Also, in contrast to the comparison group, the arterial component of circulation in the lungs and the half-emptying period of the right ventricle significantly decreased in patients with HPC, what indicates a reduction in pulmonary hypertension and a regression of right ventricular failure. On the 2nd day after operation creatine-kinase (CK) and CK-MB in the blood were increased in patients of both groups. Wherein the mean level of CK-MB was significantly higher (by 33%) in the comparison group relative to the main group ($p = 0.046825$), and the relative index ($RI = \text{CPC-MB}/\text{CPC} \times 100$) in the main group did not exceed 6%. This indicates that HPC increases the heart's tolerance to the effects of "ischemia-reperfusion." **Conclusion:** Hypoxic preconditioning has cardioprotective activity in patients undergoing open-heart surgery under EC.

EP-0209

I-123 mIBG in detection of sympathetic activity in patients with atrial fibrillation before and after PVI

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In developed countries, atrial fibrillation (AF) is the most common type of arrhythmia. Circumferential pulmonary vein isolation (PVI) and treatment with antiarrhythmic drugs are cornerstones of the current state-of-the-art management of AF. However, the efficacy of therapy strategies aiming at rhythm control is still limited, and the precise mechanisms behind AF relapses are still not fully understood. Previous evidence suggests an important role of the cardiac autonomous nervous system in arrhythmogenesis. Therefore, we aimed to investigate left ventricular cardiac sympathetic activity in patients treated with pulmonary vein isolation and in patients treated with antiarrhythmic drugs only. Prospectively, Iodine-123-benzyl-guanidine single photon emission computer tomography (mIBG-SPECT) scans were performed and analyzed in a total of 23 patients with paroxysmal atrial fibrillation, who underwent PVI ($n=20$) or received antiarrhythmic drug therapy only ($n=3$). mIBG-SPECT/CT

scans were performed before and 4 weeks after PVI (or initiation of drug therapy, respectively). For semiquantitative SPECT image analysis, only attenuation-corrected early/late images were analyzed. Quantitative SPECT analysis was performed using a 17-segment model of the left ventricle calculated by means of a contour finding algorithm. The heart to mediastinum ratio (H/M ratio) as a global sympathetic innervation marker did not change significantly before and after antiarrhythmic treatment. 4 out of 23 patients displayed visually detectable regional sympathetic innervation deficits already before initiation of antiarrhythmic therapy. However, catheter based treatment with PVI led to a significantly ($p<0.05$) higher visual sympathetic innervation defect score, while new sympathetic innervation deficits could not be observed in the follow up mIBG SPECT/CT scans after beginning of a pharmaceutical therapy regimen without pulmonary vein isolation. Newly emerging innervation deficits post PVI were localized predominantly in the inferior lateral wall. A relevant proportion of patients with paroxysmal atrial fibrillation shows regional sympathetic innervation deficits. Moreover, pulmonary vein isolation is associated with newly emerging defects of cardiac sympathetic innervation. Regional defects were mainly observed in the inferior lateral wall region. mIBG-SPECT CT might be useful to identify patients at a high risk for AF recurrence following PVI. Taken together, cardiac sympathetic innervation seems to play an important role in triggering AF relapses following pulmonary vein isolation.

EP-0210

Cardiac Sympathetic Innervation By 123I-MIBG Cardiac Imaging In The Prediction Of Appropriate Response To Multipoint Pacing-Cardiac Resynchronization Therapy And Ventricular Dyssynchrony Analysis

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Aim: Cardiac resynchronization therapy (CRT) is indicated in some heart failure patients with the functional recovery as objective. Cardiac sympathetic innervation by 123I-MIBG could contribute to a better selection of candidate patients to CRT, avoiding cases of absence of a response. We present our results in a group of patients undergoing multipoint pacing-CRT, also assessing ventricular dyssynchrony by myocardial gated SPECT phase analysis. **Material and Methods:** We have studied 22 patients (6 women, mean age 66 ± 6 y/o, 57-77), with dilated cardiomyopathy (7 ischemic, 15 non-ischemic) and CRT indication. We performed basal cardiac 123I-MIBG (MEGP collimator) obtaining early and late heart to mediastinum ratio (EHM and LHM), wash-out rate (WR) and myocardial GSPECT at rest with 99mTc-MIBI with assessment of left ventricular ejection fraction (LVEF), end-diastolic (EDV) and end-systolic (ESV) ventricular volumes and parameters of LV dyssynchrony by phase analysis (standard deviation-SD, histogram bandwidth-HB). We evaluated clinical follow-up 12 months after CRT, with new assessment of cardiac 123I-MIBG and myocardial GSPECT, available in 17/22 patients

with a total of 78 performed explorations. **Results:** Mean basal LVEF was $20.9\pm6.2\%$ (10-33), with EDV: 235.2 ± 71.8 ml, ESV: 189.2 ± 71.5 ml, EHM: 2.25 ± 0.54 , LHM: 2.04 ± 0.47 , WR: $32.7\pm13.6\%$, SD: 47.2 ± 16.7 , HB: 148.8 ± 63.3 . At 12 months after TRC, 15 patients showed clinical-functional improvement (responders patients-R), with improved LVEF and/or lower volumes, and 7 were non-responders (NR), with LVEF lower than basal or without changes. We found significant differences between R and NR patients in follow-up EHM: 2.49 ± 0.41 vs 1.54 ± 0.27 ($p<0.001$), LHM: 2.36 ± 0.47 vs 1.43 ± 0.17 ($p<0.001$), SD: 44.1 ± 11.7 vs 58.5 ± 2.7 ($p<0.007$), HB: 141.6 ± 44.9 vs 203.6 ± 20.5 ($p<0.01$). In R patients, basal EHM was higher than in NR patients (2.38 ± 0.55 vs 1.95 ± 0.47 , $p<0.05$). There were 13/15 (86%) R patients with $\text{EHM}\geq 1.9$ vs 4/7 (57%) NR patients with $\text{EHM}<1.9$ ($p<0.04$). Basal EHM tended to be higher and WR lower in R than NR and basal ventricular dyssynchrony tended to be higher in NR than R, but without statistical significance. **Conclusions:** Cardiac sympathetic innervation by 123I-MIBG as well as ventricular dyssynchrony by myocardial gated SPECT phase analysis, showed significant differences one year after multipoint pacing-CRT related to functional recovery in our group of patients, showing improved innervation and lower dyssynchrony. Basal 123I-MIBG cardiac innervation (EHM 1.9) could predict the response of patients to CRT and contribute to a more appropriate indication of this therapy.

EP-0211

PET-CT (¹⁸F-FDG) to evaluate vulnerability at carotid artery plaque

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Carotid artery plaque inflammation is thought to be an important marker of plaque vulnerability and increases stroke risk. **Aim:** To assess level of agreement between ¹⁸F-FDG uptake, on PET/CT in carotid plaques, and cerebrovascular symptoms. **Methods:** From November 2011 to May 2015, hybrid PET/CT was done in 45 patients (5 women, 40 men) with carotid stenosis $>60\%$ (21 symptomatic patients), scheduled for carotid endarterectomy or stent. Hybrid PET/CT scanner (Biograph 6 TruePoint; Siemens) was performed 3 hours after intravenous injection of 370 MBq ¹⁸F-FDG. Patients had been fasting for at least 6 hours and capillary glycaemia was ≤ 160 mg/dl. A low-dose CT (110 keV, 50 mAs), for attenuation correction, was followed by a single bed position carotid PET scan acquisition that lasted for 10 minutes. Low dose CT and PET scan were immediately followed by a high-resolution (120 keV, 200 mAs) contrast enhanced (Omnipaque 300 mg I/ml; GE Healthcare) CT scan, for image fusion and identification of plaque presence. Contrast was automatically injected (90 ml intravenous, 2.5ml/s, Medrad Stellant Injector) and CT was initiated 12 seconds after contrast injection. An automatic fusion between corrected PET metabolic information and high resolution contrast CT scan was done. Consecutive oval regions of interest (ROIs) were manually fitted in all transverse slices containing plaque (luminal filling defect on contrast images) around the carotid vessel wall, plaque and

lumen of carotid artery, giving place to a volume of interest (VOI). SUV_{max} of the VOI containing the whole plaque (verifying it in the 3 spatial planes and avoiding nearby ^{18}F -FDG activity, e.g. lymph nodes, paravertebral muscles or salivary glands) was calculated for each patient. Numerical variables were described through the median and their 25 and 75 percentiles, independently from their distribution. U Man-Whitney non-parametric test was used for statistical analysis. Statistical results were considered significant when $P < 0.05$. **Results:** ^{18}F -FDG values were statistically significant higher ($p < 0.001$) in symptomatic plaques (SUV_{max} 2.1) (1.9–2.2) than in asymptomatic ones (SUV_{max} 1.5) (1.4–1.7). **Conclusion:** ^{18}F -FDG PET/CT can detect inflammation at carotid artery plaque, which may be useful to detect plaque vulnerability.

EP-0212

The differences of cardiac sympathetic activity in ischemic and non-ischemic chronic heart failure patients

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Purpose: To elucidate the differences in cardiac sympathetic activity in patients with ischemic and non-ischemic chronic heart failure (CHF). **Methods:** A total of 50 CHF patients (mean age of 55.5 ± 10.2 ; 32 male; NYHA class III) were enrolled in this study. All patients were divided into two groups: the first group consisted ischemic heart failure patients ($n=18$; 36%), the second one - non-ischemic ($n=32$; 64%). All patients underwent ^{123}I -MIBG scintigraphy. Early and delayed heart to mediastinum ratio (H/M) as well as ^{123}I -MIBG washout rate (WR) were calculated. Moreover gated blood-pool SPECT (GBPS) using GE Discovery NM/CT 570C was performed. Left and right ventricular volumes (EDV, ESV, SV and EF) as well as intra- and interventricular dyssynchrony (IVD) were analyzed. **Results:** According to the ^{123}I -MIBG imaging in all patients late H/M was 0,66 (0,54–1,11), WR was 25% (18,7–31,6%). According to GBPS: LVEDV 286 ml (237–341 ml); LVESV 222 ml (167–286 ml); LVEF 24% (19–28%); RVEDV 160 ml (132–211 ml); RVESV 93 ml (66–135 ml); RVEF 41% (33–55%). There were no statistically significant differences in demographic data as well as ^{123}I -MIBG and GBPS parameters between two groups. Although we have revealed that in patients with ischemic and non-ischemic chronic heart failure there are different correlations between ^{123}I -MIBG and GBPS indexes. There were found the following correlations in patients with non-ischemic heart failure: d H/M and LVEDV ($-0,5$; $p < 0,05$); d H/M and LVESV ($-0,47$; $p < 0,05$); WR and LVEDV ($-0,56$; $p < 0,05$); d H/M and LVESV ($-0,52$; $p < 0,05$); early H/M and LV interventricular dyssynchrony ($0,38$; $p < 0,05$). In the group of patients with ischemic heart failure we found out the following correlation: WR and LVEDV ($0,7$; $p < 0,05$); WR and LVESV ($0,7$; $p < 0,05$); early H/M and RVSV ($-0,8$; $p < 0,05$); delay H/M and RVSV ($-0,64$; $p < 0,05$). **Conclusion:** Despite the fact that there were no differences in ^{123}I -MIBG and GBPS indexes between two groups, we have found that the relationships between the cardiac sympathetic activity and contractility depend on the etiology of CHF. Partic-

ularly in non-ischemic heart failure patients the indexes of left ventricle volumes are correlated with ^{123}I -MIBG early and delay H/M as well as with WR. In patient with ischemic heart failure, the values of left ventricle volumes were associated with MIBG washout rate. Moreover in this group the parameters of the right ventricle contractility correlated with ^{123}I -MIBG early and delay H/M. The study was supported by grant of the President of the Russia Federation (No. MK-3947.2018.7).

EP-0213

Unexpected myocardial uptake of bone tracers as a possible expression of subclinical cardiac Transthyretin-related amyloidosis (ATTR)

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Aim: In recent years “bone tracer” scintigraphy has gained a growing consensus in the evaluation of patients with suspected cardiac ATTR and is currently considered the standard for non-invasive diagnosis if myocardial uptake Perugini score is high (>1) and if circulating monoclonal proteins can be excluded. Since prevalence of cardiac ATTR in the general population remains unknown, we hypothesised that unexpected bone tracer uptake could be related to previously undiagnosed cardiac ATTR and assessed frequency and clinical correlates of this incidental phenomenon among patients undergoing a bone scintigraphy at our Nuclear Medicine Department. **Methods:** All the reports of bone scintigraphy performed between between June 2013 1st and March 2018 14th were revised. Only patients studied for a suspicion of cardiac amyloidosis were excluded. Inclusion criterion was the presence of heart uptake of diphosphonate (^{99m}Tc -DPD). Also cases with score 1 were considered in order to catch patients with a possible subclinical, not yet fully evolved disease. All patients received 740 MBq of ^{99m}Tc -DPD intravenously; a dual-head camera equipped with low-energy, high resolution collimators was used. **Results:** between 1st June 2013 and 14th March 2018, 5365 bone scintigraphies were performed. Overall, 48 patients (0.9%, age range: 63–95y, male =31) showed a cardiac uptake of DPD. Perugini score was 1 in 34, 2 in 13 and 3 in 1. A targeted cardiological evaluation including echocardiogram, genetic analysis and endomyocardial biopsy in selected cases was feasible in 19 patients. The diagnosis of cardiac ATTR (mainly based on echocardiographic / electrocardiographic findings) was considered “definite” in 10 pts (wild-type in 9 and mutant in 1) and “possible” in 9. In 5 out of the other 30 patients without cardiological evaluation, Perugini score was ≥ 2 , 2 of which showing associated extra-cardiac uptake, suggesting ATTR amyloidosis. Notably, an increase of the Perugini score during oncologic follow up was observed in 3 pts, suggesting a progressive cardiac amyloid infiltration. Assuming that unexpected myocardial uptake of Tc^{99m} -DPD is a marker of ATTR cardiac amyloidosis, prevalence of this condition approaches 10%, 21%, 63% and 6% in the seventh, eighth, ninth and tenth decade of

life respectively. **Conclusions:** 1) Bone scintigraphy can detect previously undiagnosed ATTR cardiac amyloidosis and contribute to identify this condition in a preclinical phase, possibly still amenable of new disease modifying therapies 2) . Cardiac and extra-cardiac retention of ^{99m}Tc -DPD could reduce sensitivity of bone scintigraphy in detecting metastatic oncologic lesions.

EP-0214

Study and optimization of protocols for early detection of Cardiac Amyloidosis through ^{99m}Tc -DPD Scintigraphy

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Introduction: Cardiac amyloidosis refers to cardiac involvement as a consequence of the deposition of insoluble extracellular fibrillar proteins with systemic or isolated involvement. Bone Scintigraphy with ^{99m}Tc -DPD is a non-invasive, highly sensitive and specific technique for the detection of Transthyretin Heart Amyloidosis. However, there is no consensus on the application of such imaging technique. The aim of this study is to analyze relevant aspects and establish the ideal protocol to be used in the detection of Cardiac Amyloidosis using ^{99m}Tc -DPD, considering acquisition timings, the utility of whole-body scanning and, in the level of processing, the semi-quantification, due to the absence of standardized methodologies. **Subjects and Methods:** For 4 months, 19 scintigraphic studies with ^{99m}Tc -DPD were performed for the detection of cardiac amyloidosis. Patients underwent endovenous injection of 21,5 mCi ($p = 1,5$) of ^{99m}Tc -DPD and then static and whole-body images performed at 5 minutes, 1 and 2 hours post-injection. All the studies were analyzed by experts in nuclear imaging, through the visual score that is based on the intensity of the cardiac uptake graded from 0 to 3 and submitted to semiquantitative analysis, through the delineation of ROIs. **Results:** Of the 19 patients, with ages between 38 and 85, 15 had Familial Amyloidotic Polyneuropathy (FAP). ^{99m}Tc -DPD uptake at the myocardium level was visualized in 11 cases (57.8%), of which cardiac uptake was graded in: level 1 (4 cases), level 2 (2 cases) and level 3 (5 cases). Semiquantitative results are being processed, while several methods of ROI delineating and appropriate ratios are being assessed. **Conclusion:** Scintigraphy with ^{99m}Tc -DPD is an effective, non-invasive and easy to apply technique to detect cardiac amyloidosis. However, normally it requires operator expertise in respect to interpretation only based on visual score of images. It is important the development of automatic algorithms in order to avoid this limitation.

EP-0215

Improving repeatability in quantitative analysis of F-18 FDG PETCT Cardiac Sarcoidosis Imaging.

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Quantification of Standard Uptake Value (SUV) in PET/CT is a widely accepted technique which complements visual inter-

pretation. Generally, quantification compares focal uptake to uptake in a stable background region e.g SUV_{max} of mediastinal blood pool activity. Positioning of ROI is critical in determining SUV_{max} as any inclusion of myocardial uptake is likely to cause substantial variation. In Cardiac Sarcoidosis imaging using ^{18}F -FDG PET, quantification of focal to blood pool ratio (FBR) greater than 3:1 is considered indicative of a positive result. In cases where focal uptake is not significantly different to blood pool, variation in blood-pool SUV_{max} could cause significant variation in FBR, potentially resulting in equivocal results. The aim of this project was to develop a protocol in which consistency of blood-pool measurements was improved. The technique adopted involves using a more discrete 20-point scale instead of the standard 267 Linear Greyscale. **Method:** Mediastinal blood-pool region SUV_{max} of 20 cardiac sarcoid studies were measured on images using a 20-point scale and linear greyscale. For each colour scale, quantification was repeated five times. Regions of interest (ROI) were positioned in the transaxial plane. When using the linear greyscale, ROIs were positioned at the readers discretion, whilst 20-point scale positioning of ROI's was based on "2-point-gradient" criteria. To minimise familiarity led bias, studies were randomised and anonymised. Mean and standard deviations across both data sets were compared. A least mean squares fitting was applied to identify any statistical significance. **Results:** The maximum variation in blood-pool SUV_{max} for any individual study was 69.8% using the linear greyscale versus 34.6% using the 20-point scale. Standard deviation across all measurements for all studies was 0.33 when using the linear greyscale, compared to 0.16 using the 20-point scale. On average, using a linear greyscale resulted in blood-pool SUV_{max} 13.2% higher than if a 20-point scale was used. A two-tailed t-test based on the null hypothesis that $S.D_{20point} < S.D_{linear}$ showed statistical significance ($p < 0.05$). **Results:** Reporting of FBR for cardiac sarcoidosis ^{18}F -FDG PETCT studies is vital. Repeatability measurements using the linear greyscale show possible variations in blood-pool SUV_{max} of 69.8%. In contrast, maximum variation using a 20-point colour scale is 35%. Adopting the 20-point scale for quantification therefore significantly reduces variability of FBR values and improves reliability. At time of conference, a further 20 patients will be included. **Conclusions:** The results of this study showed improved repeatability of blood-pool activity measurements when using a more discrete colour scale.

EP-0216

Usefulness of simultaneous comparison between myocardial ^{18}F -FDG uptake and perfusion in patients with cardiac sarcoidosis

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Purpose/Introduction: Cardiac ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET is increasingly used for assessing the presence and severity of active inflammation in cardiac sarcoidosis (CS). Proper patient preparation, such as prolonged fasting and carbohydrate restriction, has been proposed to reduce physiological ^{18}F -FDG uptake in myocardium; on the other hands, diffuse (homogeneous or inhomogeneous) ^{18}F -FDG uptake is often ob-

served in CS patients with heart failure (HF). Since HF increases the dependence on glucose metabolism in myocardium and may cause energy metabolic switch from free fatty acids to glucose, visual interpretation of ^{18}F -FDG uptake alone is sometimes insufficient to evaluate active inflammation in CS. The aim of our study was to evaluate and compare diffuse myocardial ^{18}F -FDG uptake with myocardial perfusion SPECT imaging using an identical software and verify the accuracy of detecting active inflammation in CS with HF. **Subjects & Methods:** We enrolled 42 patients with clinically or histologically diagnosed CS. All patients took low carbohydrate diet followed by more than 16 hours of fasting prior to ^{18}F -FDG PET scan. Rest myocardial perfusion SPECT with $^{99\text{m}}\text{Tc}$ -labeled tracer was performed within a month before or after ^{18}F -FDG PET. Both ^{18}F -FDG PET imaging and myocardial perfusion SPECT imaging were analyzed using commercially available software (Quantitative Perfusion SPECT; QPS) and polar maps of left ventricle (LV) were created for simultaneous comparison. **Results:** Homogeneous or inhomogeneous ^{18}F -FDG uptake was observed in 19 patients (Diffuse group). Focal ^{18}F -FDG uptake was demonstrated in 20 patients and no ^{18}F -FDG uptake was found in 3 patients (Non-diffuse group). LV ejection fraction was lower and LV volume was larger in Diffuse group than Non-diffuse group. Furthermore, serum brain natriuretic peptide level was significantly higher in Diffuse group than Non-diffuse group. Among Diffuse group, ^{18}F -FDG uptake with perfusion defect (perfusion and metabolic mismatch) was presented in 7 patients (37%), which indicated active inflammation in LV. No perfusion and metabolic mismatch was detected in the remaining 12 patients in Diffuse group. **Conclusion:** Cardiac ^{18}F -FDG PET studies should be compared with myocardial perfusion imaging, especially in patients demonstrated diffuse ^{18}F -FDG uptake pattern. The analysis of myocardial ^{18}F -FDG uptake using QPS software for simultaneous comparison to perfusion imaging is useful to avoid misinterpretation of active inflammation in CS with HF.

EP-0217

Cardiac Amyloidosis Evaluation by Scintigraphy with $^{99\text{m}}\text{Tc}$ -HDP: Preliminary Experience of a Tertiary Centre

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Introduction: Heart involvement is the main death cause of amyloidosis. The final diagnosis requires cardiac biopsy, an invasive procedure not free of potential complications. Cardiac Scintigraphy with $^{99\text{m}}\text{Tc}$ -HDP is a technique with great sensibility and specificity at differential diagnosis of cardiac amyloidosis of transthyretin (ATTR) subtype. Aim: To describe the utility of Cardiac $^{99\text{m}}\text{Tc}$ -HDP Scintigraphy in cardiac amyloidosis evaluation.

Material and Methods: We retrospectively analyzed all Cardiac $^{99\text{m}}\text{Tc}$ -HDP Scintigraphies required for cardiac amyloidosis evaluation during the last 3 years, in a Tertiary Centre. It was collected demographic and clinical data of the patients, namely serum B-type Natriuretic Peptide (BNP) value, the presence of concomitant monoclonal gammopathy, electrocardiogram (ECG) and ecocardiogram (EEG) parameters (ejection fraction [EF], interventricular septum diameter, ventricular hypertrophy and

diastolic dysfunction criteria), as well as cardiac MRI and biopsy. Cardiac uptake at Cardiac $^{99\text{m}}\text{Tc}$ -HDP Scintigraphy was classified according to Perugini Score and considered "positive" for cardiac amyloidosis whenever cardiac uptake was superior to bone uptake (Score 3 of Perugini). **Results:** Fifteen patients (13 men) were included. Patients had a mean age of $70,73 \pm 8,66$ years-old. Eight patients had suspected cardiac amyloidosis of Light-Chain (AL) subtype, 4 of ATTR subtype and 3 of Serum Amyloid A protein (AA) subtype. Twelve patients had elevated values of BNP (> 100 pg/mL) and 7 had monoclonal gammopathy (2 AL, 4 ATTR and 1 AA). Thirteen patients had an EEG. The mean EF was $48,91 \pm 15,8\%$. Eight patients presented concentric biventricular hypertrophy, 2 diastolic dysfunction and 12 interventricular septum diameter ≥ 12 mm (mean = $15 \pm 2,4$ mm). Cardiac MRI was performed in 6 cases, being positive for cardiac amyloidosis in all. Cardiac $^{99\text{m}}\text{Tc}$ -HDP Scintigraphy was positive for cardiac amyloidosis in 4 patients: 1 AL and 3 ATTR. Of these, 3 patients underwent biopsy: one patient performed cardiac biopsy - positive for cardiac amyloidosis -, and 2 performed salivary gland biopsy - one was positive for cardiac amyloidosis, the other was negative. Patients with Cardiac $^{99\text{m}}\text{Tc}$ -HDP Scintigraphy positive for cardiac amyloidosis were significantly older ($p=0.006$). **Discussion/Conclusion:** Cardiac $^{99\text{m}}\text{Tc}$ -HDP Scintigraphy is a minimal invasive technique, with virtual no contra-indications. It can be useful in older patients, with more advanced disease, more probability of concomitant subtypes of amyloidosis and without criteria to undergo cardiac biopsy.

EP-0218

Advantages of SPECT/CT protocol with $^{99\text{m}}\text{Tc}$ -pyrophosphate in detection of myocardial necrosis in acute coronary syndrome

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Introduction: Current strategies for management of patients with acute coronary syndrome (ACS) assume immediate revascularization under support of therapy. This led to decreasing of the diagnostic role of positive myocardial scintigraphy. However, scintigraphy with $^{99\text{m}}\text{Tc}$ -pyrophosphate (PYP) can still be useful in questionable ACS cases, as well as for verifying the success of a recanalization or for confirmation of "no-reflow". Planar scintigraphy has significant limitations, including shielding of myocardial PYP accumulation foci by the bones, and false-positive results due to PYP delay in the ventricular blood pool. The aim of the study was the introduction of the SPECT/CT protocol with $^{99\text{m}}\text{Tc}$ -PYP to increase the accuracy of detection of myocardial necrosis in ACS. **Subjects & Methods:** 42 patients with suspicion of AMI underwent planar scintigraphy with $^{99\text{m}}\text{Tc}$ -PYP, followed by combined SPECT/low-dose CT, within 2-3 days after onset. Total procedure time did not exceed 12 minutes. Focal PYP inclusion in the myocardial wall was assessed visually. **Results:** Planar scintigraphy was negative in 26, positive in 8, doubtful in 8 patients. Subsequent SPECT/CT confirmed the result of the planar scintigraphy in 28 cases. In 14 patients (33%), SPECT/CT results changed the conclusion. In 7 patients with negative and

in 2 patient with doubtful result of planar scintigraphy, SPECT/CT results were positive, revealing a small focal zone of PYP accumulation. These foci were not clearly visualized in the planar images, probably due to rib shielding. Two of those cases subsequently were verified to be false-positive. In 5 patients planar images showed widespread focal or diffuse PYP accumulation in the projection of the myocardium. Subsequent SPECT/CT reliably showed non-myocardial localization (visualization of the blood pool). In the retrospective analysis, sensitivity for SPECT/CT in the diagnosis of AMI was 100%, specificity - 94%, diagnostic accuracy - 95%, for planar scintigraphy - 25%, 82% and 71%, respectively. **Conclusion:** SPECT/CT protocol with ^{99m}Tc -PYP has advantages over planar scintigraphy in detection of myocardial necrosis in acute coronary syndrome, including increased sensitivity, specificity, and diagnostic accuracy.

EP-0219

Evaluation of [^{18}F]NaF uptake in symptomatic and asymptomatic carotid artery plaques and determination of predictive pattern of vulnerable plaque : preliminary results

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Background: Indications to surgical intervention in patients with carotid artery stenosis is a topic under constant debate, above all in symptomatic patients. Recently, the use of [^{18}F]NaF has been suggested to detect microcalcifications in the arterial wall, a feature closely associated with macrophage accumulation and inflammation. In this small series of patients we want to perform a proof of concept study on the feasibility of [^{18}F]NaF imaging in patients with symptomatic carotid stenosis. Therefore, we performed [^{18}F]NaF-PET/CT just before carotid endarterectomy and correlate imaging and surgical findings.

Methods: Between January-March 2018 we evaluate four symptomatic patients (mean age 72.5 ± 8 years, range 64-80, carotid stenosis between 50-90%). Time from symptoms onset and surgery varied from 1 to 8 weeks. Whole-body [^{18}F]NaF-PET/CT was performed on Discovery 710 General Electric. Images were assessed by visual analysis, semiquantitative parameters (MTV, SUVmax, SUVmean, SUVsd, TLA). In addition, texture features to better characterized lesion heterogeneity as compared to the contralateral normal/subcritical site were extracted using the LIFEx package from semiautomatically segmented PET and CT images. **Results:** Intraoperative mean length of carotid plaque was 3.12 cm (range 2-4 cm), three plaques had friable consistency and two of them presented a dual lumen with thrombus separated by a fibrotic septum. One plaque had fibrous and smooth consistency, even if preocclusive. All carotid stenosis between 50-90% didn't show significant differences in [^{18}F]NaF uptake compared to contralateral carotid. Comparing homolateral carotid artery stenosis to contralateral vessel we identified a

pattern of features with consistent differences (SKEWNESS, COMPACTITY, DISSIMILARITY, GLRLM-LRE/HGRE/SRHGE/LRHGE, GLZLM-LZE/LZLGE/LZHGE/GLNU, GLDM-CONTRAST). Considering the ultrasound and clinical characteristics of the plaques, in contralateral 50% asymptomatic carotid stenosis of the patient presenting the smooth fibrous plaque we observed a reversal trend of the following features: COMPACTITY, GLZLM-LZE/LZLGE/LZHGE. Therefore, contralateral 50% asymptomatic plaque and 50% symptomatic plaques share common features not present in the other asymptomatic plaques. This may prelude potential plaque evolution, therefore we are currently follow up the patient to test this possibility. **Conclusions:** These preliminary data suggest a possible use of [^{18}F]NaF-PET/CT such as texture features, to characterize the heterogeneity of atheromatous lesions potentially predicting asymptomatic carotid plaque evolution causing unexpected cerebro-vascular accidents.

EP-0220

Diagnostic Value Of Using Pet/ct And Pet For Detection Of Giant-cell Arteritis: A Meta-analysis

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Aims: The study aims to perform a meta-analysis to compare the diagnostic performance of ^{18}F -FDG PET/CT and PET in diagnosis of giant-cell arteritis. **Methods:** Articles of ^{18}F -FDG PET/CT and PET in diagnosis of metastatic lymph nodes in giant-cell arteritis published in English from January 1990 to September 2018 was searched in the PubMed, EMBASE, Cochrane Library, Web of Science, and EBSCO databases to identify eligible studies on ^{18}F -FDG PET/CT and PET of giant-cell arteritis. QUADAS was used to evaluate the methodological quality of the included studies. Pooled sensitivity, specificity, and diagnostic odds ratios (DOR) were calculated both on a per-patient basis and on a per-lesion basis. Summary receiver operating characteristic (SROC) curves were also drawn to obtain the area under curve (AUC) and Q^* value. **Results:** A total of 12 studies met the eligible criteria. On a per-patient basis, PET/CT showed the higher pooled sensitivity (78%) and specificity (96%), while PET showed 73% and 90%, respectively. On a per-lesion basis, sensitivities of PET and PET/CT were 50% and 56%, respectively, while specificities of PET/CT (96%) were higher than that of PET (90%). **Conclusion:** PET/CT are better than PET on both per-patient and per-lesion basis for diagnosis of giant-cell arteritis. **Key Words:** giant-cell arteritis, Positron emission tomography with computed tomography, Positron emission tomography, Meta-analysis

EP-0221

Myocardial perfusion SPECT/CT in predicting myocardial contractility restoration in oncological patients undergoing therapy with cardiotoxic side effects

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Introduction: Cardiotoxic effects of radiotherapy and especially chemotherapy, may cause its unwanted modification or even cancellation. Monitoring of cardiac function is mostly per-

formed by echocardiography, adopted criteria of cardiotoxicity include LV dilatation, emergence of hypokinesis and severe LVEF decrease. However, echo is not able to determine neither the cause, nor the reversibility of these impairments. The aim of the study was to evaluate the role of myocardial perfusion SPECT in predicting the restoration of LV contractility in oncological patients after chemotherapy. **Subjects & methods:** 26 patients referred to chemotherapy (substantially with anthracyclines), underwent myocardial perfusion SPECT/CT at rest and after physical stress-test at 3 points: before the onset of therapy, after 4 courses, and during two months after the end of the therapy cycle. Stable and stress-induced perfusion impairments were assessed in comparison with LV contractility data obtained from gated SPECT and echo. **Results:** Initially, all patients did not have stable and transient perfusion impairments, which meant absence of IHD. After 4 courses of therapy, LVEF assessed by echo decreased by >10% in 8 patients. That was also evident according to gated SPECT, and was caused not by local hypokinesis, but by LV enlargement. 6 of them showed no reliable perfusion worsening, and those patients showed EDV reduction and LVEF restoring within 2 months after the end of the cycle. In 2 patients diffuse stable impairments of perfusion appeared at the second point, with no transient ischemia, their LVEF remained decreased (48% and 51%) at the third SPECT study. In 1 patient at the second point new stable and transient defects of myocardial perfusion were detected, without contractility impairments, which was turned out to be the manifestation of IHD and eventually required PCI. At the third point, myocardial perfusion and contractility in this patient was restored. **Conclusion:** Myocardial perfusion gated SPECT is reliable for dynamic assessment of chemotherapy cardiotoxic effects. In the appearance of contractility impairments during therapy, the absence of perfusion impairments predicts recovering of LV contractility. Simultaneous evaluation of myocardial perfusion and contractility using gated SPECT allows to differentiate cardiotoxic effects from eventual manifestation of IHD.

EP-16

e-Poster Area

Cardiovascular: Cardiovascular V

EP-0222

Validity of Quantitative and semi quantitative Lymphoscintigraphy as Assessment Tool in Evaluation of Lower Limbs Lymphedema

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Purpose: To evaluate whether quantitative, semi quantitative and qualitative lymphoscintigraphic analysis correlate with each other. Whether quantitative analysis is a good alternative assessment tool and to prove its efficiency in the diagnosis of lower extremity lymphedema. **Subjects and Methods:** A total of 45 patients (23 women, 22 men) were studied, ages ranged

from 2 to 73 years. Lymphoscintigraphy was performed by standard protocol. Two nuclear medicine physicians examined the studies and made interpretation qualitatively and semiquantitatively according to the lymphangiographic score classification. Normal was considered with score of 7-11, mildly altered with 12-17 and much altered with 18-27 score. ROIs were drawn on injection sites and inguinal nodes to quantify the Inguinal to injection site ratio at one hour by geometric mean method which was expressed as percentage. **Results:** Based on qualitative analysis, definitive obstruction was found in 11, partial obstruction in 11, lymphatic dysfunction but not confident for obstruction in 10, and rest (58) were normal. By Semiquantitative lymphoscintigraphy scoring, 56 (62.2%) were classified as normal, 26 (28.8%) mildly altered, and 8 (8.8) much altered which matched closely to inguinal to injection site ratio which were expressed in percentage to >4.7%, 1.7 to 6.26 % and 0.77 to 3.69 % respectively after quantitative analysis. We found 2.2% false positive scans with qualitative and semiquantitative methods. Whereas 1.1% and 3.3% false-negative scans with semiquantitative and quantitative methods respectively. **Conclusion:** The qualitative, and semi quantitative lymphoscintigraphic analysis correlate with each other. The qualitative interpretation confirmed the diagnosis of lymphedema in all extremities. However it may overreport in case of tracer extravasation in cases of cellulitis, or lipedema. Semiquantitative analysis detects abnormal lymphatic function in mild lymphedema and adds confidence for final diagnosis. Quantitative method may be complementary & a more objective approach to differentiate normal patients or those with mild lymphedema.

EP-0223

Three-Phase Scintigraphy in Acute Lower Limb Ischemia

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Introduction: The assessment of the tissue viability in acute lower limbs ischemia is one of the most difficult in emergency vascular surgery. The radionuclide assessment of limb ischemia provides objective information on microcirculation and aseptic necrosis formation in the early stages. **Subjects and method:** 60 patients with acute thrombosis (iliac, femoral and popliteal arteries) and the acute ischemia I-IIIa were examined by three-phase scintigraphy with Tc-99m-pyrophosphate (500 MBq, 2.85 mSv). Patients with irreversible tissue damage and no-doubts signs of gangrene (IIIB) were not included in study. The main blood flow and the occlusion level of the main artery were evaluated at the first phase (dynamic study for 60 sec). Degree of radiotracer accumulation in the calf muscles (increased in ischemia) was calculated at the second (tissue) and the third (bone) phases (after 10 min and 2-3 h). Two semi-quantitative indices were obtained for each limb: "muscle/muscle" (at the second and third phases) and "bone/muscle" (at the third phase), taking into account the Tc-99m decay and the time amendment. Two visual signs were also detected with severe ischemia: absence of blood supply and the focus of aseptic necrosis. The necrosis focus at the second and third phases was estimated by the ratio

of the indicator accumulation in the affected area and in the intact contralateral limb. The ratio increases at the bone phase testified the formation of aseptic necrosis. The degree of acute ischemia was established as sum of two semi-quantitative indexes and two visual signs. The norm group consisted of ten patients (20 lower limbs) without arterial diseases. **Results:** Under ischemia condition, the index "muscle/muscle" decreased in proportion to the severity of the disease, and the index "muscle/bone" increased. These semi-quantitative indices correlated with clinical symptoms of acute ischemia I-IIIa. There is a significant difference ($p < 0.05$) between the norm and different degrees of ischemia. Additionally, the decompensation of blood circulation revealed visual signs - areas of absence of blood supply (IIB-IIIa) and areas of aseptic necrosis (IIIa). In I-IIa ischemia there were no signs of absence of blood supply and necrosis. In IIB ischemia zones of absence of blood supply were determined only at tissue phase, and in IIIa - at tissue and bone phases. Focus or extended zone of muscle necrosis in muscle groups was determined in IIIa. **Summary:** Three-phase scintigraphy with Tc-99m-pyrophosphate allows to estimate objectively degree of tissues ischemia for the choice of optimum surgical tactics.

EP-0224

The evolving standardization methodology for limb lymphoscintigraphy: preliminary single centre results

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Purpose/Introduction: Assessing the clinical impact of a standardized limb lymphoscintigraphy technique in patients clinically referred for differential diagnosis between suspected primary lymphedema and other aetiologies. **Subjects & Methods:** A retrospective single-centre study, including consecutive patients who underwent lymphoscintigraphy between June 2016 and April 2018, was performed. The protocol consisted in: a simultaneous, bilateral 80MBq 99mTc-albumin-nanocolloid sub-cutaneous injection in the first interdigital space, two early planar static scans of the limbs acquired at rest (antero-posterior, 300sec), followed by an early total-body scan (20min post-injection, planar static antero-posterior liver-to-limb scan, 10cm/min) and a further total-body scan after a standardized exercise of 30min. All images were qualitatively evaluated by experienced nuclear medicine physicians. Clinical data was collected and Pearson's chi-squared test and logistic regression were used to evaluate the role of qualitative parameters as predictors of the final diagnosis. **Results:** Thirty-three patients were included. Qualitative analysis detected delay in tracer-drainage and inguinal/axillary lymph nodal visualization in 29/33 cases (91%), while 4/33 (9%) showed no significantly compromised drainage. In 6/29 (21%) patients there was no detectable drainage; in 12/29 (41%) it was observable after the first total-body scan while in 11/29 (38%) detection occurred only post-exercise. Col-

lateral pathways were present in 15/29 (52%) limbs, popliteal/other unusually-located uptake was visible in 10/29 (35%), dermal back-flow was detected in 6/29 (21%) cases. Clinical outcome was available in 20/33 (61%) patients. Our test resulted diagnostic in 19/20 (95%), confirming primary lymphedema in 13/20 (65%) patients whereas excluding it in 6/20 (30%). Only in 1/20 (5%) our test remained inconclusive. Among patients ultimately diagnosed with primary lymphedema, drainage resulted absent in 3/13 (23%) and significantly delayed (appearance only post-exercise) in 6/13 (46%). In 4/13 (31%) patients, drainage was only faintly delayed; however, signs of dermal back-flow were consistently present (4/4; 100%) and altered tracer-distribution was observed in 1/4 (25%) cases (popliteal uptake). Although our regression model did not reach statistical significance, our chi-square test underlined a significant difference ($p = 0.035$) between the degree of delay in tracer-drainage (early vs. late) and the resulting diagnosis (positive vs. negative), as did the presence of collateral pathways ($p = 0.081$). **Discussion/Conclusion:** This standardized lymphoscintigraphy technique, recently implemented in our centre, may provide reliable information about compromised limbs' lymph-drainage. Although only qualitatively interpreted, it seemed to accurately assess the severity of functional impairment. Further analyses are ongoing (including i.e. quantitative interpretative method reflecting transport kinetics) to clearly establish its diagnostic role and potential effect on patient management.

EP-0225

Diagnostic impact of pulmonary ventilation and perfusion SPECT/CT for differentiating lung diseases

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Objectives: Combined study of pulmonary ventilation and perfusion scintigraphy is helpful to differentiate pulmonary thromboembolism (PTE) from other pulmonary diseases. However, this diagnostic performance was measured mainly using free-breathing planar images, and the reliability of diagnosis may be limited. The purpose of this study was to estimate the diagnostic performance of combined pulmonary ventilation and perfusion SPECT/CT using short-time deep-inspiratory breath-hold (STDIBH) acquisition. **Materials and Methods:** Consecutive 75 patients with suspected PTE who underwent both STDIBH perfusion SPECT/CT (each breath-hold duration: 10 sec) and non-breath-hold ventilation SPECT were included in this study. Among these, 56 patients (35 men and 21 women, 57 ± 21 y) who solely have either PTE, pulmonary emphysema (PE), or pulmonary inflammatory disease (PID) were analyzed. Of these, 4 patients underwent a ventilation SPECT/CT test with CT attenuation correction (CTAC) and the remainder received a non-attenuation corrected (NAC) SPECT/CT test. Their diagnoses were confirmed based on the combination of clinical symptoms, serum D-dimer levels, CT pulmonary angiography, and pulmonary SPECT/CT. In the pulmonary ventilation SPECT or SPECT/CT images, %PVD was calculated by dividing ventilation defect volume (cut-off percentage for counts: 17% for NAC SPECT, 22% for SPECT/CT) in SPECT images by lung

volume in CT images. In the pulmonary perfusion SPECT/CT images, %PPD was calculated by dividing perfusion defect volume (cut-off percentage for counts: 31%) in SPECT images by lung volume in CT images. The percentage of ventilation to perfusion mismatch (%VPM) was calculated by subtracting %PVD from %PPD. The sensitivities and specificities for differentiating PTE from non-PTE, PTE from PE, and PTE from PID were measured using receiver-operating-characteristic curve analyses. **Results:** This study population included 28 patients with PTE, 12 with PE, and 16 with PID. While %VPM in PTE patients or PE patients was significantly higher than in PID patients [29 (16–48), 30 (18–46), 17 (8–26); $p = 0.048$, $p = 0.042$, respectively], that in PTE and PE patients did not differ ($p = 0.884$). The sensitivity and specificity of %VPM for differentiating PTE and non-PTE were low at 61.2% and 59.9%, respectively; the sensitivity and specificity of %VPM for differentiating PTE and PID were high at 70.3% and 81.7%, respectively. **Conclusions:** Detailed pulmonary ventilation to perfusion mismatch in PTE, PE, and PID patients was quantified calculating %VPM from pulmonary ventilation and perfusion SPECT/CT images. All analyzed disease may have recognizable VPM. Moreover, %VPM cannot differentiate PTE and PE patients.

EP-0226

Quantification of lower extremity lymphoscintigraphy

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Introduction: Lymphoedema is the abnormal accumulation of fluid within the soft tissue as a result of impaired lymphatic drainage. In order to differentiate from other causes of soft tissue oedema, lymphoscintigraphy is used as an invaluable diagnostic tool. It involves the intradermal injection of Tc-99m-nano-colloid at the feet with subsequent imaging of the limbs and body to assess the lymphatic drainage. We aim to use a method of quantification to aid the interpretation of this investigation.

Method: Data was obtained from Hermes and PACS for all patients who had undergone lymphoscintigraphy from 1st January 2014 to 31st December 2015. Only patients with lower limb lymphoscintigraphy were included in this study. In order to quantify the data, we compared the initial number of counts at the injection site to the number of counts at the iliac and inguinal nodes at the end of the study to determine a ratio. This data was then correlated with the diagnostic opinion of two expert consultant radionuclide radiologists to determine whether a cut off ratio could be used to aid in the diagnosis of impaired lymphatic drainage. **Results:** A total of 82 patients were identified, 11 had bilateral impaired lymphatic drainage, 25 had single leg impaired lymphatic drainage and 46 did not demonstrate impaired lymphatic drainage. Statistical analysis was performed using Graphpad prism version 5 applying the ROC analysis. This determined a threshold value of <7.5 ratio of feet to node activity for an abnormal result. This would result in a sensitivity of 79% and a specificity of 93% for impaired lymphatic drainage.

Conclusion: We have demonstrated a method of quantification in lymphoscintigraphy to aid the interpretation of this investigation.

EP-17

e-Poster Area

Neuroimaging: Neurology

EP-0227

Yoga practitioners have decreased glucose metabolism in midbrain, limbic and motor areas correlated to their experience: a simultaneous [¹⁸F]FDG PET-MR study

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Purpose/introduction: Yoga is becoming increasingly popular worldwide, with several physical and mental benefits. Under the hypothesis that yoga stimulates parasympathetic tone, it can be expected that it would lead to reduced neuronal activity and connectivity in motor and limbic brain areas. We therefore conducted a simultaneous [¹⁸F]FDG PET-MR cross-sectional study by comparing experienced yoga practitioners and yoga-naïve healthy subjects and relating metabolism to years of experience.

Subjects and Methods: Ten experienced yoga practitioners (8 women; age = 36.8±7.0 years) and 15 age-matched healthy controls (13 women; age = 34.6±9.7 years) were included in a prospective 2x2 design. On consecutive days, both groups underwent simultaneous [¹⁸F]FDG PET, resting state functional MRI (rs-fMRI), and diffusion tensor imaging (DTI) on a GE Signa 3T PET-MR, with baseline and intervention scan randomized. The intervention consisted of a 75min standard ashtanga yoga practice for the yoga group, and a 75min indoor cycling at moderate power (60–70% of max heartrate) including 30min stretching exercises for the control group. Static [¹⁸F]FDG-PET scans were acquired for 30min at 45min post-injection and regional cerebral metabolic rate of glucose (rCMRglu) images were calculated according to the Hunter method. [¹⁸F]FDG PET images were analysed using SPM12 ($P_{\text{uncorr}} < 0.001$) and volume-of-interest (VOI) approach using both N30R83 Hammers probabilistic and AAL atlases (PMOD v3.9). **Results:** At baseline, yoga practitioners showed a significant relative hypometabolism in the (para)hippocampus, insula, pallidum and midbrain, compared to controls (peak cluster difference -9%). Midbrain and parahippocampal glucose metabolism was correlated to the years of yoga experience ($r = -0.63$, $p = 0.049$ and $r = -0.65$, $p = 0.041$, respectively). A single yoga practice resulted in relative hypermetabolism in the cerebellum bilaterally (+5%) and decreased metabolism (-12%) in the temporal lobe and brainstem. In contrast, no metabolic differences were detected within controls after the physical exercise intervention. No robust differences were found in rs-fMRI or DTI between groups or conditions. **Conclusion:** [¹⁸F]FDG PET shows that yoga practitioners have highly significant hypometabolism in brainstem and limbic regions, that is correlated with the years of yoga experience. Furthermore, short-term effects of yoga practice were observed in brainstem, motor circuitry and temporal areas, but not in the active cycling control group. Reduced neuronal activity may be due to increased regional parasympathetic effects (e.g. controlled breathing induced) or indicate more efficient metabolic activity in experienced yoga practitioners. Further studies in yoga-naïve individuals that undergo prospective training are warranted to further investigate the causality of these findings.

EP-0228

Glucose metabolism in the hippocampus is negatively correlated with blood cholesterol level in geriatric patients with cognitive impairment of varying etiology

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Motivation/Aim: High blood cholesterol is a risk factor not only for cerebrovascular but also for neurodegenerative diseases. FDG PET is widely used to support the etiological diagnosis of clinically uncertain cognitive impairment. Aim of the present study was to test for possible associations between blood cholesterol and regional cerebral glucose metabolism as measured by brain FDG PET in a clinical sample of geriatric inpatients with cognitive impairment. **Methods:** The retrospective analysis included 86 inpatients (81.7 ± 5.4 y, 56 females) with newly manifested cognitive impairment during hospitalization in a geriatric unit for an acute indication. Brain FDG PET had been performed as part of a prospective study (ICTRP DRKS00005041). PET images were stereotactically normalized to MNI space using SPM8, then scaled to mean FDG uptake in brain parenchyma. Regional FDG uptake was obtained by applying standard ROIs predefined in the Automated Anatomical Labeling (AAL) atlas. Regional FDG uptake was tested for correlation with blood cholesterol level in all AAL ROIs except cerebellar and vermis ROIs. **Results:** Blood cholesterol ranged between 97 and 296 mg/dl (mean 185 ± 43 mg/dl). The strongest correlation between blood cholesterol and parenchyma-scaled FDG uptake was observed in the hippocampus in both hemispheres (left/right: Pearson correlation coefficient = $-0.330 / -0.270$, $p = 0.002 / 0.012$). Hippocampal FDG uptake was also correlated with LDL (left/right: $-0.280 / -0.213$, $p = 0.009 / p = 0.049$). The correlation between blood cholesterol and parenchyma-scaled FDG uptake in the left hippocampus remained a statistical trend after correction for gray matter volume of the left hippocampus (partial correlation coefficient = -0.210 , $p = 0.054$). It also remained a trend when corrected for both, gray matter volume of the left hippocampus and presence (versus absence) of cerebrovascular disease (partial correlation coefficient = -0.194 , $p = 0.077$). **Conclusion:** These findings suggest that high blood cholesterol is associated with lower glucose metabolism in cognitively impaired geriatric patients specifically in the hippocampus, independent of hippocampal atrophy and independent of the presence of prominent cerebrovascular pathology according to MRI. This is in accordance with previous studies demonstrating hypercholesterolemia to be an adverse factor promoting neurodegeneration.

EP-0229

Brain ¹⁸F-FDG PET/CT in early Diagnosis of Primary Progressive Aphasia (PPA) Variants

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Introduction: The correct diagnosis of PPA variants in early stage represents a crucial clinical point since Logopenic Apha-

sia (LPA) variant is related to AD, while Progressive non-Fluent Aphasia (PNFA) variant and Semantic variant (SV) might develop FTD. We evaluated ¹⁸F-FDG PET/CT usefulness in PPP variant early initial diagnosis. **Methods:** We investigated 31 consecutive patients, 16 with uncertain symptoms attributable to early PPA (Group A) and 15 with ascertained PPA but also with symptoms suspected for early AD or FTD (Group B). All patients underwent brain ¹⁸F-FDG PET/CT using GE Discovery tomograph. Images were evaluated both qualitatively and quantitatively with automated analysis program (Cortex ID, GE Healthcare); brain metabolic map and normal age matched control group comparative analysis was produced. **Results:** ¹⁸F-FDG PET/CT showed different degrees of cortical hypometabolism in the two Groups. Group A: widespread in 2/16 cases, bilateral temporo-parietal regions in 5/16, left frontal/parietal inferior regions in 5/16 cases, bilateral inferior-frontal and temporal regions in 2/16 and left inferior-frontal regions in 1/16. Group B: diffuse in 2/15 cases, bilateral frontotemporal and fronto-parietal regions in 6/15, bilateral temporo-parietal regions in 5/15 and bilateral temporal regions in 2/15. The eight Group A patients with hypometabolic areas only in inferior-frontal regions as well as in inferior-parietal and temporal regions were clinically classified as PNFA at risk to develop FTD, while the six patients with bilateral hypometabolism in temporo-parietal regions was classified as LPA, eventually anticipating AD. However, in the two patients with diffuse hypometabolism, diagnosis remained uncertain. The six Group B patients with hypometabolism in fronto-temporal and fronto-parietal areas and the two with hypometabolism in temporal lobe were considered PNFA and SV, respectively, both associated to FTD, while the five patients with temporo-parietal hypometabolism were classified as LPA associated to AD. However, diagnosis remained uncertain in the remaining two cases with diffuse hypometabolism. **Conclusions:** Our study evidenced brain ¹⁸F-FDG PET/CT elevated performance in early diagnosis of PPA different variants contributing to clarify clinical differential diagnosis in 87.1% of cases and concurring to define subsequent possible development in AD or FTD. However, brain ¹⁸F-FDG PET/CT could not clarify the four cases, belonging to two groups with diffuse cortical hypometabolism, in which the diagnosis remaining uncertain; in these cases, more accurate clinical and instrumental investigation and close follow up are necessary to achieve a correct diagnosis. A larger series of patients must be enrolled to confirm these preliminary data.

EP-0230

Intrastriatal analysis of FDOPA PET scans for differentiation of Parkinsonian Disorders

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Aim: L-3,4-dihydroxy-6-18F-fluorophenylalanine (FDOPA) PET allows quantification of presynaptic dopaminergic functioning *in vivo*. It assesses the function of nigrostriatal projection neurons, particularly dopamine release in the striatum. Previously, it was postulated that Idiopathic Parkinson's disease (IPD) preferentially affects the posterior putamen. This study aims to investigate

the potential of FDOPA PET scans to differentiate atypical parkinsonian disorders (APD), idiopathic parkinson's disease (IPD) and healthy controls. **Materials & Methods:** 58 patients (28 IPD, 13 APD and 17 controls) who underwent FDOPA PET scan as part of the clinical evaluation and who were diagnosed by movement disorder specialists, were retrospectively analyzed. Average age of IPD, APD and controls was 61.0, 69.6 and 65.4 respectively. All were scanned on a Siemens HR+ camera, with injected dose of 200MBq and pretreated with carbidopa, 2.5 mg/kg orally. After spatial normalization of images in standard MNI space (Montreal Neurological Institute), predefined sets of volumes of interest (VOIs) were used to sample values from striatum and the occipital reference region. Outcome values were striatal-to-occipital ratios (SOR), intrastriatal ratios and slope of multiple in-line spherical VOIs through the striatum anterior to posterior (gradient analysis). All values were compared between groups using ANOVA test and ROC curves were calculated. **Results:** SOR values showed no statistically significant difference between APD and IPD patients. When analyzing intrastriatal ratios, caudate-to-putamen was found to be statistically significant when comparing APD and IPD ($p < 0.001$; anterior putamen: 0.94 ± 0.06 vs. 1.05 ± 0.10 ; posterior putamen: 1.10 ± 0.12 vs. 1.26 ± 0.19 , respectively). Gradient analysis also showed statistically significant differences between APD and IPD ($p = 0.006$, 0.07 ± 0.05 vs. 0.12 ± 0.07). In ROC curve, separating controls from parkinsonian patients, the caudate-to-posterior putamen ratio showed the highest area under the curve ($AUC = 0.930$), while for differentiating APD from IPD the highest AUC was the caudate-to-anterior putamen ratio (0.824). **Conclusion:** SOR value is currently used in clinical routine to discriminate healthy from parkinsonian patients. However, results from this study have shown that the best value for this differentiation seems to be the caudate-to-posterior putamen ratio. In addition, caudate-to-anterior putamen is capable to discriminate between atypical and idiopathic parkinsonian patients. These results are in agreement with previous publications, and support the implementation of this ratios in clinical routine. Moreover, the positive results of the gradient analysis support further exploration of this approach, and its possibilities of creating a model that combines different image measurements and/or clinical information to improve the accuracy for discriminating APD and IPD.

EP-0231

Utility of 18F-Florbetaben PET/CT in patients with mild cognitive impairment and cerebrospinal fluid biomarkers non-conclusive: preliminary results

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Introduction/Purpose: The use of biomarkers has supposed a considerable advance in the clinical diagnosis of Alzheimer Disease (AD). In a proportion of patients CSF-biomarkers can

offer inconclusive results and it is in this subgroup that imaging biomarkers, such as amyloid PET with Florbetaben (FBB-PET/CT), can be especially useful. To evaluate the usefulness of FBB-PET/CT in patients with mild cognitive impairment (MCI), with inconclusive result in the determination of cerebrospinal fluid biomarkers (CSF). **Subjects and methods:** Observational and retrospective study (years 2015-2018), including patients with MCI and inconclusive results in the values of beta-amyloid (A β), total TAU (t-TAU) and phosphorylated TAU (p-TAU) determined in CSF (ELISA technique). It was considered a "non-conclusive" results when no congruence was found between A β , t-TAU and p-TAU; when they were in the limit of reference value, or when they were not consistent with the patient's clinic. For the FBB-PET/CT study, a dose of 296 MBq of FBB was administered with acquisition of the images at 90min-p.i.; (Siemens Biograph 16). **Results:** A total of 30 patients were included (60.3 ± 6.84 years, 16 men). The FBB-PET/CT was positive in 20 patients (66.7%). Result of biomarkers: A β positive in 17 patients (56.7%), t-TAU in 18 patients (62.1%) and p-TAU in 15 patients (50%). No significant differences were found in the mean values of the different CSF biomarkers between the positive vs. negative FBB-PET group. The behavior of the biomarkers was different in the group of patients with positive FBB-PET (positive result of A β in 13/20 (65%) patients, t-TAU 14/19 (73.7%) patients and p-TAU 11/20 (55%) patients), unlike the negative FBB-PET group (positive result of A β in 4/10 (40%), t-TAU 4/10 (40%) and p-TAU 4/10 (40%) of patients), although this difference didn't reach statistical significance ($p > 0.05$). The ROC curve analysis showed that the CSF biomarker that best correlates with the FBB-PET result was A β (AUC of 0.686, $p = 0.125$). **Conclusion:** In our series FBB-PET/CT has been clinically useful in the evaluation of patients with MCI and inconclusive CSF biomarkers in both senses: FBB-PET/CT result [+/-] or [-]; with a positive correlation between the levels of biomarkers in CSF and the result of the FBB-PET/CT, with the advantage of being a non-invasive technique.

EP-0232

Diagnostic Utility of CT-based Attenuation Correction in Brain SPECT/CT over Traditional Chang Method in Predicting the Exacerbation of Alzheimer Changes from Mild Cognitive Impairment utilizing a Voxel-Based Statistical Analysis

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Purpose/Introduction: In predicting the progression of Alzheimer's dementia from mild cognitive impairment(MCI), we sought to examine the diagnostic value of non-uniform CT-based attenuation correction (CT-AC) utilizing voxel-based statistical analysis in comparison to that of attenuation correction (AC) with Chang's method. **Material and Methods:** We retrospectively recruited two groups of elderly individuals with matched age, education and baseline mini mental state exam-

ination (MMSE) score. All of them were initially diagnosed as MCI with MMSE score of more than 24 by neurological specialists, and also underwent brain perfusion single-photon emission computed tomography (SPECT) with N-isopropyl-p-[123I] iodoamphetamine (IMP). Stable MCI (S-MCI) group was consisted of 11 patients who have maintained MMSE score (27.0 ± 1.6), and progressive MCI (P-MCI) group was consisted of 15 patients who have at least 3 or more decreased MMSE score from the baseline test (baseline score, 26.4 ± 1.7 and the latest score, 21.4 ± 2.0) during at least 1 year follow-up (mean 37.2 ± 16.7). All SPECT images were reconstructed using 3D-OSEM with both CT-AC and Chang's AC. Z-scores of gyri and lobules were calculated by voxel-based Z-statistics analysis referring to normal subject data base of our institution. In the two AC methods, the difference of Z-scores in lobes and lobules between P-MCI and S-MCI was examined using receiver operating characteristic (ROC) analysis. **Results:** To discriminate the two group with the extent of Z-score >1.65 in a single gyrus or lobule, the 5 highest area under the ROC curves (AUC) were seen in left middle temporal gyrus (0.855), left superior temporal gyrus (0.773), left cingulate gyrus (0.770), left uncus (0.764) and right cingulate gyrus (0.739) in CT-AC, and left middle temporal gyrus (0.821), left angular gyrus (0.764), right angular gyrus (0.745), left superior parietal lobule (0.730), and left superior temporal gyrus (0.730) in Chang's AC. When combining the all 5 gyri or lobules, AUC reached 0.909 in CT-AC and 0.812 in Chang's AC. If the best cut-off value was applied, sensitivity, specificity and accuracy of SPECT with CT-AC were 100%, 72.7% and 88.8%, respectively. As for Chang's AC, sensitivity, specificity and accuracy were 73.3%, 90.9% and 80.8%. **Conclusion:** To detect the progression of Alzheimer's disease from mild cognitive impairment, the voxel-based statistical analyses with non-uniform CT-based AC by integrated SPECT/CT might improve the diagnostic accuracy compared with the conventional uniform Chang's AC.

EP-0233

Long-term follow-up of amyloid brain deposition assessed by ^{11}C -PIB-PET/CT in patients with amnesic mild cognitive impairment: preliminary experience

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Aim: To assess the 5-year amyloid brain deposition changes in patients with amnesic mild cognitive impairment (a-MCI) and baseline positive ^{11}C -PIB PET/CT (PIB-PET). **Materials and methods:** Twenty-three consecutive a-MCI patients with a baseline positive PIB-PET were asked for a new PIB-PET 5 years later. Eleven patients underwent PIB-PET and in 12 it was not possible (7 bad clinical situation, 1 dead, 2 declined and 2 lost). General deterioration scale (GDS) was used to assess clinical situation. A static PIB-PET was acquired 60-90 min after the intra-

venous administration of 555MBq ^{11}C -PIB in patients (n=11) and in healthy controls (n=3). SUV regional indices were obtained in cerebellar, temporal, frontal, anterior cingulate, occipital, parietal and posterior cingulate cortex. Using the cerebellar cortex as reference region, SUVratios (SUVr) and global SUVratios (gSUVr) were obtained. Mean gSUVr and regional SUVr (rSUVr) were obtained and compared at baseline and 5-year follow-up. The percentage of increment of gSUVr at 5 years was calculated for a-MCI and healthy controls. **Results:** a-MCI patients showed an increase in cerebral ^{11}C -PIB retention compared with healthy controls over 5-year follow-up ($p < 0.01$). When amyloid brain deposition was globally compared at baseline and after 5-year follow-up, lower differences were found in the mean gSUVr. The analysis of mean rSUVr was as follows: temporal (1.7646 ± 0.3277 vs 2.2434 ± 0.6390) ($p < 0.05$), occipital (1.8160 ± 0.4050 vs 2.0921 ± 0.4887) ($p = \text{ns}$), frontal (2.0895 ± 0.4207 vs 2.5704 ± 0.6395) ($p < 0.1$), parietal (1.9292 ± 0.3612 vs 2.2966 ± 0.5876); anterior cingulate (2.2246 ± 0.4558 vs 2.5578 ± 0.5935) ($p = \text{ns}$) and posterior cingulate (2.2343 ± 0.3061 vs 2.6723 ± 0.534) ($p < 0.05$). The outcome at 5-year (n=11) was: 1 patient stayed as GDS 3, 2 progressed to GDS 4, 2 to GDS 4-5, 5 to GDS 5 and 1 to GDS 5-6. One healthy control progressed to a-MCI with PIB-PET positive. The percentage of increment of mean gSUVr at 5 years for a-MCI and healthy controls were 22.23% and 6%, respectively ($p < 0.01$) and no correlation between the percentage of increment of gSUVr and GDS was observed. **Conclusion:** a-MCI patients showed significant increase of ^{11}C -PIB uptake at 5-year follow-up compared with healthy controls. Compared to baseline, a slight global increase in cortical ^{11}C -PIB uptake over 5 years was detected. Regionally, that increase was in frontal, temporal and in the posterior cingulate areas. Further deeper analysis with more patients are ongoing after this preliminary experience.

EP-0234

Early cerebral blood flow scan from F-18Florbetapir. Provides useful extra-information in the evaluation of neurodegenerative disorders?

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Purpose: To evaluate whether early scan from F18-florbetapir could provide relevant cerebral blood flow information, complementary to amyloid plaque assessment, in neurodegenerative disorders. **Subjects & Methods:** Prospective longitudinal observational study of 18 patients with neurodegenerative disorder, without definitive diagnosis, submitted for a F18-florbetapir PET scan. Imaging acquisition: early blood flow scan from 1-10 min, and late amyloid plaque scan from 40-60 min, after intravenous injection of 370MBq of F18-florbetapir. Imaging analysis: both scan were evaluated visually by 2 experienced nuclear medicine physician and also using MIMneuro software for quantification. **Results:** A high level of interreader agreement was achieved, kappa index 0.80. Interobserver agreement percentage was 100% in positive amyloid PET studies. Correlation between visually and quantification analysis in late amyloid plaque

was also very high. Thirteen of eighteen late amyloid plaque scans were positive. Hypoperfusion of posterior cingulate and/or bilateral posterior parietotemporal lobes, increase the probability of Alzheimer disease (6 of 13 patients). In patients with early hypoperfusion of others brain regions as basal ganglia, frontal or occipital lobes, clinical revaluation and extra-studies were required. 2 Lewy body dementia were diagnosed. Five late amyloid scans were negative. 4 patients had also a normal blood flow scan and they remained still in clinical follow up. A patient with bilateral frontal hypoperfusion was finally diagnosed of frontotemporal dementia. **Conclusion:** Early regional cerebral blood flow scan provides complementary extra-information added to amyloid plaque late scan from F18-florbetapir, which helps in a better evaluation of neurodegenerative disorders.

EP-0235

Comparison Between Early-onset And Late-onset Alzheimer Disease Patients With Amnesic Presentation: A 18f-fbb Pet Study

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Background/Aims: To investigate the differences in amyloid burden in brain between patients with early onset of Alzheimer's disease (AD) (EOAD, aged ≤ 65 years) and patients with late onset of Alzheimer's disease (LOAD, aged > 65 years). **Methods:** We examined 60 patients with clinical diagnosis of Alzheimer's disease according to NINCDS-ADRDA criteria. Of them 22 were EOAD and 38 were above LOAD. All of them underwent a brain Positron Emission tomography 90 minutes after the injection of 18F Florbetaben (18F FBB; 300 ± 10 MBq). Qualitative analysis of PET data was positive for increased amyloid burden in brain in all of them. Differences in amyloid burden in brain between the groups have been evaluated by means of Statistical Parametric Mapping version 8, with the use of age, sex, Mini-Mental State Examination as covariates in the comparison between EOAD and LOAD. We performed a multiple regression for age using SPM8. **Results:** We did not find significant differences when comparing LOAD vs. EOAD patients. Multiple regression analysis did not show significant correlation between age of onset and amyloid deposition in brain. **Conclusions:** The results of our study suggest that amyloid burden in brain is not related to the age of onset of AD.

EP-0236

Amyloid burden identifies neuropsychological phenotypes of Mild Cognitive Impairment at increased risk of progression to Alzheimer's disease

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Purpose: The extent of amyloid burden associated to cognitive decline in amnesic Mild cognitive impairment is unknown.

Subjects & Methods: In this prospective study 66 participants with amnesic mild cognitive impairment underwent clinical, neuropsychological and PET amyloid imaging tests. Composite scores assessing memory and non-memory domains were used to identify two clinical classes of neuropsychological phenotypes expressing different degree of cognitive impairment. Detection of amyloid status and definition of optimal amyloid +/- cutoff for discrimination relied on unsupervised k-means clustering method. The primary aim of the study was to determine the extent at which amyloid burden is associated to the cognitive impairment. The secondary objective was to test the relationship between amyloid accumulation and memory or cognitive decline. **Results:** Threshold for identifying low and high amyloid retention groups was of $SUVr=1.3$. A β + participants showed poorer global cognitive and episodic memory performance than subjects with low amyloid deposition. A β positivity significantly identified individuals with episodic memory impairment with a sensitivity and specificity of 80% and 79% ($\chi^2=21.48$; $P<0.00001$). Positive and negative predictive values were 82% and 76% respectively. Amyloid deposition increased linearly as function of memory decline with a rate of 0.13/ point of composite memory score ($R=-44$, $P=0.0003$). **Conclusion:** The amyloid burden of $SUVr=1.3$ identify amyloid positivity in MCI. Being A β positivity associated to cognitive impairment and episodic memory decline, it thus allows to differentiate neuropsychological phenotypes at increased risk of progression to Alzheimer's disease from those with a lower likelihood of progression (Trial number, EudraCT 2015-001184-39).

EP-0237

ATN. A new biomarkers classification in Alzheimer's disease.

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Aim: To establish the usefulness of the amyloid deposition, tauopathy and neurodegeneration classification (ATN) in the diagnosis of Alzheimer's disease (AD). **Materials and methods:** 27 patients, 10 men and 17 women with an average age of 67.2 years They were performed a 18F-amyloid PET/CT study (PETa) (average dose 8.543mCi), magnetic resonance imaging (MRI), amyloid beta and protein TAU determination in cerebrospinal fluid (CSF) and 18F-FDG PET/CT. Patients were stratified according to the ATN classification that divides into three binary categories the seven known biomarkers of AD (Clifford, 2016). The variable that has the greatest influence on the decision of the final diagnosis and the influence of the findings on the modification of the initial diagnostic suspicion is identified. **Results:** According to the neuropsychological study and clinical symptoms, 8 of them were referred with high likelihood of AD, 6 with a diagnosis of depression refractory to treatment and 13 with a diagnosis of mild cognitive impairment (MCI) without labeling. After carrying out the proposed studies, they were classified as: A+T+N+ (n:2), A+T-N+ (n:2), A+TxN- (n:2), A+TxN+

(n:7), A-T+N- (n:1), A-T-N- (n:3), A-T+N- (n:3), A-TxN- (n:2), A-TxN+ (n:5) where x is data not available or not performed. The rates of true positive in A was 100%, with a chi-square correlation $\chi^2=20$ ($p<0.05$) according to the final diagnosis; in T was 66% with a $\chi^2=1.59$ ($p>0.005$, not significant that could be justified as a low sampling bias); in N categories was 81.3%, $\chi^2:13.07$ ($p<0.05$). In terms of modifying the initial diagnostic suspected, 100% of the patients referred with high likelihood of AD were confirmed as positive; those referred by DCL only 4/13 (32.5%) were labeled as AD; those referred with depression psychiatric disease 3/6 (50%) with A+ result were confirmed as AD and in the other 3/6 (50%) all of them with A-, AD was ruled out. **Conclusion:** The new classification of the AD based on ATN allows the characterization of patients with high likelihood of AD. According to our study A+ biomarker seems to be the category that provides highest reliability and weight in making diagnostic/therapeutic decisions.

EP-0238

¹⁸F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) and DaTSCAN® single-photon emission computed tomography (SPECT) in the diagnosis of dementia with Lewy bodies (DLB) - A quantitative analysis
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Introduction: DaTSCAN SPECT has been largely used in Europe as a diagnostic imaging method in movement disorders. FDG-PET imaging identifies typical patterns of cortical and subcortical hypometabolism in DLB, however, the visual diagnosis is sometimes challenging since there are other neurological diseases with similar patterns. The combination of both is a common approach in the diagnosis of DLB. Quantitative programs such as DaTQUANT for DaTSCAN and CortexID for FDG-PET can be of help when reporting these studies. Our aim is to see the degree of correlation between the quantification of the FDG-PET and DaTSCAN SPECT. **Materials and methods:** Retrospective review of 15 adult patients with a combined approach of FDG PET and DaTSCAN SPECT (From 2015-01-01 to 2018-02-12) and suspected diagnosis of LBD (For at least 1 yr). The FDG PET study was quantified using CortexID (GE, Healthcare) and the basal ganglia in the DaTSCAN SPECT using DaTQUANT, Xeleris 4.0 (GE, Healthcare). A score ranging from 0 to -2 was considered as "normal", from -2,1 to -4 as "mild" change, from -4,1 to -6 as moderate and from -6,1 to > -7 as severe according to the Z-score observed in the CortexID, taking the most pathological score as reference. For DaTQUANT a score ranging from +0,6 to -0,44 was considered as "normal", from -0,45-0,99 as "mild" change, from -1,0 to -1,79 as moderate and from -1,8 to > -3,3 as severe according to the most pathological score as reference. **Results:** The DaTQUANT showed 3 patients (20%) with mild changes, 4 (27%) with moderate and 7 (47%) with severe changes. One patient had no changes in the DaTQUANT (7%). With respect to the CortexID 8 patients (53%) showed mild changes, 4 moderate (27%) and 1 severe changes (7%) showed. Two patients (13%) had no changes in CortexID. These last 2 patients without changes detected by CortexID did showed mild changes in the DaTSCAN. **Conclusions:** There is not a strong correlation with

the severity of changes observed in the quantitative analysis of the DaTQUANT and in the CortexID. The results from DaTQUANT show that the DaTSCAN study will almost always be pathological (93%) and the detected changes more severe. When considering performing both studies, the DaTSCAN should probably be performed first. Pathological scores, in the borders of what is considered normal or pathological in quantitative studies, are challenging and should be correlated with visual findings. Larger studies are needed to confirm our results.

EP-0239

Quantification Of Amyloid Regional Burden Using 18F-Florbetaben PET For Clinical Assessment Of Alzheimer'S Disease In A Multidisciplinary Team Study
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Scope: to assess the impact of 18F-Florbetaben PET using a SPM MRI-less and AAL Atlas in correlation with clinical data, neuropsychological assessment and CSF analysis to diagnose Alzheimer's disease in-vivo. **Materials and Methods:** Forty-four patients with clinical evidence of dementia, underwent Amyloid-PET, were retrospectively evaluated by a MDT (neurology, nuclear medicine, radiology, neuropsychology and laboratory medicine physicians). Amyloid-PET images were processed with SPM and converted in standard space (MNI space) by normalizing them with tissue probability map as template. Automated anatomical labeling atlas was used to mask each VOI followed by extraction of SUVR, normalized on the cerebellum. The regional SUVR and scores from clinical and cognitive tests were used to create ROC curves and obtain the best thresholds for the clinical diagnosis. Leave-one-out cross-validation was carried out in order to validate the results. **Results:** A total of 26/44 patients showed elevated amyloid burden at Amyloid-PET scan. After integration with 18F-FDG PET, clinical data and CSF protein levels, 22 of them were classified by MDT as AD, the remaining 4 as vascular or fronto-temporal dementia. Among the variables ordered by area under curve (AUC), Amyloid and 18F-FDGPET (qualitative evaluation), CDR value 1, CSF Tau and p-tau levels presented the best true positive and true negative rates (Amyloid-PET: AUC= 0.85, sensitivity 0.91, specificity 0.79; 18F-FDG PET: AUC= 0.76, sensitivity 0.86, specificity 0.67; CDR 1 AUC 0.72, sensitivity 0.75, specificity 0.67; CSF-Tau: AUC=0.75, sensitivity=0.84, specificity=0.64; CSF p-TAU AUC 0.66, sensitivity 0.72, Specificity 0.65). At semi-quantitative

evaluation of Amyloid-PET a SUVR value of 1.006 in the inferior frontal cortex and a SUVR of 1.03 in the precuneus region were the best cutoff SUVR value and good correlation for the diagnosis of AD (inferior frontal cortex AUC 0.883; precuneus region AUC 0.826). By using two-tailed Pearson correlation between SUVR values of all brain region and neuropsychological tests, a significant moderate inverse correlation has been found especially for inferior frontal cortex and Attentive-memory test ($R=-0.455$; $p=0.008$), Rey Auditory-verbal learning Test ($R=-0.459$; $p=0.006$), Corsi-Span Test ($R=-0.408$; $p=0.017$), Raven Test ($R=-0.405$; $p=0.022$). Similarly, an inverse correlation was found also between precuneus brain region and Raven Test ($R=-0.420$; $p=0.017$) and rolandic operculum region and Rey Auditory-verbal learning Test ($R=-0.426$; $p=0.012$), Attentive-memory test ($R=-0.477$; $p=0.005$) and Corsi-Span Test ($R=-0.427$; $p=0.012$). **Conclusion:** Amyloid-PET, especially when using SPM normalized SUVR analysis, confirms high predictive power for the differential diagnosis of dementia over 18-F-FDG PET, neuropsychological tests and CSF analysis

EP-0240

Brain Perfusion Differences Between Behavioral Variant of Frontotemporal Dementia And Language Variants With Behavioural Impairments. A Spect Study With Brodmann Areas Analysis

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Purpose: Behavioural variant frontotemporal dementia (bvFTD) is characterized by behavioral alterations and executive impairment due to prefrontal cortex degeneration of the non-dominant (usually right) hemisphere. Progressive non-fluent aphasia (PNFA) and semantic dementia (SD) are characterized by non-fluent effortful speech and loss of semantic knowledge, anomia and single-word comprehension deficits, respectively. SD patients may present behavioural disorders similar to bvFTD, while in PNFA, although less frequently, socially inappropriate behaviours may emerge over time. The aim of our study was the evaluation of brain perfusion differences between bvFTD and SD-PNFA in specific Brodmann areas (BAs) of left(L) and right(R) hemispheres. **Subjects-methods:** We used the Diagnostic and Statistical Manual-IV (DSM-IV) and the Neary criteria for the clinical diagnosis, as well as a battery of neuropsychological tests including the mini-mental state examination (MMSE). We studied 60 right-handed patients (21 bvFTD, 12 PNFA, 27 SD, 17 men, 43 women, aged 62-68 years, MMSE=14-18). All the patients underwent a brain SPECT 20 min after the i.v. administration of 740MBq 99mTc-HMPAO. We applied the NeuroGam software on the reconstructed data, for the semi-quantitative evaluation of BAs perfusion. **Results:** Compared with SD, bvFTD patients had lower mean perfusion values in BAs 8LR (intermediate prefrontal), 9LR-46LR (dorsolateral prefrontal), 10LR (anterior prefrontal), 11R (orbitofrontal), 23R (ventral posterior cingulate), 32LR (ventral anterior cingulate), 44R (inferior frontal), 45LR (pars triangularis-inferior frontal), 47LR (inferior prefrontal). Multiple logistic regression analysis showed that 8R could discriminate SD from bvFTD. Compared with normal data base, statistically significant hypoperfusion in bvFTD patients with respect to SD patients, was found in BAs 6LR (premotor-supplementary motor cortex), 8LR, 9LR, 10LR, 11LR, 23R, 24LR-32LR (anterior cingulate), 44R, 45LR, 46LR (dorsolateral prefrontal cortex), 47LR. PNFA patients, compared to bvFTD, had lower mean perfusion values in BAs 25LR (subgenual cortex) and 28L (posterior entorhinal cortex). BA 25R could discriminate bvFTD from PNFA according to multiple logistic regression analysis. Compared with normal data base, statistically significant hypoperfusion in bvFTD patients with respect to PNFA, was found in BAs 9R and 10R, while BA 25R was found hypoperfused in PNFA patients with respect to bvFTD ones. **Conclusion:** Behavioural disorders in SD and bvFTD may be attributed to damage of different neuronal circuits. Impairment of BA 8R, as it was found in bvFTD, is associated with executive dysfunction and psychiatric symptoms. Right hemisphere hypoperfusion in PNFA has been rarely reported, based on the hypothesis of crossed aphasia and our results need further investigation.

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EP-0241

Clinical Impact of MR-based Attenuation Correction in Dementia Evaluation with ¹⁸F-FDG PET/MRI

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Purpose/introduction: Combined PET/MRI is a promising diagnostic tool in the evaluation of patients with suspicion of dementia. However, accurate attenuation correction (AC) of PET images is a prerequisite for calculation of z-scores, which is used to aid the diagnosis of dementia by comparing ¹⁸F-FDG uptake with statistical population databases of healthy controls. The aim of this study was to evaluate whether clinical available MR-based AC (MRAC) methods, in addition to a promising research MRAC method, have an impact on z-scores compared to CTAC. **Subjects & methods:** 17 patients with suspicion of dementia underwent an ¹⁸F-FDG PET/MRI brain examination subsequent to a PET/CT brain examination. Simultaneous to the PET acquisition, MR images for generating MRAC-maps were acquired (Dixon, ultra-short echo time (UTE), T1w MPRAGE) on the PET/MRI system. Five PET reconstructions were performed for each patient, one with CTAC (PET_{CTAC}) and four with MRAC (PET_{MRAC}): DixonNoBone (4-class: air, fat, soft tissue, (lung)), DixonBone (5-class: air, fat, soft tissue, continuous bone from an atlas-based bone template, (lung)), UTE (3-class: air, soft tissue, bone), and UCL (University College London) (continuous pseudo CT, not clinically available). Z-scores for all PET reconstructions were calculated in Cortex ID (GE Healthcare, Waukesha WI, USA) in 26 brain regions, with pons and cerebellum as reference regions. The z-scores from the four PET_{MRAC} reconstructions were quantitatively compared to z-scores from PET_{CTAC} (Wilcoxon signed

rank test, $p < 0.01$, MATLAB). **Results:** With pons as reference region, PET_{UCL} had the smallest absolute deviation in z-score from PET_{CT} in the brain regions on average ($0.14 \pm 0.06 \sigma$), and the deviation was increasing for $PET_{DixonBone}$ ($0.43 \pm 0.15 \sigma$), $PET_{DixonNoBone}$ ($0.50 \pm 0.24 \sigma$), and PET_{UTE} ($0.89 \pm 0.18 \sigma$). The same tendency was also found when using cerebellum as reference region, but with smaller differences between the MRAC methods and the CTAC method (PET_{UCL} : $0.11 \pm 0.05 \sigma$, $PET_{DixonBone}$: $0.19 \pm 0.15 \sigma$, $PET_{DixonNoBone}$: $0.25 \pm 0.23 \sigma$, PET_{UTE} : $0.45 \pm 0.24 \sigma$). All MRAC methods gave z-scores significantly different from CTAC. **Discussion/conclusion:** UCL was found to be the best MRAC method in evaluation of dementia with ^{18}F -FDG PET/MRI, while DixonBone was found to be the best clinically available MRAC method. The differences in z-scores between MRAC and CTAC were smallest with cerebellum as a reference region. It should however be evaluated whether these differences in z-scores between CTAC and MRAC will affect the clinical diagnosis of dementia.

EP-0242

Digital PET/CT compared to analog PET/CT in ^{18}F -Flutemetamol studies.

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Aim: To assess the quality image of digital PET/CT compared to analog PET/CT to differentiate between gray and white matter in ^{18}F -Flutemetamol studies and to optimize the image acquisition procedure. **Material and methods:** Twelve consecutive patients underwent dual imaging with digital PET/CT (Philips Vereos) and analog PET/CT (Philips Gemini TF) after the i.v. injection of 185MBq of ^{18}F -Flutemetamol. Seven patients underwent scans on the analog PET/CT (60 minutes after the i.v. injection with 15 minutes of acquisition duration) and then followed by the digital PET/CT (90 minutes after the i.v. injection with 20 minutes of acquisition duration). In the remaining 5 patients, we performed the reverse, first they underwent digital PET/CT (60min after i.v. injection with 15 min of acquisition duration) and then analog PET/CT (90 min after i.v. injection and 20 min of acquisition duration). The parameters reconstructions were similar in the two scanners (LOR RAMBLA 3it33subsets, 2mm). Three independent readers reviewed the 2 sets of PET/CT images for differentiation between grey and white matter on a binary scale (0 good differentiation and 1 poor differentiation), and for overall image quality on a 1-5 scale (1 poor and 5 excellent) based on the pixilation, noise and resolution. **Results:** In all patients the digital PET/CT image quality improves compared to analog PET/CT (mean 4,3 vs 3,1, Wilcoxon signed-rank test < 0.02). No differences were observed in the image quality between early and late acquisition duration. The Flutemetamol images in 3 of the 12 patients were considered negative (good differentiation between grey and white matter) and in the remaining 9 were considered positive (poor differentiation) by the three readers regardless the acquisition time, time of duration of the scan and

the type of scanner used. **Conclusion:** Digital PET/CT provides better image quality to differentiate between grey and white matter in ^{18}F -Flutemetamol studies compared to analog PET/CT, regardless the acquisition time or time of duration of the scan, without improving the diagnostic accuracy.

EP-0243

Prefrontal Activation After Group Psychotherapy in Alzheimer's Disease Patients.

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Introduction: Stimulation of the compensatory response of the brain through non-pharmacological interventions can provide a valuable complementary alternative to drug therapy to improve the quality of life of patients with Alzheimer's disease (AD) and their caregivers. **Aim & Methods:** The aim of the study was to evaluate the effects of a group psychotherapeutic intervention designed for patients with AD on brain function. Subjects and Methods: 11 patients with mild to moderate AD (Age 64-86 ys, mean 75.5; 7 female; 3 or more years of formal education; GDS stage 5 or less with preserved language, without behavioral disorders; non-institutionalized) and 18 family caregivers participated in 27 sessions of group psychotherapy of 75 minutes during 7 months. Cognitive, psychological and functional brain imaging (^{99m}Tc -ECD SPECT) evaluations were conducted immediately before and after the intervention (mean follow-up of 9 months). AD diagnosis was based on probable AD criteria supported by a consistent brain SPECT pattern. Paired t-tests were used to compare conditions. Images were analyzed in SPM8. Uncorrected p values lower than 0.001 at the voxel level and 0.05 at the cluster level were considered significant. Trends were also reported at $p < 0.01$ for clusters greater than 100 voxels. **Results:** No significant differences were found in MMSE (18.6 ± 5.5 vs 18.2 ± 5.5 , mean $\pm$ SD; $p = 0.66$), ADAS-cog (24.3 ± 10.5 vs 23.2 ± 10.6 , $p = 0.29$), NPI-Q (7.7 ± 15.1 vs 5.4 ± 14.2 , $p = 0.67$) or Zarit caregiver Burden Interview (26.6 ± 15.6 vs 24.5 ± 16.5 , $p = 0.62$). SPECT showed a cluster of progression in left posterior temporoparietal cortex ($kE = 223$, $p = 0.073$), consistent with the natural course of AD. Significant clusters of activation after therapy were detected in right dorsolateral prefrontal and inferolateral frontal cortex ($kE = 2643$, $p = 0.000$ corr.) and bilateral dorsal anterior cingulate ($kE = 697$, $p = 0.004$ uncorr.). A trend to activation was present in left dorsolateral prefrontal cortex. Prefrontal activations might be related with brain plasticity phenomena, an attempt to compensate for the impaired brain function in the posterior cortex in early clinical stages of AD. The absence of significant changes in cognitive tests during the period of the study may also support this hypothesis. **Conclusion:** Prefrontal activations in early stages of AD can represent compensatory mechanisms underlying cognitive plasticity that may be stimulated by psychotherapeutic and psychosocial interventions. Studies including control groups are needed to clarify to what extent these changes are a direct consequence of the intervention or a natural response to the pathological process of AD.

EP-0244**Prospective comparative evaluation of brain with F-18 FDG PET/CT in diabetics and non-diabetics to look for Alzheimer's like reduction in brain glucose metabolism in diabetics in Indian population group**

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Aim/introduction: Type 2 diabetes and Alzheimer's disease (AD) are chronic diseases. Chronic hyperglycemia and cerebral microvascular disease may contribute to neuronal damage, brain atrophy and cognitive impairment. The management of AD depends on early diagnosis. Several studies using PET scan reported reduction in glucose metabolism in posterior cingulate gyrus, precuneus and parietal cortices even before the clinical diagnosis of probable AD. Few studies suggested presence of AD like pattern in diabetics on FDG brain PET. There is no literature of such studies available on Indian population, hence, decided to do the study to see the Alzheimer's like pattern in brain on FDG PET scan in diabetic Indian population. **Subjects & Methods:** Diabetic (n=39) and non-diabetic (n=39) adult patients (age group 43-87 years) were included in the study. Mini Mental Status Examination (MMSE) was done prior to FDG PET scan in every patient. Each patient underwent dedicated brain PET scan in addition to the whole body FDG PET/CT scan for which they were referred. Patients with known neurological disease or structural abnormalities on CT scan were excluded from the study. Images were processed using CORTEX-ID application in automatic 3D-stereotactic surface projection (3-D SSP) comparison to age matched normal. PET to PET Regional hypometabolism normalized by thalamus in different projections were recorded. Appropriate statistical tests of significance were applied. **Results:** AD like pattern in brain on FDG PET scan was seen in 2 patients in Indian diabetic group (5.1%). Rest of the 37 diabetic patients didn't show AD like pattern (94.9 %). We didn't see AD like pattern in any non-diabetic control group patient. Abnormal but no AD type pattern was seen in 41% of brain scans in the diabetic group (25.6% abnormal scan but no AD type pattern in non-diabetic control group) with mainly global hypometabolism - were suggestive of depression. Mean MMSE score was 25.28 in diabetic group and 26.82 in non-diabetic control group. In this study, statistically significant association was not observed between Alzheimer's like pattern on FDG Brain PET and diabetes (p value 0.494). **Conclusions:** No significant incidence of an 'Alzheimer's like pattern' found on FDG brain PET images on Indian diabetic population.

EP-0245**Brain Spect Perfusion In Bad Responder Psychiatric Patients**

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Introduction: Nowadays, the use of functional neuroimaging as Brain Perfusion SPECT (BPS) in psychiatry is getting attention. Especially, BPS might be helpful identifying or discarding

neurodegenerative diseases that could overlap with psychiatric disorders (PD) in patients with a bad response to conventional therapies. **Aim:** To evaluate the role of BPS in psychiatric patients in our health area. **Methods:** We reviewed all psychiatric adult bad-responders patients referred by their specialists to perform a BPS from April of 2007 to September of 2016 selecting 202 patients, 129 with depressive disorder (DD), 46 with psychotic disorder (PSD) and 27 with bipolar disorder (BPD). In all of them a BPS was performed after the ev administration of 740 MBq of Tc99m-HMPAO employing two dual-head gammacamaras. 64 images were acquired, 20 seconds each one using 128 x 128 matrix. Chang attenuation was employed. The studies were reported in a qualitative way. No quantification was performed. Findings were divided in four main scintigraphic patterns: normal, cerebrovascular, Alzheimer and frontotemporal. We collected the BPS reports in the different disorders and the induced changes in the management of patients. **Results:** The scintigraphic patterns founded by the 202 BPS were: 99 (49%) normal, 37 (18%) cerebrovascular, 40 (20%) frontotemporal and 26 (13%) Alzheimer's patterns. BPS was pathological in 103 out of 202 patients (51%). The distribution of these patterns in the different PD was: In the DD patients the patterns founded were 52% normal, 15% cerebrovascular, 16 % frontotemporal and 19% Alzheimer's. In PSD the patterns found were: 41% normal, 29% cerebrovascular, 27% frontotemporal and 4% Alzheimer's. In BPD the patterns described were: 49% normal, 17% cerebrovascular and 29% frontotemporal patterns; no Alzheimer's patterns were found. **Conclusion:** BPS is a useful tool for the study of bad-responder psychiatric patients and could potentially change their management in half of them. All BPS patterns founded were similar in frequency in all PD except Alzheimer's pattern that was more frequent in DD.

EP-0246**Functional Evaluation Of Primary Auditory Cortex In Normal Subjects And Alzheimer Disease**

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Background: Age related hearing loss (presbycusis) is a gradual, irreversible, bilateral and symmetrical sensorineural hearing loss, resulting from degeneration of the cochlea or associated structures of the inner ear or auditory nerves and is often associated with Alzheimer Disease (AD) and incident cognitive impairment in older adults. People affected by AD generally undergo to acoustic prosthesis, often without clinical improvement. Sensory impairment is related to increased risk of dementia. The present study is aimed to investigate a) differences in auditory stimuli processing (as detectable by means of ¹⁸F FDG PET/CT) and b) connectivity of primary auditory cortex in AD patients and normal subjects. **Materials and methods:** We examined

131 newly diagnosed AD patients (mean ($\pm$ SD) age 70 ($\pm$ 7 years); 74 males, 57 females) according to the NINCDS-ADRDA criteria and a control group (CG) of 36 subjects. A complete clinical investigation, including medical history, neurological examination, mini-mental state examination (MMSE) and a complete neuropsychological evaluation was conducted in both groups. All AD patients were taken off cholinesterase inhibitor treatment throughout the study. All the subjects underwent a brain PET/CT after the injection of ~ 185 MBq of ^{18}F FDG. Statistical Parametric Mapping (SPM 8, implemented in Matlab 2015b) was used in order to investigate differences in brain glucose consumption between AD and CG. A selected inclusive mask that included the primary auditory cortex was generated (WFU Pickatlas[®]) and then used for a two sample t-test comparison. Then, cortical ^{18}F FDG activity was extrapolated and normalized for the counts of the cerebellum and then used as a regression factor in SPM8 for the connectivity analysis using gender, age and MMSE as covariates. **Results:** AD subjects vs. CG showed a reduced glucose consumption in BA 6,7,8,39, whereas we did not find significant differences in primary auditory cortex. Connectivity analyses showed a significant positive correlation of primary auditory cortex in AD with BA6,8,21,31,39,40,42 (P fwr and fwe corr $<0,001$; k_e 565–6347) and a negative correlation with BA19, cerebellum, basal ganglia (P fwr and fwe corr $<0,001$; k_e 607–2034). In CG a positive correlation of primary auditory cortex was reported in with BA10,22,32,39,42 (P fwr and fwe corr $<0,001$; k_e 1550–3948) **Conclusions:** the results of our study suggests that primary auditory cortex metabolism and its connectivity is not affected by AD. The connectivity with cortical areas whose hypometabolism is significant in AD may affect the processing of acoustic stimuli and, consequently, acoustic prosthesis may lead to limited benefits.

EP-0247

Combined FDG PET and event-related potentials study of the cognitive impairment mechanisms in patients with Parkinson's Disease

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Different neuroimaging techniques allow researcher to study the pathogenesis of neurodegeneration from different point of view that is of great importance for its understanding and early diagnostics of cognitive impairment.

Objective: The study was aimed to matching the positron emission tomography with ^{18}F -fluorodeoxyglucose (FDG PET) and event-related potentials (ERP) data in patients with Parkinson's Disease (PD) with and without cognitive impairment. **Methods:** We implemented FDG PET (standard protocol) and ERPs during the execution of the two-stimulus task in the Go/NoGo paradigm in 40 patients with PD and age-matched healthy control group. Application of the novel method of blind source separation to the ERPs allowed to isolate latent components of the ERPs which are generated in specific regions and assumed to reflect various cognitive processes. To evaluate cognitive state, the Mini-mental state examination (MMSE) and the Frontal assessment battery (FAB) were used. **Results:** In PD patients, ce-

rebral glucose metabolism was decreased in frontal (Brodmann areas (BA) 9-11,46,47), parietal (BA 39), temporal (BA 20,37), and cingulate cortex (BA 32) compared to the control group. In the group of cognitively impaired PD patients glucose metabolism was decreased in the frontal (BA 8-10, 45-47), parietal (BA 7,39,40) and cingulate cortex (BA 23,24,31,32). The analysis of ERPs in PD patients revealed decrease of P300 amplitude in Go and NoGo conditions compared to controls. Also changes in the amplitude of latent components generated in the occipital, inferior temporal, parietal and frontal cortex were revealed. These components are supposed to reflect the stages of visual stimuli processing and operations of the executive system. Correlations were found between P300 amplitude of ERP in NoGo condition and CMRglu in frontal (BA 8-11), parietal (BA 7,39,40), temporal (BA 20,21,37), and cingulate cortex (BA 32), $r=0.4-0.5$; $p<0.05$.

Conclusion: The analysis revealed that ERP amplitude decline was accompanied with the decreased glucose metabolism in several cortical areas associated with cognitive impairment in PD. Correlations of glucose metabolism in these areas with ERP amplitude in NoGo condition confirm the important role of executive functions decline in the pathogenesis of cognitive impairment in PD.

EP-0248

C9orf72-related fronto-temporal dementia: clinical and neuroimaging features as compared to the sporadic form

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Purpose: The C9orf72 pathogenic GGGGCC hexanucleotide repeat expansion is one of the most common causes of frontotemporal dementia, in particular the behavioural variant (bvFTD). In contrast to the sporadic form (sFTD), bvFTD patients with C9orf72 expansion (C9orf72-FTD) often show a more malignant prognosis, and an association with motor symptoms. Our aim is to identify the brain metabolic profile of patients with C9orf71-FTD as compared to sFTD, and to understand how the C9orf72 metabolic profile interact with the clinical variables in order to predict the C9orf72 expansion in bvFTD patients. **Method:** 38 bvFTD (13 with -C9orf72-FTD- and 25 without C9ORF72 expansion - sFTD) patients were included in the study. Among them, 28 subjects underwent FDG PET. We analyzed the differences between these groups and with 25 cross-matched neurologically normal controls. **Results:** sFTD patients showed significant hypometabolism in anterior cingulate, medial frontal and anterior temporal cortices, as compared to controls. C9orf72-FTD patients showed a widespread hypometabolism involving all frontal regions, caudate nuclei and thalamus, as compared to controls. Moreover, C9orf72-FTD patients showed significant hypometabolism in dorsolateral prefrontal cortex and thalamus as compared to bvFTD patients. This metabolic profile, in association with the presence of positive family history and motor symptoms, was capable to correctly classify almost 90% of the patients. **Discussion:** bvFTD with C9orf72 expansion had a more widespread cerebral involvement than sFTD patients, involving

in particular frontal lobes. This metabolic signature, combined with other clinical characteristics, could be used to identify bvFTD patients eligible to genetic testing.

EP-0249

The role of ^{123}I -MIBG myocardial scintigraphy in the differential diagnosis of different forms of Parkinsonism

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Aim: The differential diagnosis in neurodegenerative parkinsonism is usually established through certain clinical criteria, however in the early stage, it remains challenging. ^{123}I FP-CIT (DaTscan) is a highly sensitive technique for imaging nigrostriatal dopaminergic degeneration but it is not specific enough to distinguish amongst different types of neurodegenerative parkinsonism (multiple system atrophy-MSA, progressive supranuclear palsy-PSP, corticobasal degeneration-CBD, Lewy body dementia-LBD). ^{123}I -MIBG myocardial scintigraphy displays the functional status of cardiac sympathetic nerves, which is reduced in Parkinson disease (PD) and normal in atypical parkinsonian syndromes and secondary parkinsonism. The aim of the study is to evaluate the impact of ^{123}I -MIBG on a) the final diagnosis of patients with clinically uncertain parkinsonian syndromes and b) the differential diagnosis of PD from other parkinsonisms. **Material-Methods:** During the last 10 years, a total of 473 patients underwent ^{123}I FP-CIT for the differential diagnosis between parkinsonism and essential tremor (ET). DaTscan was abnormal in 196/473 and normal in 277/473. The differentiation of PD from other forms of parkinsonism was not feasible through clinical criteria in 33/473 cases. Therefore they underwent ^{123}I -MIBG myocardial scan. Anterior planar images of the chest were obtained at 10min and 4hours p.i. For semiquantitative analysis, ROIs over the heart and upper mediastinum were used and heart to mediastinum (H/M) uptake ratio was calculated. The reference cut-off values were H/M (10min): 1.48 and H/M (4hr): 1.43. Patients had no medical condition or therapy that could interfere with the results. **Results:** The ^{123}I -MIBG myocardial uptake was reduced in 15/33 and normal in 18/33 patients. The final diagnostic findings of combined imaging modalities (DaTscan and MIBG) were in full agreement with the clinical diagnosis in 28/33 patients (8/11 PD, 9/10 MSA, 1/1 PSP, 3/3 DLB, 1/2 ET, 1/1 drug-induced parkinsonism, 1/1 frontotemporal dementia, 2/2 dystonia, 2/2 dysautonomia). There was disagreement in 3/11 with PD, 1/11 with MSA and 1/2 with ET. **Conclusion:** ^{123}I -MIBG myocardial scintigraphy provides a complementary imaging technique to ^{123}I FP-CIT in making the correct diagnosis of parkinsonism and differentiating between PD and other forms of neurodegenerative parkinsonism.

EP-0250

A Comparison of Dopamine Active Transporter (DAT) Quantification Applications (HERMES BRASS v2.5 and GE DaTQUANT v1.01

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Aims: Quantitative assessment of DAT has proved valuable for many centres across the UK as it provides clinicians with greater confidence in differentiating Parkinson's disease. Two commercial semi-automated DAT scan applications were made available to Guy's and St Thomas' Hospital (GSTT); HERMES BRASS v2.5 and GE Healthcare DaTQUANT v1.01 which both use the results of the ENC-DAT project (EANM Research Ltd) to define the normal database. This work compares the quantification and use of the two programmes. **Methods:** Tomographic acquisition data from a set of 50 patients (21 originally reported as normal and 29 abnormal) were retrospectively processed on BRASS and DaTQUANT. The images were iteratively reconstructed with no scatter or attenuation correction within the applications to match the reconstruction parameters for each of the normal databases. An assessment of the Specific Binding Ratio (SBR) and z score of the left and right putamen and caudate was performed. A z-score threshold of more than 2 standard deviations was defined as an abnormal scan. **Results:** There is excellent linear agreement between both the specific ratios and z-scores of each anatomical region (average $R^2 = 0.93 \pm 0.004$). However a systemic difference is observed with HERMES BRASS giving an overall higher the specific ratio and the subsequent z-score when compared to GE DaTQUANT. This was observed using Bland-Altman plots of the difference in specific binding ratio for each anatomical region. The lines of equality do not lie within the 95% confidence interval of the mean differences (mean difference = 0.44 and SD = 0.21). The plots show increases in differences with mean SBR for both putamen regions. No significant correlation was observed for both caudate regions. A retrospective comparison found 8 cases for HERMES BRASS and 6 cases for GE DaTQUANT of which the z-score threshold of 2 SD for abnormal scans did not correspond to the original Nuclear Medicine clinical report. Practically, it was found that GE DaTQUANT required less steps during post processing as the reconstruction and calculations were performed in one application. However with HERMES BRASS, acquisition images had to be reconstructed and aligned using HERMES Hybrid Recon-Neurology application before quantification could be done in BRASS. **Conclusions:** Processing time was reduced when using GE DaTQUANT. The systematic difference between the two applications must be considered when defining abnormal scans as 2 standard deviations.

EP-0251

Evaluating the role of Brain SPECT imaging in the Diagnosis and Treatment of Traumatic Brain Injury

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Introduction: Traumatic brain imaging (TBI) is defined as an alteration in the brain functions resulting from a blunt or penetrating force to the head. Common manifestations include confusion, seizure, coma, focal sensory, altered level of consciousness etc. Stem cell therapy is emerging as a promising therapeutic option for the treatment of TBI. We evaluated the clinical utility of single photon emission computed tomography (SPECT) in TBI. **Subjects and Methods:** In the present study, seven patients with TBI were treated with human embryonic stem cell (hESC) therapy. A baseline SPECT was done following intravenous injection of Tc99m ECD to identify areas of hypoperfusion. The patients underwent hESC therapy in gap periods to allow stem cells to grow, repair and regenerate the affected area. Subsequent Brain SPECT after a gap phase of 4-6 months was done to evaluate interval changes. **Results:** The results were elaborated as mild improvement when 10%- 30% changes were noted, moderate improvement when 30%-60% changes were noted and significant improvement when 60%-90% changes were noted. Following the treatment, all the seven patients showed significant changes and improvement in their clinical condition. No adverse event was reported during the course of therapy. **Conclusion:** Brain SPECT is an extremely useful tool in monitoring the treatment response to stem cell therapy in patients of traumatic injury. It showed changes at the molecular level, hence indicating improvement even before the clinical changes were manifested. Despite the positive results, this investigation needs further research in order to understand the clinical utility of hESC therapy.

EP-0252

Different Patterns Of Brain Glucose Consumption In Alzheimer Disease. Is Cerebral Glucose Metabolism Related To Epsilon Phenotype?

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Aim: The aim of our study was to investigate the impact of epsilon phenotype in brain glucose consumption in a population with Alzheimer disease. **Materials and methods:** Statistical Parametric Mapping (SPM8) was used in order to investigate differences in brain glucose consumption (as detectable by means of ¹⁸F FDG PET/CT) in the population examined. A total of 140 patients (77 females and 63 males) with a diagnosis of probable AD according to the NINCDS-ADRDA criteria underwent the PET/CT examination. The mean (SD) age of the patients was 70 (± 7) years; mean mini mental state examination was 19(±5.6). 59 expressed epsilon 4 phenotype (E4), 70 the epsilon 3 phenotype (E3) and 12 the epsilon 2 phenotype. Cerebro spinal fluid amyloid, tau and t-tau have been measured resulting equal to 367.4 (±149.1), 584.7 (±312.1) and 79.2(±45.9)

pg/ml respectively. Age, sex, MMSE, scholarship and CSF parameters were used as covariate in the SPM analyses. **Results:** We did not find significant differences in age, gender, MMSE and CSF values among groups. As compared to E3, E4 subjects show a significant reduction of brain glucose consumption in frontal lobe bilaterally and in the right insula (BA 47, 11, 13). As compared to E2, E4 showed a reduction of brain glucose consumption in the left frontal lobe (BA6). As compared to E4, E3 subjects showed a significant reduction of brain glucose consumption in right parietal lobe (BA7, 40). We did not find significant differences in brain glucose consumption when comparing E3 vs. E2 and when subtracting E2 to E4. **Conclusions:** epsilon phenotype is related to different metabolic patterns in Alzheimer Disease. In particular, E4 is related to a major involvement of frontal cortex while E3 is related to a major involvement of parietal cortex in AD.

EP-0253

Brain 18 F FDG Abnormalities In Neurobechet Disease

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Objectives: Neuro-Behçet's disease (NBD) is a relatively uncommon but potentially life-threatening manifestation in individuals affected Behçet's disease (BD). Despite the well-established usefulness of magnetic resonance imaging (MRI), patients may present with neurological symptoms unexplained on the basis of MRI findings. Aim of this preliminary study was to investigate brain glucose consumption in a selected population of patients with NBD by means of 18F-FDG positron emission tomography/computed tomography (PET/CT) scan. **Methods:** Three groups of subjects were recruited: A) NBD patients (n = 6); B) BD patients (n = 7); C) Healthy subjects (n = 17). Relevant clinical data were collected before performing ¹⁸F-FDG PET/CT scan. **Results:** As compared to healthy subjects, NBD patients showed a significant reduction of brain glucose consumption in left and right cingulate gyrus. At a sub-cortical level, we found a significant reduction of brain glucose consumption in right brainstem. As compared to BD patients, NBD showed a significant reduction of brain glucose consumption in right and left parahippocampal gyrus and in right posterior cingulate cortex. We did not find significant difference in brain glucose consumption when subtracting BD to CG and vice versa. **Conclusion:** Our data, although limited by the explorative, proof-of- concept nature, suggest that cerebral glucose metabolism abnormalities, detected by means of ¹⁸F-FDG PET/CT, may represent a distinctive feature of NBD patients. Notably, these findings are independent of the MRI-evident lesion sites in individual patients and therefore may underlie a different, preclinical, pathophysiological phenomenon.

EP-0254**Nigrostriatal degeneration in the cognitive part of the striatum in Parkinson's disease is associated with frontomedial hypometabolism**

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Aim: Cognitive decline in Parkinson's disease (PD) is associated with nigrostriatal degeneration, especially in the ventral "cognitive" subdivision of the striatum. The relationship between nigrostriatal degeneration and its brain metabolic correlates is, however, not fully understood. The present study examined the association between cerebral glucose metabolism according to brain FDG PET and the specific FP-CIT binding ratio (SBR) in striatal subregions defined by cortico-striatal connections with emphasis on cognitive striatal associations. **Methods:** The retrospective study included 41 patients (61.4 ± 12.8 y, 17 females) with PD-typical reduction of striatal FP-CIT SBR and no sign of atypical neurodegenerative parkinsonian syndrome (MSA, PSP, CBD) or other disease than PD or PDD or LBD in brain FDG PET. SBR reduction was more pronounced in the left hemisphere in 22 patients. SPECT and PET of the remaining patients were left-right flipped so that DAT reduction was more pronounced in the same (left) hemisphere in all patients. FP-CIT SBR was determined in the cognitive (=executive+limbic) part of the left striatum according to the Oxford-GSK-Imanova Striatal Connectivity Atlas based on cortico-striatal connections derived from diffusion weighted MRI and probabilistic tractography in healthy subjects. FDG PET images were stereotactically normalized to MNI space using SPM8, smoothed with an isotropic Gaussian kernel of 16 mm FWHM, and scaled to mean voxel intensity in brain parenchyma. Scaled FDG uptake was tested voxelwise for correlation with FP-CIT SBR including both cognitive and sensorimotor SBR in the same multiple regression model (uncorrected $p < 0.001$ or fwe-corrected $p < 0.05$; cluster volume ≥ 1 ml). **Results:** Positive correlation between FDG uptake and cognitive SBR (corrected for sensorimotor SBR) was observed in bilateral medial frontal cortex including anterior cingulate cortex, left caudate and left thalamus. After correction for multiple testing only the correlation between FDG uptake in the bilateral medial frontal cortex and anterior cingulate cortex remained significant. **Conclusions:** The observed association between nigrostriatal degeneration in the cognitive part of the striatum and altered cerebral glucose metabolism in PD was restricted to the medial parts of the frontal cortex including the anterior cingulate cortex. This might be a biological correlate of impaired inhibitory control in PD, as previous fMRI studies demonstrated that inhibitory control is associated with functional connectivity between the anterior putamen and the frontomedial cortex.

EP-0255**Assessment of the incremental diagnostic value of ¹²³I-loflupane brain imaging in patients with uncertain parkinsonian syndrome: a single-center experience in a large population**

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Introduction: in parkinsonian syndromes (PS) nigrostriatal projections loss gives a decrease of dopaminergic transporters (DAT). Brain single photon emission computed tomography (SPECT) with ¹²³I-loflupane a dopamine transporter radioligand, marker of nigro-striatal degeneration is the most employed technique for differential diagnosis of PS. The aim of the study was to evaluate the incremental diagnostic value of ¹²³I-loflupane SPECT in addition to the routine clinical diagnostic assessment of subjects with a clinically uncertain PS, performing a visual analysis. **Materials and Methods:** One thousands hundred fifty eight consecutive patients (600 male;558 female) median age 68 (range 18-88) referred to our Nuclear Medicine Department between 2004 and 2016 to undergo a ¹²³I-loflupane SPECT for an as yet unclassified parkinsonian syndrome were retrospectively evaluated. All patients underwent a baseline clinical examination by a movement disorder specialist before imaging. Visual assessment of ¹²³I-loflupane striatal uptake was performed. Among this population, 654 patients with at least 2 year follow up were included. **Results:** Patients, based on pre-imaging diagnosis, were classified into three groups: 241 suspected degenerative PS, 87 non-degenerative PS and 326 with clinically uncertain PS. At the clinical reevaluation after a minimum 2 year follow up (reference standard diagnosis) diagnoses were 488 (74.6%) degenerative PS (51,2% IPD, 5,5% CBD, 1,4% PSP, 15,4% LBD, 1.07% MSA) and 141 (21.6%) non degenerative PS (19,57% ET, VP 0.6%, 1,4 % DIP). In 25 patients (3.8%), neurologists were still unable to provide a definite diagnosis after the follow up (inconclusive cases). ¹²³I-loflupane striatal uptake was normal in 168/654 patients (26%) and abnormal in 479/654 patients (73%) with a mild, medium or severe unilateral or bilateral decreased striatal uptake. Seven SPECT were reported as doubt or inconclusive due to artefacts. In the cohort ¹²³I-loflupane SPECT showed a Sensitivity of 96.8%, Specificity of 95%, Positive Likelihood Ratio of 19,5, Negative Likelihood Ratio of 0.03, Positive Predictive Value of 98,5%, Negative Predictive Value of 89,9% for degenerative parkinsonism. Seventeen patients (7%) with a pre-imaging diagnosis of degenerative PS and negative SPECT diagnosis were changed to non degenerative PS, while eight patients (9.1%) with pre-imaging diagnosis of non degenerative PS and a positive SPECT had a final diagnosis of degenerative PS. **Conclusions:** Our data based in the largest series in the literature, strongly support the high diagnostic accuracy of ¹²³I-loflupane SPECT in the diagnosis of patients with PS and the significant clinical impact especially when clinical features are uncertain or patients fail clinical diagnostic criteria.

EP-0256**To evaluate the role of ^{99m}Tc-TRODAT-1 SPECT/CT and ¹⁸F-FDOPA PET/CT and their comparative performance in Parkinson Disease (PD), Parkinson Plus Syndrome (PPS) and Essential Tremor (ET).**

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Aim: The purpose of this prospective study was to evaluate the role of dopaminergic imaging using ^{99m}Tc -TRODAT-1 SPECT/CT and ^{18}F -FDOPA PET/CT and their comparative performance in Parkinson disease (PD), Parkinson plus syndrome (PPS) and Essential Tremor (ET). **Material & Methods:** A total 83 patients; 43 patients of PD (M:F=33:10, age: 24-83years), 15 patients of PPS (M:F=10:5, age: 52-76 years) and 26 cases of ET (M:F=13:12, age range 47-79years) were enrolled. Hoehn and Yahr staging (HnY) and MDS-UPDRS was done for PD and PPS patients. All the patients underwent ^{99m}Tc -TRODAT-1-SPECT/CT and ^{18}F -FDOPA PET/CT brain scan. The scans were analyzed visually for symmetry in bilateral striatal tracer uptake and specific uptake ratio of striatum (SURs) was calculated for quantitative analysis. Average pixel count (APC) of the striatal region of interest (ROI) in SPECT imaging and standardized uptake value mean (SUVmean) of ROI in PET imaging was calculated to determine the SURs ($\text{SURs} = \text{Striatal ROI} - \text{Occipital ROI} / \text{Occipital ROI}$). Comparison of scan findings and SURs values among different groups and correlation between MDS-UPDRS score, disease severity (HnY) and SURs was done for both modalities. **Results:** Symmetrical comma shaped uptake was seen in bilateral striatum in ET while reduced tracer uptake was seen either in caudate or putamen in PD and PPS except in two cases of early PD which showed normal uptake in the ^{18}F -FDOPA images and reduced uptake in putamen on ^{99m}Tc -TRODAT-1 images. On visual interpretation, 50/58 patients showed comparable uptake in both, ^{99m}Tc -TRODAT-SPECT/CT and ^{18}F -FDOPA-PET/CT (Weighted Kappa-0.659). Remaining 8 patients showed discordant findings between ^{18}F -FDOPA and ^{99m}Tc -TRODAT-1 where ^{99m}Tc -TRODAT-1 images showed relatively greater reduction in tracer uptake. Quantitatively, patients with ET showed significantly higher value of SURs than PD ($p < 0.001$) and PPS ($p < 0.001$) patients both on ^{99m}Tc -TRODAT-1 [$\text{SUR}_{\text{Left striatum}} (\text{SUR}_{\text{sl}}) = 0.66 \pm .25$; $\text{SUR}_{\text{Right striatum}} (\text{SUR}_{\text{sr}}) = 0.67 \pm .28$] and ^{18}F -FDOPA ($\text{SUR}_{\text{sl}} = 2.0 \pm 0.51$; $\text{SUR}_{\text{sr}} = 2.0 \pm 0.52$) images. However, between PD (^{99m}Tc -TRODAT-1- $\text{SUR}_{\text{sl}} = 0.29 \pm 0.30$; $\text{SUR}_{\text{sr}} = 0.28 \pm 0.12$) (^{18}F -FDOPA- $\text{SUR}_{\text{sl}} = 1.1 \pm 0.41$; $\text{SUR}_{\text{sr}} = 1.1 \pm 0.41$) and PPS (^{99m}Tc -TRODAT-1- $\text{SUR}_{\text{sl}} = 0.24 \pm 0.12$; $\text{SUR}_{\text{sr}} = 0.29 \pm 0.19$) (^{18}F -FDOPA- $\text{SUR}_{\text{sl}} = 1.0 \pm 0.49$; $\text{SUR}_{\text{sr}} = 0.99 \pm 0.42$) patients no significant difference in the SURs value was noted ($p = 0.97$). No significant difference was found between the SURs and severity of disease (HnY) ($p = 0.238$). A negative, but non-significant correlation was found between the MDS-UPDRS score and SURs. **Conclusion:** Our study showed substantial agreement for evaluation of dopaminergic dysfunction in PD and PPS. Both, ^{99m}Tc -TRODAT-1 SPECT/CT and ^{18}F -FDOPA PET/CT are potential imaging biomarkers which can help in differentiation of cases of ET from PD/PPS with ^{99m}Tc -TRODAT-1 SPECT/CT performing better than ^{18}F -FDOPA PET/CT in detection of PD in early stages.

EP-0257

A back-to-back comparison of ^{18}F -FE-PE2I-PET/CT and ^{123}I -FP-CIT-SPECT dopamine transport imaging in the diagnostic work-up of patients with clinical features of Parkinsonism

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Introduction: Recently a new PET-tracer, ^{18}F -FE-PE2I, with suitable dopamine transporter (DAT)-characteristics, has been developed with the possibilities of exploiting the advantages of PET-imaging, such as improved spatial resolution. The aim of this project was to compare the clinical back-to-back performance of ^{18}F -FE-PE2I-PET/CT and ^{123}I -FP-CIT-SPECT for DAT-imaging in the diagnostic work-up in a cohort of out-patients with clinical features of Parkinsonism. **Methods:** In the diagnostic workup for Parkinsonism, 47 unselected patients were recruited (17 women, median age 70 years, range 36-86 years) for DAT-imaging with ^{18}F -FE-PE2I-PET/CT and ^{123}I -FP-CIT-SPECT on two separate days with a median time-interval of 15 days (range 1-64 days). For the PET-examination the patients received a median dose of 187 MBq (range 66-232 MBq), and a 25-minute static PET-scan was performed after a 17-minute uptake-period. For the SPECT-examination the patients received a dose of 185 MBq, and SPECT-images with attenuation correction were obtained three hours post-injection. Both SPECT and PET-scans were categorized as either normal or abnormal independently and blinded by two readers based on a combination of visual and semiquantitative assessment calculating the ROI-based specific binding ratio (SBR) of striatum and putamen using the occipital lobe and cerebellum as reference, respectively. Pathology on CT-scan was noted. The semiquantitative data were compared using Pearson's correlation analysis with SPECT as reference, and the test accuracy was measured using leave-one-out cross-validation. **Results:** Twenty-one of the SPECT-DAT-scans were rated normal, and 26 abnormal, while 20 of the PET-DAT-scans were rated normal and 27 abnormal. Four of the abnormal PET-DAT-scans were caused by infarctions in the basal ganglia. In one case, SPECT-DAT-scan was rated normal and the PET-DAT-scan abnormal due to an infarction in the basal ganglia not detectable on the SPECT-scan. For three SPECT-DAT-scans the vascular etiology of tracer reduction was only identified correctly when compared with CT. Excluding patients with infarctions, there was significant correlation of semiquantitative measures between SPECT- and PET-DAT-scans of worst-hemisphere putamen/caudate ratios ($r = 0.7$) and putamen SBR ($r = 0.9$) and striatum SBR ($r = 0.8$). The worst-hemisphere PET putamen/caudate ratio was the best semiquantitative measure with a test accuracy of 100 % in separating normal from abnormal SPECT-DAT-scans. **Conclusion:** There was an excellent correspondence of ^{18}F -FE-PE2I-PET compared to reference standard ^{123}I -FP-CIT-SPECT-DAT-imaging, and ^{18}F -FE-PE2I-PET seems promising for clinical use. In 10 % of the patients the PET/CT combination performed better than SPECT alone because of the identification of previously unreported basal ganglia infarcts on CT.

EP-0259

[^{18}F]FDG-PET-based Parkinson's Disease-related Metabolic Brain Pattern (PDRP) As A Progression Biomarker: A 4-year

Follow-up In A Cohort Of Patients With Idiopathic Rem Sleep Behavior Disorder (iRBD)

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Background: iRBD is commonly considered to be a prodromal stage of alpha-synucleinopathies such as Parkinson's disease (PD), Dementia with Lewy Bodies (DLB), or Multiple System Atrophy (MSA). The characteristic brain pathology in PD results in a pattern of abnormal cerebral glucose metabolism known as the PD-related pattern (PDRP). The degree of this pattern expression can be quantified in any [¹⁸F]FDG-PET brain scan. Previous reports have shown that this pattern is a useful biomarker of disease progression and of phenoconversion from iRBD to PD. It may also be useful for identifying the approximately 10–20% of iRBD patients who will **not** convert to a parkinsonian disorder so that they may be excluded from future parkinsonian drug trials targeting the prodromal phase. **Methods:** In our first study ("REMPET1"), 21 iRBD patients without parkinsonism or dementia, 19 controls, 20 PD patients, and 22 DLB patients underwent static [¹⁸F]FDG-PET brain imaging. PDRP expression values were then computed using spatial covariance (SSM/PCA) analysis and z-transformed to control values. In our follow-up study ("REMPET2"), we have begun rescanning the 21 iRBD subjects to follow the progression in their PDRP expressions since their last scans. **Results:** In our baseline study (published November 2017 in the Movement Disorders Journal), PDRP expression was higher in iRBD patients compared to healthy controls ($p=0.048$), but lower compared to PD ($p=0.001$) and DLB patients ($p<0.0001$). 12/21 iRBD subjects (57%) already had a suprathreshold PDRP expression. In our preliminary follow-up results so far, it appears that PDRP expression has significantly increased in most iRBD subjects rescanned compared to their initial scans from approximately 4 years ago. Additionally, some of the subjects appear to have developed early signs of parkinsonism according to the MDS-UPDRS. **Conclusion:** Our preliminary findings show that abnormal metabolic expression begins years before clinical manifestation of parkinsonian symptoms in iRBD patients, and that changes in PDRP expression over time may provide a useful metric for predicting phenoconversion to alpha-synucleinopathy diseases.

EP-0260

FPCIT SPECT in parkinsonism predicts survival: a data-driven analysis

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Dopamine transporter SPECT is an established method to investigate nigrostriatal integrity in case of clinically uncertain parkin-

sonism. The present study investigated whether a completely data-driven analysis of FPCIT SPECT is able to stratify patients according to mortality after SPECT. This was tested in a clinical patient sample. Patients from our clinical registry were included if they had received FPCIT SPECT between 10/2008 and 06/2016 for diagnosis of parkinsonism and if their vital status (alive or date of death, if applicable) could be determined in 07/2017. Atlas-based regions of interest were used to extract individual specific binding ratios (SBR; occipital cortex as reference) of the whole striatum and striatal subregions (caudate nucleus, anterior and posterior putamen) of both hemispheres. SBR of the whole striatum, its asymmetry (asymmetry index, AI; absolute value), and the rostrocaudal gradient of striatal binding (C/pP: caudate SBR divided by posterior putamen SBR) were used as input for hierarchical clustering of patients into three subgroups. A Cox proportional hazards model was computed in order to test whether survival (adjusted for age) was different between the subgroups. Vital status could be determined in 518/566 patients. 77/518 patients had died within the median follow-up duration of 3.3 years [95% C.I. 3.1 to 3.7]. The subgroups identified by hierarchical clustering were characterized by relatively (1) low striatal SBR, high AI, and low C/pP, (2) low striatal SBR, high AI, and high C/pP, and (3) high SBR, low AI, and low C/pP. Mortality was significantly higher in group (1) compared to each of the other two groups: compared to group (2), HR = 1.9 [95% C.I. 1.1 to 3.3], $p = 0.029$; compared to group (3), HR = 2.2 [95% C.I. 1.3 to 3.8], $p = 0.003$. In patients with parkinsonism, data-driven analysis of FPCIT SPECT identified a subgroup of patients with significantly increased mortality during follow-up. This high-risk group showed an FPCIT signature suggestive of atypical parkinsonian syndromes, whereas the other groups had either normal scans or showed an FPCIT profile suggestive of Parkinson's disease. This suggests that FPCIT SPECT might not only serve as a diagnostic tool but also provide valuable prognostic information ("red flag", e.g. triggering additional examinations like FDG PET for differential diagnosis of parkinsonism or intensified clinical follow-up).

EP-0261

Corticostriatal hypometabolism in the motor circuit of Huntington's disease patients

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Aim: To assess corticostriatal metabolic changes in brain 18F-FDG PET/CT in presymptomatic (preHD) and symptomatic (sHD) Huntington's disease (HD) patients related to motor circuits. **Materials and methods:** Fifty-eight patients (26 male, mean age = 47 ± 12) carrying the HD mutation (mean CAG = 43 ± 3) were prospectively included. Based on the Unified Huntington's Disease Rating Scale (UHDRS), motor score and Total Functional Capacity, patients were classified as presymp-

tomatic (preHD=20; UHDRS <4, mean age $\pm$ SD: 42.7 $\pm$ 11.7y/o; CAG $\pm$ SD: 40 $\pm$ 3.8) and symptomatic (sHD=38; UHDRS>4, mean age $\pm$ SD: 54 $\pm$ 14.3y/o; CAG $\pm$ SD: 44.2 $\pm$ 3.1). A separate group of 18 healthy subjects, matched with patients by age and gender, was used as control group (mean age $\pm$ SD: 45 $\pm$ 13.2y/o) (CG). Brain PET/CT was performed 60 minutes after i.v. injection of 277 MBq of 18F-FDG on a Philips Gemini TF. Images were initially assessed by 2 nuclear medicine physicians identifying qualitative metabolic changes in the striatum and sensorymotor Cortex (SMC). Analysis and quantitative assessment of regional cerebral activity was performed using the Statistical Parametric Mapping (SPM8). **Results:** In the visual analysis, sHD patients presented a significant hypometabolism in striatum compared to preHD patients. No other cortical metabolic changes were observed in sHD compared to preHD. The quantitative analysis, demonstrated a significant bilateral striatal hypometabolism in HD subjects (sHD and preHD) relative to CG ($p<0.05$ FWE; extent voxel threshold $k=200$). It also showed a marked bilateral striatal hypometabolism in sHD patients compared to preHD patients ($p<0.05$ FWE; extent voxel threshold $k=200$). As new finding, the quantitative analysis showed hypometabolism in the sensory-motor cortex in sHD patients compared to preHD patients ($p<0.05$ FWE; extent voxel threshold $k=200$). **Conclusion:** The striatal and SMC hypometabolism observed in sHD compared to preHD in the cerebral 18F-FDG PET/CT is associated with neurodegeneration within corticostriatal circuits, circuits from the principal network, which mediate motor symptoms.

EP-0262

The diagnostic accuracy of DAT SPECT using DaTQUANT software: discrimination among patients with non-Parkinsonian disease, Parkinson's disease, and atypical Parkinsonian syndromes

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Purpose: The purpose of this study was to evaluate the diagnostic utility of the quantitative values of dopamine transporter (DAT) single photon emission computed tomography (SPECT) in differentiating among patients with Parkinson's disease (PD), atypical parkinsonian syndromes (APS), and non-parkinsonian syndrome (NPS). We used and compared three typical quantitative values derived with DaTQUANT: the specific binding ratio (SBR), Putamen-to-Caudate ratio (PCR), and asymmetry index (AI). At present, there are few study comparing these three quantitative indices and thus we evaluated the diagnostic accuracy of each index. **Materials and Methods:** Forty patients without parkinsonian syndrome (PS) and 110 patients with PS were included in this study. Out of 110 PS patients, 71 including 51 patients with PD and 20 patients with APS were diagnosed clinically and enrolled for differentiating between PD and APS. The SBR, PCR, and AI were calculated from their SPECT images and compared between datasets for evaluating the diagnostic utility. Mann-Whitney test and Receiver-operating characteristics (ROC) analysis were used for analysis. **Results:** ROC analysis

revealed that the SBR value had high diagnostic performance (The areas under the curve (AUC) = 0.960) compared with the other two values in differentiating between PS and NPS patients. While in differentiating between PD and APS, the PCR value had the highest performance of the three (AUC = 0.865). The sensitivity, specificity, and accuracy respectively were 90.0%, 92.5%, and 90.7% with SBR, 72.7%, 95.0%, and 78.7% with PCR, and 63.6%, 92.5%, and 71.3% with AI in differentiating between PS and NPS, while 40.0%, 82.4%, and 70.4% with SBR, 90.0%, 68.6%, and 74.6% with PCR, and 60.0%, 64.7%, and 63.4% with AI in differentiating between PD and APS. **Conclusion:** SBR was the most useful index when differentiating between PS and NPS patients, while concerning the discrimination between PS and APS patients, PCR was the most useful.

EP-0263

Memory Performance Associates With Serotonin Transporter In Healthy Subjects

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Purpose: We aimed to evaluate the association between availability of serotonin transporter (SERT) measured by ¹²³I-FP-CIT single-photon emission computed tomography and memory function of healthy subjects. **Methods:** Specific binding of ¹²³I-FP-CIT regarding SERT was calculated using a region of interest analysis. Spherical volumes of interest for midbrain and pons were defined. The cerebellum was chosen as a reference region. Specific binding ratios (SBRs) of midbrain and pons representing SERT availability were measured as follows; SBR= (target- cerebellum)/cerebellum. **Results:** 181 healthy subjects (117 male, 64 female) were included in this study. SBRs of both midbrain ($p=0.025$) and pons ($p=0.006$) of males were higher than those of females. However, among HVLT-R scores, total recall score ($p=0.008$), delayed recall score ($p=0.013$), and discrimination score ($p=0.017$) of males were lower than those of females. None of SBRs showed the correlation with age in males (midbrain; $p=0.736$, pons; $p=0.875$), and females (midbrain; $p=0.294$, pons; $p=0.170$). In 181 healthy subjects, SERT availability of midbrain correlated positively with total recall score ($\rho=0.159$, $p=0.033$), and delayed recall score ($\rho=0.149$, $p=0.046$). In females, the correlation between SERT availability of midbrain and delayed recall score was significant ($\rho=0.320$, $p=0.010$), however, not in males ($\rho=0.112$, $p=0.229$). **Conclusion:** We demonstrated that SERT availability was associated with memory function in healthy subjects. Further studies are needed to clarify underlying mechanisms of this phenomenon.

EP-0264

Effects Of Rs591323 On Serotonin Transporter Availability In Healthy Male Subjects Effects Of Rs591323 On Serotonin Transporter Availability In Healthy Male Subjects

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Objectives: We aimed to investigate the association between genetic factors of SNPs dopamine transporter (DAT) and serotonin transporter (SERT) availabilities in healthy controls. **Methods:** The study population consisted of healthy controls with screening ^{123}I -FP-CIT single-photon emission computed tomography. Specific binding of ^{123}I -FP-CIT regarding DAT and SERT was calculated using a region of interest analysis. VOI template was applied to measure specific binding ratios (SBRs) of caudate nucleus, putamen, striatum, midbrain, and pons. **Results:** One hundred sixty healthy controls (male 106, female 54, 61.0 ± 11.5 years) were included in this study. Sex difference did not exist in DAT availabilities of caudate nucleus ($p=0.5344$), putamen ($p=0.5006$), and striatum ($p=0.5056$). However, male subjects had higher SERT availabilities of both midbrain ($p=0.0436$), and pons ($p=0.0061$). We analyzed the effect of SNP on DAT availabilities of subjects in all, and that on SERT availabilities of males and females separately. None of 19 SNPs included in this study showed the effect on DAT availabilities. However, rs591323 in Fibroblast Growth Factor 20 on chromosome 8 had a significant impact on SERT availability of pons ($p=0.0007$). **Conclusion:** SNP rs591323 of risk loci for Parkinson's disease is associated with SERT availability of healthy male subjects.

EP-0265

Incidence of balanced loss of dopaminergic nerve terminals in striata in patients with Lewy body diseases referred for DaTSCAN - should we always do quantification?

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Introduction: In DaTSCAN™ (ioflupane) reporting, detecting balanced loss (BL) of dopaminergic nerve terminals in the striata could be difficult to diagnose by visual assessment alone. We investigated the incidence of BL in DaTSCAN referrals to determine if routine use of quantification is of value. **Method:** We performed a retrospective data analysis of patients referred to our institution from 2012 to 2018. Images were processed using GE recommendations. Striatal specific binding ratio (SBR) was measured using DaTQUANT (GE Healthcare). Scans were assessed by two experienced reporters. Four groups of referrals were identified: to establish diagnosis of idiopathic Parkinson's disease (?PD), possible drug-induced PD (?DIP), possible vascular PD (?VP) and suspected Lewy Body Dementia (?DLB). The reports for these were categorised into four groups: Normal (comma shaped with normal SBR), classic abnormal (dot appearance with reduced SBR), nigrostriatal pathway infarct (infarct, with contralateral normal SBR) and BL (normal comma shaped with reduced SBR). The percentage of report categories were calculated for each group of patients. To assess significance of BL, we looked at the final clinical diagnosis for patients reported BL with minimum follow up of 3 years. **Results:** There were 370 scans; 39% were normal, 45% classic abnormal, 5% (19/370) striatal infarct and 11% (41/370) showed BL. The incidence of BL in "?PD" group of patients was 10% (27/281), in "?DIP" group was 7% (3/23), in "?DLB" group 33.3% (5/15), and in "?VP" was 21% (6/29). The incidence of striatal infarct in "?PD" group was

6% (16/281), in "?VP" group was 10% (3/29), and none in "?DLB" or "?DIP" groups. 12 patients with BL had 3+ years of accessible documented follow up. The final diagnosis was PD in 8 (67%), DLB in 3 (25%) and dementia with possible DLB in 1 patient. **Discussion:** Quantification is essential for accurate recognition of BL, and helpful in identifying patients with possible nigrostriatal pathway infarcts. BL and infarcts comprise a significant proportion of our referral patient population (16%). Without quantification, 60 scans could have been misreported. High incidence of BL in DLB is well documented in literature, but we also noted a significant proportion of BL in our "?PD" referrals. **Conclusion:** Although visual assessment remains the primary method of DaTSCAN reporting, quantification is essential for improving interpretation accuracy in cases of BL and nigrostriatal pathway infarct, of which there was a significant proportion in our group of patients.

EP-0266

Semiquantitative analysis of 18F-FDOPA brain PET-CT in Idiopathic Parkinson Disease Patients in correlation with clinical rating scale and in tremor predominant subgroup

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Objective: To evaluate striatal-to-occipital ratios (SOR) on L-3,4-dihydroxy-6-F-18 fluorophenylalanine (18F-FDOPA) PET in early and advanced Idiopathic Parkinson's disease (IPD) based on clinical rating scales- Unified Parkinson disease rating scale (UPDRS) and Hoehn and Yahr (H&Y) scale. Since an underlying serotonergic deficit is the pathophysiology in tremor predominant IPD we derived midbrain to occipital ratio (MOR) on 18F-FDOPA brain PET-CT in this subgroup. **Materials and methods:** We evaluated 43 IPD patients with 18F-FDOPA brain PET-CT studies. Each patient underwent dopaminergic imaging after undergoing a detailed clinical examination at the movement disorder clinic of our institute. This included 25 early IPD (UPDRS = 34.3 ± 5.8 ; range 14-42, H&Y < 2.0 and disease duration = 3.4 ± 0.9 ; range 2-5 years) and 18 advanced IPD (UPDRS = 54.3 ± 7.2 ; range 39-72 and H&Y = 2.0-4.0, disease duration = 6.6 ± 4.2 ; range 5-18 years). Twenty age matched subjects who undergone 18F-FDOPA PET-CT for indication other than Parkinsonism, were included as control. Brain 18F-FDOPA PET-CT images were interpreted visually and semi-quantitatively using SUVmax value. ROI were generated for the caudate, putamen, occipital regions and midbrain on fused PET-CT images for structural correlation. SORs were generated for caudate, and putamen and MOR for midbrain. Statistical analysis using Mann-Whitney U Test was performed between controls to early and advanced IPD separately. MOR was compared between non-tremor dominant and tremor predominant IPD (assessed by UPDRS tremor score). **Results:** SOR clearly differentiated between controls and early as well as advanced IPD (p value 0.006 and 0.003 respectively). SOR between early and advanced IPD patients was also significantly different ($p=0.018$). Comparison between contralateral SOR (to predominant symptom sidedness) to ipsilateral SOR was significantly different in early IPD ($p=0.032$) while no significant difference was noted for advanced IPD ($p=0.507$). MOR in trem-

or predominant subgroup showed significant difference from non-tremor dominant subgroup group ($p=0.002$). **Conclusion:** SOR is a good diagnostic tool for IPD patients and can differentiate between early and advanced IPD. SOR correlates well with clinical sidedness in early IPD but not in advanced IPD. MOR can be used in the tremor predominant patient subgroup when SOR's may not be useful.

EP-0267

Correlation Of ^{99m}Tc -trodat-1 Spect Findings And Clinical Staging Of Parkinson's Disease

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Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder that results in loss of dopaminergic neurons in the striatum. Its clinical diagnosis relies on the presence of cardinal motor symptoms of bradykinesia, rigidity, resting tremors and postural instability. ^{99m}Tc -TRODAT-1 is a sensitive diagnostic test for early detection of PD. This study was conducted with the aim of evaluating ^{99m}Tc -TRODAT-1 SPECT imaging patterns in clinically diagnosed patients of Parkinson's disease and to assess the correlation between the decline in ^{99m}Tc -TRODAT-1 uptake with increasing disease severity as assessed by clinical staging. **Subjects and Methods:** The study included 241 diagnosed patients with clinically probable PD who underwent ^{99m}Tc -TRODAT-1 SPECT scan. Binding ratios (BR) were calculated for each striatum, caudate, and putamen individually, by drawing region of interest (ROI). Occipital cortex was taken for background correction. Correlation of binding ratio with increasing clinical stage as given by Modified Hoehn and Yahr scale was derived. **Results:** Median binding ratio was least in the contralateral putamen for all stages of Modified Hoehn and Yahr. A statistically significant negative correlation was found between increasing disease severity and BR in all sub-regions of the striatum. A significant decline was noted in the binding ratio of the putamen as compared to caudate. Patients were clinically categorized into postural-instability gait disorders (PIGD) group and tremor-dominant PD (TD) group. No significant asymmetry was found between the left and right striatum in patients belonging to PI GD group and in those with bilateral tremors without lateralization. A significant correlation was found between the decline in the striatal binding on both the sides, even in early stages of the disease when patients manifested with unilateral symptoms. **Conclusion:** ^{99m}Tc -TRODAT-1 uptake was significantly reduced in the putamen as compared to caudate nucleus. A significant asymmetry with the contralateral side being affected more than the ipsilateral side can be attributed to patients with lateralization of symptoms and particularly in tremor-dominant PD patient. A significant negative correlation exists between decline in binding ratio in all the sub-regions with increasing stage of Modified Hoehn & Yahr scale. The binding ratio of the ipsilateral striatum may serve useful in following the progression of the disease and in prognosticating the clinical course, as it represents the level of remaining functional dopaminergic neuronal reserve in the striatum.

EP-0268

Selecting reference regions to model neurodegeneration in Huntington's disease using 18F-FDG PET/CT images and clinical parameters

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Objective: Normalization to an appropriate reference region in 18F-FDG-PET imaging may enhance diagnostic performance in Huntington's disease (HD). We aimed to identify brain areas that could be used to model neurometabolic degeneration in HD correlating imaging (SUVr values at the basal ganglia [BBGG]) and clinical parameters (disease burden score [DBS]). **Materials and methods:** Fifty-eight patients (26 male, mean-age = 47 ± 12) carrying the HD mutation (mean CAG = 43 ± 3) were prospectively included. Based on the Unified Huntington's Disease Rating Scale (UHDRS), motor score and Total Functional Capacity, patients were classified as presymptomatic (preHD=20; UHDRS <4, mean-age $\pm$ SD: 42.7 ± 11.7 y/o; CAG $\pm$ SD: 40 ± 3.8) and symptomatic (SHD=38; UHDRS >4, mean-age $\pm$ SD: 54 ± 14.3 y/o; CAG $\pm$ SD: 44.2 ± 3.1). A separate group of 18 healthy subjects, matched with patients by age and gender, was used as control group (CG; mean-age $\pm$ SD: 45 ± 13.2 y/o). Brain PET/CT was performed 60 minutes after i.v. injection of 277 MBq of 18F-FDG on a Philips Gemini TF. For quantitative analysis performed using the Statistical Parametric Mapping (SPM8), we selected: a) predefined reference regions from the MNI space-atlas [pons, whole cerebellum, cerebral white matter, thalamus, and a ROI pons-vermis] and b) reference-clusters obtained by voxelwise statistical comparison across groups ($p < 0.05$ FWE; extent voxel threshold- $k=200$). The performance of each candidate reference region was quantitatively assessed using imaging and clinical parameters (correlation between SUVr values at the BBGG and DBS using the predefined reference region from the MNI space-atlas and the reference-clusters obtained by voxelwise statistical comparison, as well as comparing the minimum variance of SUVr values relative to the CG). **Results:** Comparing HD and CG groups we obtained a reference-cluster in the cerebellum, and in temporal and frontal lobes. Comparing symptomatic-HD and presymptomatic-HD patients we observed reference-clusters in the cerebellum, pons, thalamus, parietal lobe, and cuneus. The set of reference regions showed a significant correlation between SUVr values at the BBGG and DBS in patients carrying the HD mutation. In presymptomatic-HD patients, the correlation between SUVr values at the BBGG and DBS was significant using the ROI pons-vermis and thalamus as defined reference regions and pons and thalamus as refer-

ence-clusters. In symptomatic-HD patients, the correlation was significant using the temporal and white matter frontal lobe clusters. Variance between SUVr values in the set of reference regions was minimal within CG. **Conclusion:** The pons and thalamus may be reliable choices to calculate SUVr values to model the neurometabolic degeneration in quantitative 18F-FDG PET imaging in Huntington's disease.

EP-0269

Spectrum of Autoimmune Encephalitis: Pattern recognition on FDG PET CT and correlation with specific antibody sub type

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Introduction: Autoimmune encephalitis (AE) is a diverse group of neuro-psychiatric disorders, caused by auto antibodies and may be of para neoplastic or non-para neoplastic etiology. F-18 Fluoro-deoxy glucose (FDG), a glucose analog which accumulates in the neuronal tissue whenever there is increased metabolic demand. A distinctive pattern of hyper and hypo metabolism is emerging on FDG PET CT scan, specific to the particular antibodies involved, which changes with disease evolution and progression. FDG PET/CT may have an important role both in the identification of AE itself and in the detection of the unknown malignancy that might have caused it. **Purpose:** To establish specific FDG uptake patterns in different antibody sub types of autoimmune encephalitis. **Material and methods:** We present a retrospective analysis of 25 serologically proven cases of AE. All the subjects underwent whole body F-18 FDG scan including brain and the studies were analyzed both qualitatively (visually) and semi quantitatively. Areas of cortical hypo/hyper metabolism in the cerebral or cerebellar cortex that were two standard deviations from the mean were considered as abnormal. The pattern of FDG uptake in specific antibody sub types were recorded and a correlation with normalized data was attempted. The patients were also analyzed based on a visual assessment of the Z score surface maps of the 3D SSP image and their ability to differentiate the commonly encountered sub types of AE. **Results:** All the subjects had an abnormal pattern of F-18 FDG uptake on PET scan, both on visual inspection and semiquantitative analysis. The subjects who had Voltage gated potassium channel (VGKC) complex receptor antibody encephalitis, had typical hyper metabolism in bilateral medial temporal regions and bilateral basal ganglia with relative global hypometabolism in rest of the cortical and sub cortical structures. The subjects with N-methyl-D-aspartate-receptor antibody (NMDAR-Ab) encephalitis showed variable degrees of focal hyper metabolism in bilateral fronto-temporal regions, basal ganglia, thalami and cerebellar hemispheres with inhomogeneous parieto-occipital hypometabolism. The scans normalized with treatment on follow up FDG PET scans. **Conclusion:** FDG PET scan may act as a non invasive diagnostic modality in the early diagnosis and management of patients with clinical suspicion of Auto immune encephalitis. **Keywords:** Autoimmune encephalitis, Auto antibodies, F-18 FDG PET CT, MRI, NMDAR, VGKC

EP-0270

18F-FDG PET/CT and MRI co-registration plays a role during pre-surgical evaluation of patients with drug-resistant focal epilepsy: SEEG validation and predictive outcome

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Purpose: Primary aim was to determine sensibility and positive predictive value (PPV) of 18F-FDG PET/CT and MRI in a series of patients surgically treated for drug-resistant focal epilepsy. Secondary aims were to assess the pre-surgical contribution of PET in Stereo-EEG (SEEG) electrodes positioning during evaluation and to investigate the possible role of PET, MRI and clinical parameters as predictors of postoperative outcome. **Subjects & Methods:** Retrospective single-centre study including 25 consecutive patients (16F; mean age 32 years old; range 16-47) enrolled between July 2013 and November 2015. All patients underwent ictal video-EEG, MRI, functional MRI, 18F-FDG PET/CT, SEEG, surgery and clinical follow-up (mean 31 months; range 12-50). PET co-registered with MRI and MRI alone were compared with the epileptogenic zone (EZ) determined by SEEG (as the gold standard for EZ localization). A survey was administered to the neurologist before and after performing 18F-FDG PET/CT in order to assess its contribution during the placement of intracranial electrodes. Student's t-test, Pearson's chi-squared test and logistic regression were employed to estimate factors associated with the post-operative outcome (Engel's classes). **Results:** Visual PET analysis disclosed an hypometabolism in 23/25 cases (92%) while MRI resulted positive in 13/25 (52%). PET was positive in all 12/25 (48%) patients with a negative MRI scan. PET/MRI co-registration detected single-lobe uptake reduction in 10/25 patients (40%), which conversely affected more than one lobe in 13/25 (52%). Location of single-lobe PET abnormalities was temporal in 8/25 (32%) cases, parietal in 1/25 (4%) and occipital in 1/25 (4%). Histology showed 16/25 (64%) cases of gliosis, 7/25 (28%) dysplasia, and 2/25 (8%) sclerosis. PET/CT sensibility and PPV were respectively 91,7% (95% CI=72,1-98,5) and 95,7% whereas those of MRI were 54,2% (95% CI=33,6-73,5) and 100% respectively. Regarding SEEG electrode placement 18F-FDG PET/CT gave a major contribution (>50%), particularly in case of inconclusive MRI imaging. According to multivariate analysis, the number of involved lobes in PET (p=0,046) and the frequency of seizures (p=0,049) were the only statistically significant predictors (Engel's class I). **Conclusion:** 18F-FDG PET/CT co-registered with MRI is highly sensitive to detect the EZ in our series of patients operated for drug-resistant focal epilepsy and it may play a relevant role during pre-surgical evaluation guiding the SEEG electrode-placement. PET-detected lobe-number

involvement was found to be the only significant predictor, combined with seizure frequency, of seizure freedom after surgery, though further studies are needed to clarify their role.

EP-0271

Lewy body dementia and Posterior cortical variant Alzheimer's disease: Similarities and differences on FDG PET and TRODAT scan

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Introduction: Posterior cortical atrophy (PCA), first described by D. Frank Benson in 1988, is a form of dementia considered to be an atypical variant of Alzheimer's disease (AD). There is atrophy of the posterior part of the cerebral cortex, resulting in the progressive disruption of complex visual processing. Dementia with Lewy bodies (DLB) is a type of posterior dementia characterized by fluctuating levels of cognition, changes in behavior, visual hallucinations with variable degrees of extrapyramidal motor symptoms. The two differ in etiopathology as PCA is characterized by deposition of senile B amyloid plaques and neurofibrillary tangles, whereas, DLB is characterized by clumps of alpha-synuclein protein in the affected areas of the brain. The two can be differentiated with the help of Dopamine transporter imaging agent Tc 99m- TRODAT-1, which is abnormal in DLB and normal in AD including PCA. This study is an attempt to identify specific core areas on FDG PET imaging which are common to both and also to establish the differences which may be helpful to differentiate the two. **Aims:** To illustrate the similarities and differences in the imaging patterns of PCA and LBD on FDG PET. **Material and methods:** We present a retrospective analysis of 30 patients of clinically suspected posterior dementia. The subjects underwent F-18 FDG PET and 99 m TRODAT scan of the brain and the studies were analyzed qualitatively (visually) and semi quantitatively. The subjects were divided into possible PCA with TRODAT scan normal (n=10) and possible DLB with abnormal (n=20). Areas of cortical hypometabolism that were two standard deviations from the mean were considered as abnormal. **Results:** Both on visual inspection and semiquantitative analysis, bilateral parieto-occipital hypometabolism was consistently found in all the subjects. Hypometabolism in precuneus, posterior cingulate and the cortex around the angular gyrus was present in all the subjects of PCA with relative sparing of the medial occipital cortices. DLB subjects showed variable degrees of involvement of the medial occipital cortices with relative sparing of posterior cingulate and precuneus. **Conclusion:** FDG PET and TRODAT may act as non invasive diagnostic modalities in differentiating the two posterior cortical dementias. **Keywords:** Posterior cortical atrophy (PCA), Dementia with Lewy bodies (DLB), FDG PET, Tc99m-TRODAT-1

EP-0272

Multi-Parametric Cerebral ¹⁸F-FDG PET/MRI in Patients Referred for Chronic Fatigue

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Purpose: To evaluate cerebral PET/MRI profile in patients with chronic fatigue, including glucose metabolism, perfusion and tissue biochemicals. **Methods:** We performed cerebral PET/MRI in 23 patients (mean age, 42 y) with chronic fatigue on a Biograph mMR (Siemens, Erlangen, Germany) 30 min after injection of 190±65 MBq ¹⁸F-FDG. Simultaneously, anatomical MR sequences were performed at 3 Tesla, as well as ¹H MR spectroscopy in 10 patients and 3D perfusion arterial spin labelling (ASL) in 7 patients. PET was interpreted visually for characterization of regional glucose metabolism and quantitatively (SUVmean) after spatial normalization to the Talairach space by applying a set of predefined cortical and subcortical volumes-of-interest (Syngovia®). MRI was interpreted for structural abnormalities, perfusion and spectroscopy profiles. **Results:** All patients presented chronic fatigue >6 months (major criterion); 7 of them presented 2-3 minor criteria of the Fukuda scale and 16 at least 4 minor criteria. Symptoms started an average 9 y before imaging and were related to aluminium-containing vaccines in 11 patients, viral infection in 4, autoimmune reaction to silicone in 1, and unknown in the remaining 7. Decreased glucose metabolism was found in the temporal areas in all patients, precuneus in 22, cerebellum in 22, amygdalo-hippocampal complexes in 20, internal occipital cortex in 17, and parietal areas in 13 patients. All but 1 patient had normal frontal metabolism. Quantitatively, SUVmean was significantly lower in the occipital cortex (6.05±1.0), amygdalo-hippocampal complexes (4.77±0.83) and cerebellum (5.19±0.95), compared to the frontal cortex (6.56±1.34), Wilcoxon P<0.0001. Morphological MR sequences did not show relevant abnormalities outside white matter FLAIR hypersignals in 7 patients and cortical atrophy in 3. ASL perfusion was not significantly different between frontal (197±61 mL/min/100g) and occipital areas (235±126 mL/min/100g). Interestingly, choline-to-creatine (Cho/Cr) ratio were significantly higher in the frontal (1.04±0.34) than in the occipital cortex (0.75±0.22, Mann-Whitney P=0.008). No significant difference was found for N-acetyl aspartate-to-creatine ratio, 1.91±0.40 vs. 1.66±0.40, respectively). An optimal cut-off of SUVmean ≤6.71 and Cho/Cr >0.602 in the occipital cortex allowed to separate patients with Fukuda score ≥4 vs. those with score 2-3, with Chi² P=0.01 and P=0.04, respectively. **Conclusion:** Multi-parametric ¹⁸F-FDG PET/MRI seems useful to characterize patients with chronic fatigue, showing metabolic and biochemical abnormalities in the posterior cortical regions. Larger studies including comparison to a normal database are warranted.

EP-0273

Synchronous EEG and brain-perfusion-SPECT measurements reveal networks of speech understanding during a speech-discrimination task

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Introduction: In the majority of cases, cochlear implantation results in successful therapy of inner ear deafness; however unexplained limitations of speech understanding still occur in some patients. We evaluated a multi-modal approach including synchronous brain-perfusion-SPECT and EEG to elucidate the underlying mechanisms. **Methods:** 14 CI-users (58±11y, 12 right-handed) performed a speech-discrimination task with sentences, being either semantically correct or incorrect. Speech was presented via one CI (6 right-, 7 left-sided) with simultaneous registration of a 96-channel-EEG plus injection of 740MBq ^{99m}Tc-HMPAO after 2min. A dual-head-SPECT scan (count-rate-dependent for approximately 50min) was acquired 1.5h p.i. ("speech condition"). A second SPECT was performed at rest ("rest condition"). SPM8 was used to compare the two conditions and correlate their difference to EEG (e.g. N400 response), speech-audiometry (HSM-sentence-test, Freiburg-monosyllabic-word-test), linguistic competence (Multiple-choice-word-test-B) and working-memory (Size-comparison-span-test) data. To compare the cortical activation patterns between CI users with poor and good speech recognition abilities, two subgroups were created by means of a median-split procedure (HSM-sentence-test in noise (10dB SNR): bad performers <48%; good performers >48%). **Results:** The speech-discrimination task resulted in bilateral activation of auditory regions (Brodmann areas (BAs) 21, 22, 41, 42; $p<0.001$) and BA45 (right; $p<0.001$). An enhanced N400 response, reflecting the detection of the semantic violation during the speech-discrimination task, was related to a stronger left-sided activation in temporal areas (BA20; $p<0.01$). A higher working-memory capacity and higher linguistic competence were related to a stronger activation during the speech-discrimination task in the auditory cortex (BA41, 42, 22, 21), Broca's area (BA44/45), as well as left frontal (BA8) and premotor areas (BA6; all $p<0.001$). In bad compared to good performers higher activation of left parietal (BA40, 2; $p<0.001$), frontal (BA8; $p<0.01$) and prefrontal regions (BA9, 46; $p<0.01$), as well as of the left premotor cortex (BA6; $p<0.01$) and Broca's area (BA45; $p<0.01$) were seen. By contrast, good performers showed higher activation of auditory regions (BA21 left; $p<0.001$; BA21 right and BA22 left; $p<0.01$) and temporal regions (BA20 and BA38 left and right; $p<0.01$). **Conclusion:** Synchronous functional measurements of SPECT and EEG in the context of a speech discrimination task revealed recruitment of a temporo-frontal network during speech processing as well as a connection between SPECT and EEG measures, the performance in speech understanding and cognitive tests. CI-users with good and bad speech discrimination abilities showed differences in their cortical activation patterns. These results can help to understand/improve results of auditory rehabilitation after CI-implantation.

EP-0274

Recurrent cerebral ischemic events in symptomatic carotid stenosis are related to plaque inflammation

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Background and aims: Severity of symptomatic carotid stenosis often determines the treatment approach. However, severity explains only the regional hypoperfusion as the mechanism of cerebral ischemia. Artery-to-artery embolisation remains an important pathogenic mechanism in patients with high-risk carotid plaques. Inflammation is considered as the initiating event for plaque rupture and cerebral embolism. Using 18F-fluorodeoxyglucose positron-emission tomography (FDG-PET)/computed tomography (CT) and high-resolution magnetic resonance imaging (HR-MRI), we investigated the role of plaque imaging in stroke recurrence in our patients with recently symptomatic carotid stenosis. **Methods:** This prospective study included consecutive patients within 30-days of recent stroke and ipsilateral carotid stenosis ($\geq 50\%$). FDG uptake was quantified as mean standardized uptake values (SUV, g/ml). The ratio of T1 hyperintensity of carotid plaque to the ipsilateral sternocleidomastoid muscle (SCM) was recorded on T1-weighted fat suppressed HR-MRI. Patients were followed-up for stroke recurrence within 90-days. **Results:** Of the 85 patients included in the study, 12 (14%) suffered from recurrent cerebral ischemic event in the stenosed carotid territory within 90-days. Compared to patients who remained asymptomatic, patients with recurrent cerebral ischemia showed higher mean T1 carotid-SCM ratio (2.16 versus 1.42; $p<0.0001$) and higher mean SUV value in the carotid plaque (3.12g/ml versus 1.39g/ml; $p<0.0001$). Higher T1 carotid-SCM ratio on HR-MRI (OR 3.625, 95%CI 1.416-5.334; $p<0.0001$) and higher mean SUV on FDG-PET (OR 3.328, 95%CI 3.014-8.172; $p=0.005$) were independent predictors of recurrent cerebral ischemia. **Conclusions:** FDG-PET/CT and HR-MRI of carotid stenosis are useful tools for risk stratification and may aid in better therapeutic decision-making.

EP-0275

Effect of insulin resistance in [¹⁸F]FDG uptake in brain in Diabetes Mellitus Type 2 (DMT2) patients compared to non diabetic subjects

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Aim: The main objective is to assess glucose metabolism in different areas of the brain using [¹⁸F]Fluorodeoxyglucose Positron Emission Tomography ([¹⁸F]-FDG PET/CT) and to evaluate the uptake differences between diabetic and non diabetic subjects. **Materials & Methods:** 73 patients diagnosed with DMT2 and 50 non diabetic subjects with similar age underwent a [¹⁸F]FDG PET/CT, after 6 hours fast and oral glucose overload (25 mg for DMT2 and 50 mg for non diabetic subjects). When blood glucose level was < 125 mg/ml, a dose of 3.7 MBq/kg [¹⁸F]FDG

was administered. Insulin was administered when necessary to reduce high glucose levels. Brain images were obtained 45–60 minutes post-injection. Axial PET/CT images were analysed to calculate [^{18}F]FDG standardize uptake value (SUVmax) in different regions of interest (ROI): bihemispheric cortex, basal ganglia, hypothalamus and cerebellum. Student T test was applied to compare differences between T2DM and non-T2DM groups. Additionally, all patients underwent whole body PET/CT, assessing SUVmax and SUVmean in liver and vascular background regions. **Results:** DMT2 was associated with lower [^{18}F]FDG uptake compared to non diabetic individuals in all brain regions, showing statistically significant difference ($p < 0.05$). The most relevant differences were observed in bihemispheric cortex. DMT2 SUV max in bihemispheric cortex = 10.728 vs. Non-DMT2 SUV max = 14.848 ($p = 5.3 \cdot 10^{-6}$). DMT2 SUV in basal ganglia = 11.217 vs. Non-DMT2 SUV max = 14.847 ($p = 0.0003$), DMT2 SUVmax in hypothalamus = 9.694 vs. Non-DMT2 = 13.230 ($p = 1.0 \cdot 10^{-5}$). DMT2 SUV max in cerebellum = 7.762 vs. Non-DMT2 SUV max = 9.777 ($p = 0.002$). We did not find statistically significant difference in liver [^{18}F]FDG uptake between diabetic and non diabetic subjects: SUV for DMT2 was 1.861 and for non-DMT2 1.773 ($p = 0.33$). In both groups, no significant correlation was found between glycaemia and liver and vascular [^{18}F]FDG uptake. The insulin administration during oral glucose overload do not correlate with liver and vascular SUV levels. **Conclusions:** This study was conducted to evaluate the influence of insulin resistance in brain glucose metabolism. Significant reduction of [^{18}F]FDG uptake was consistently shown in DMT2 group suggesting a disorder of cellular glucose uptake in diabetes type 2 patients.

EP-0276

The effects of bariatric surgery on the brain glucose metabolism and its biological mediators: an insight from dynamic 18F-FDG PET/CT study.

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Aim: Obesity and glucose metabolism disorders are associated with accelerated age-related cognitive decline, deterioration of plasticity and metabolic homeostasis in the brain. Gut hormones act upon central circuits and exert an important role in the homeostasis of glucose metabolism. We aimed to evaluate the impact of bariatric surgery (RYGB) on the brain glucose metabolism and to access the possible relationship between cerebral metabolic rate of glucose (MRGlu) and gut hormones changes at 6 months after RYGB. **Materials and methods:** Eleven obese subjects with normal glucose tolerance (BMI 45.8 ± 4.9 kg/m²; HbA1c 41.5 ± 5.4 mmol/mol; age 43.7 ± 9.5 years) underwent an oral glucose tolerance test (OGTT) followed by 60 minutes 18F-FDG (185 ± 100 MBq) dynamic PET study before and

6 months after RYGB. Gut hormones, leptin and brain derived neurotrophic factor (BDNF) were assessed at baseline and 6 months after RYGB. Arterial input function was obtained by the first-pass of FDG from a manually drawn carotid artery region (PMOD software). Continuous venous samples were collected to scale image derived input curves and to correct for spill-in/spill-out. The two tissue compartment Patlak approach was used to calculate the MRGlu. Parametric MRGlu images were then created and spatially normalized in MNI space. Within-subject ANOVA and voxel-wise paired t-test were used to assess the changes of the mean substrates values. To determine within-individual association for paired measures the repeated measures correlations (*rmcorr*) were performed. **Results:** Six months after RYGB a significant BMI reduction ($p < 0.001$) was observed. Post-OGTT GLP1 was increased (5336 ± 2263 to 11132 ± 3412 pmol/l x 120min; $p < 0.05$) as well as GIP (4140 ± 3659 to 5791 ± 4537 pg/ml x 120min; $p = 0.01$). VIP and BDNF levels did not change 6m after RYGB, while fasting plasma leptin decreased (73.8 ± 45.5 to 14.3 ± 5.9 pmol/l; $p < 0.008$). Voxel-wise paired analysis displayed clusters of decreased MRGlu 6 months after RYGB ($p = 0.005$, $k^E > 100$, uncorrected) in the wide-spread brain regions. At the intra-individual level, *rmcorr* yields a strong positive relationship between MRGlu in the brain clusters and BMI ($r_m = 0.74$, 95% CI, $p = 0.006$) and leptin ($r_m = 0.78$, 95% CI, $p = 0.003$). Inverse association was depicted between MRGlu in the brain clusters and pre-OGTT active GLP-1 ($r_m = -0.6$, 95% CI, $p < 0.05$). **Conclusion:** Our findings imply a synergistic link between changes of circulating gut hormone levels and cerebral metabolism following the bariatric surgery. Further studies are needed to perceive the interplay between modulated gut homeostasis and the behavioral/cognitive changes after RYGB.

EP-0277

Utility Of The Portable Gamma Camera In The Diagnosis Of Brain Death

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Objective: Evaluate the usefulness of cerebral perfusion scintigraphy with a portable gamma camera as a diagnostic test for brain death, established in Annex I of Royal Decree 1723/2012 of December 28, regulating the activities of obtaining and using clinical of human organs. **Material and method:** Cerebral perfusion scintigraphy (CPS) with portable gamma camera was performed on 46 patients with a clinical diagnosis of brain death (BD) referred by the ICU of our hospital from January 2016 to December 2017. Transcranial Doppler (TD) or electroencephalogram was also performed (EEG), or the two tests in certain cases, in order to confirm the diagnosis of brain death. The GPC is performed by administering 925 MBq of Tc99m-HMPAO stabilized via I.V in bolus, washing with 10 cc of physiological saline. Static brain images of 300 seconds are acquired in lateral projections at 15 minutes post injection, with a pin-hole collimator

of 2.5 mm diameter (sentinella portable gamma camera). The BD scintigraphy criteria are established as: absence of tracer uptake in cerebral cortex and posterior fossa. Any uptakes in said regions or images of doubtful interpretation are considered not compatible with BD. The results of the CPS are compared with the TD. The EEG is not taken into account because it has very few cases. **Result:** The CPS was positive for BD in 41 of the 46 patients studied, 41 scintigraphy's were positive with other positive auxiliary tests (EEG or Doppler). Of the 5 negative scintigraphy's 4 were clearly negative and 1 was doubtful that it was considered negative or non-diagnostic. No patient presented two different negative ancillary tests for brain death. **Conclusion:** Cerebral perfusion scintigraphy with a portable gamma camera is emerging as a reliable, useful and easy to perform test, avoiding patient displacement.

EP-0278

Regional Cerebral Blood Flow Correlates of Formal Education and Socioeconomic Level in Cognitively Normal Non-elderly Subjects.

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Introduction: Evidence support that formal education can influence brain activity as measured by functional imaging in elderly subjects. The protective effects of education on dementia are well known. Education is an essential condition always taken in account in neuropsychological evaluations, but the same situation is not so clear in imaging studies. The effect of socioeconomic level is even more controversial. The objective is to assess correlations of the regional cerebral blood flow (rCBF) measured by SPECT with formal education and socioeconomic level in cognitively normal non-elderly subjects.

Methodology: 41 normal subjects (19–65 ys, mean 37.5, 22 male) evaluated by 99mTc-ECD SPECT in a Mediso NuLine Spirit DH-V dual-head gamma camera were included. Acquisition was performed in 128 steps 60 minutes after injection in a 128x128 matrix with a pixel size of 2.66 mm. Attenuation was corrected using first-order Chang with a 0.12 cm⁻¹ coefficient. Iterative OSEM reconstruction with 10 subsets and 2 iterations was carried out after Butterworth filtering (order 10, 0.20 cut-off frequency). Intellectual level was evaluated measuring abstract thinking with the analogies test. Subjects scored 12 to 24 (mean 19.2) for a normal limit of 11. Years of formal education considering an upper limit of 21 (university post-graduate) scored 9 to 21 with a mean value of 16.8. All subjects completed school and only 6 did not complete high school. The Socioeconomic Level Index commonly used in our country (INSE) classified the sample in 4 subjects of low level, 17 of medium level and 20 of high level. Regression analysis was performed in SPM8 using age and gender as covariates. Correlations with years of formal education were tested first and then INSE values were entered to the model. Voxels were interrogated at $p < 0.001$ uncorrected and cluster level was extended to $p < 0.05$ uncorrected. **Results:** Positive correlation with formal education was found in left anterior lateral and inferior temporal cortex ($kE=678$, $p=0.012$ FEW-corr), a region implicated in semantic knowledge and so-

cial-emotional information. Negative correlation was found in right dorsolateral prefrontal cortex ($kE=294$, $p=0.033$ unc). No significant correlations with INSE were detected. **Conclusion:** Formal education can condition rCBF distribution in cognitively normal subjects even with relatively high intellectual level. No changes associated with socioeconomic level were detected, although the proportion of subjects in the low level was small, potentially affecting the sensitivity of the analysis. The level of formal education should be taken in account when comparing groups of SPECT images.

EP-0279

Left Temporal Hypometabolism in FDG-PET underlines Cognitive Reserve Hypothesis in Frontotemporal Dementia

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Introduction: Frontotemporal lobar degeneration as the second most cause of presenile dementia shows a characteristic pattern of hypometabolism in frontal and temporal regions in [¹⁸F]-fluorodeoxyglucose positron-emission-tomography (FDG-PET). In ageing and dementia, the concept of cognitive reserve as a mediating factor between neuronal injury and clinical symptoms has been proposed for many years. Years of education (YoE) has been demonstrated as a proxy of cognitive reserve in Alzheimer's disease. We aimed to test how the paradigm of cognitive reserve is reflected in FTD. **Subjects and methods:** FDG-PET of 93 subjects (age 68 ± 9 years) with FTD were analysed retrospectively. Mini-mental-state-examination (MMSE) and YoE were recorded. A voxel-wise regression analysis was used to identify regional glucose metabolism associated with declining MMSE. Individual FDG-PET values were extracted from the resulting significant cluster (FWE correction, $p < 0.05$). The residuals of the partial correlation between FDG-PET and MMSE were correlated with YoE. **Results:** Cognitive deterioration (MMSE) was only correlated with left temporal hypometabolism whereas the contralateral temporal lobe and bilateral frontal cortices did not indicate significant associations. Regression analysis with values deriving from the left temporal cluster indicated a significant positive association with MMSE ($\beta = 0.62$, $p < 0.001$). The residuals of the correlation of FDG-PET and MMSE showed a significant correlation with the YoE ($\beta = 0.29$, $p = 0.005$). **Conclusion:** Cognitive decline is mainly associated with left temporal hypometabolism in FTD. Cognitive reserve expressed by a higher level of education is also present in FTD and needs to receive attention as a potential modifying factor in prevention and treatment of FTD.

EP-0280

Differential diagnosis of patients with parkinsonian syndrome using multilinear regression to disease-specific ^{11}C -PE2I-PET templates and classification tree learning

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Purpose: The selective dopamine transporter ligand ^{11}C -PE2I can provide images of both relative cerebral blood flow (rCBF) and dopamine transporter (DAT) availability using a single 40 min PET protocol. The aim of the present work was to investigate an automatic method for differential diagnosis of patients with parkinsonism based on multilinear regression to disease-specific mean rCBF and DAT image and classification tree learning. Initially, patients diagnosed as idiopathic Parkinson's disease (PD) and dementia with Lewy bodies (DLB) as well as healthy subjects (HS) were included. **Methods:** ^{11}C -PE2I-PET data from 9 PD, 9 DLB, and 9 HS were included. Subjects were referred for PET examination due to suspicion of neurodegenerative disease and differential diagnosis was performed by visual assessment of the ^{11}C -PE2I-PET images by experienced nuclear medicine physicians and neuroradiologists combined with clinical diagnosis. All rCBF and DAT images were normalised to MNI space. Each subject's images were then expressed as a linear combination of mean PD, DLB and HS images of all other subjects using non-negative regression. Classification of patients was performed by selection of the largest regression parameter for rCBF and BP_{ND} as well as by a decision tree model using regression parameters. Outcome was evaluated as sensitivity and specificity. **Results:** Classification only based on rCBF regression parameters resulted in 9/9 correct classifications for HS and DLB, but performed poorly for PD, whereas classification based only on DAT availability could not differentiate between DLB and PD. A classification tree model could correctly classify all subjects except for one PD patient that was misclassified as DLB. Hence, the classification tree model showed 89% sensitivity and specificity for DLB and 89% sensitivity and 100% specificity for PD, respectively. Leave-one-out cross-validation showed a misclassification rate of 8% using this simple model. Including only rCBF regression parameters did not affect accuracy for DLB, but reduced sensitivity and specificity to 67% and 78% for PD, respectively. **Conclusion:** The classification tree model was able to provide a correct differential diagnosis between HS, PD and DLB in nearly 90% of cases in this small subject sample. The small patient sample and the fact that the ground truth was partly an image-based diagnosis are limitations of the present work, as is the lack of using asymmetry information, but it nevertheless seems promising. The classification tree model is currently being extended to larger samples, considering other atypical parkinsonian disorders using data from 250 patients.

EP-18

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Cardiovascular -> Perfusion, metabolism and receptors

EP-0292

Value of calcium scoring in addition to MPI in patients with CAD

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Introduction: Coronary artery calcium CAC may be a marker of an increased risk of coronary artery disease events. CAC score represents an assessment of the presence and extent of atherosclerosis and may therefore be useful in predicting future events. Calcification may actually reflect stabilization and maturation of atherosclerotic plaques and lead to fewer myocardial infarctions and CHD deaths. **Purpose:** Find out the correlation between MPI and calcium scoring in patients with different risk factors of coronary heart disease. **Subject and methods:** 50 patients had been subjected to clinical examination looking for risk factors, body mass index BMI, and multislice CT for CAC score and gated myocardial perfusion SPECT MPI. **Results:** the current study included 58% male (aged 58.1+7.9) and 42% female (aged 58.3+9.6) ($P>0.05$). thirty one patients (62%) showed +ve MPI with 8 cases (26%) had infarct alone or with ischemia. Multivariate analysis revealed that in the presence of obesity, diabetes mellitus, hypertension, there is a strong impact of sex, age and high CAC score to diagnose +ve MPI and higher value of SSS score. **Conclusion:** high total CAC score in elderly male patient is strongly predictable for coronary artery disease with high SSS. In similar aged females, further assessment is needed.

EP-0293

Cardiac Amyloidosis. Utility of bone seeking tracers scintigraphy in differentiation the subtype of Amyloid

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Aim: Cardiac amyloidosis is an infiltrative cardiomyopathy, caused by the deposition of insoluble fibrils in the myocardium. The aim of the study was to assess the value of myocardial scintigraphy using $^{99\text{mTc}}$ PYP in the diagnosis of cardiac amyloid deposition derived from transthyretin and the differentiation of the amyloidosis subtype. **Materials and methods:** 7 patients with heart failure, concentric left ventricular hypertrophy, diastolic dysfunction and normal systolic function, findings revealed by transthoracic echocardiogram, were involved in our study with the suspicion of cardiac amyloidosis. All of them underwent genetic testing and myocardial scintigraphy using $^{25\text{mCi}}$ $^{99\text{mTc}}$ -PYP. Planar image of anterior thorax with the heart centred in the field of view was obtained 1 hour

post injection with a dual head tomographic γ camera (Philips Forte Jet Stream). A qualitative visual scoring of cardiac retention (0: absent cardiac uptake, 1: mild uptake less than bone, 2: moderate uptake equal to bone, 3: high uptake greater than bone), and a semiquantitative analysis of heart retention was calculated by drawing a region of interest (ROI) over the heart and on the contralateral chest. The fraction of mean counts in the heart ROI-to-contralateral chest ROI was calculated as the heart-to-contralateral (H/CL) ratio. **Results:** Scintigraphic findings revealed in all 7 patients a very intensive tracer uptake in the heart region compared to bone tissue (score 3). The (H/CL) ratio was > 1.5 (reference value > 1.5). The above findings were suggestive of transthyretin-related (TTR) cardiac amyloidosis. ATTR amyloidosis is associated with less heart failure and a much better long-term survival compared to AL cardiac amyloidosis. Current management remains symptomatic. **Conclusion:** Planar myocardial scintigraphy using ^{99m}Tc -PYP could be able to establish the diagnosis of cardiac amyloidosis and to provide useful information about the cardiac amyloidosis subtype and the therapeutic management.

EP-0294

The diagnostic role of ^{99m}Tc -PYP scintigraphy in the differential diagnoses of cardiac amyloidosis: preliminary results

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Introduction: Cardiac involvement in Patient with amyloidosis it's the most unfavorable prognostic factor. Most common types of cardiac amyloidosis (CA) are caused by fibril deposits of immunoglobulin light chains (AL) and transthyretin (TTR, m or wild type). The gold standard for diagnosis is endomyocardial biopsy, an invasive procedure with possible risks and complications. There is a need of noninvasive reliable diagnostic test to select patient for this procedure. To diagnose CA are commonly used morphological imaging modalities (echocardiography-lacks sensitivity and specificity, and cardiac-RM not enough specific to differentiate AL or TTR). Radionuclide scintigraphy with bone seeking tracers has been a valuable tool in the differential diagnosis of CA (AL vs TTR). Most European Center use ^{99m}Tc -diphosphonates while we use ^{99m}Tc -PYP: we conducted our study to ascertain the diagnostic value of ^{99m}Tc -PYP scintigraphy in suspected CA. **Subjects-Methods:** From December 2016 to April 2018 14 patient were addressed to our Nuclear Medicine Unit from Cardiology Department with morphological imaging suspected for CA. Our study population was composed from 9 males and 5 females, age (range 39-83, median 65.7 years). All Patients were injected with 740 MBq of ^{99m}Tc -PYP and static chest images were acquired 60-80' post injection. Then, if there was myocardial retention of radiolabeled tracer, a cardiac SPECT/CT was performed. Cardiac retention of ^{99m}Tc -PYP was visually evaluated and graded with the score suggested by Rapezzi (JACC, 2011) and also with a semiquantitative score Heart-to-Contralateral ratio. **Results:** The study was clearly positive for 5 patients and suggestive for ATTR (grade=3), with SPECT/CT confirming a diffuse concentration in the left

ventriculum (pathological infiltration from amyloid). One patient had a grade=2, and follow up confirmed a cardiac AL amyloidosis in mieloma. Of the remaining 7 patients negative for ATTR (grade $\leq$ 1), 3 were diagnosed with AL amyloidosis in monoclonal gammopathy, in 3 AL was excluded (RM not suggestive and/or biopsy of periumbilical adipose tissue), while 1 had a positivity at periumbilical fat for AL, but wasn't supported in follow up, so it was considered a false positivity. **Conclusions:** Our preliminary results show promising use of ^{99m}Tc -PYP scintigraphy as a valid alternative to ^{99m}Tc -diphosphonates with a potential better compliance of the patient (scanned at 60-80' vs 3 hours). The positivity of the study was related with a good accuracy to ATTR while a low grade was highly related to AL form. It can be useful in selecting patients for endocardial biopsy, being safe and fast.

EP-0295

The Value of Myocardial Perfusion Scintigraphy Findings on Early-Onset Cardiac Event Risk in Patients with Coronary Artery Bypass Graft and Percutaneous Coronary Intervention: Single Center Preliminary Results

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Introduction: The role of myocardial perfusion scintigraphy (MPS) in determining of early event risk in patients with known coronary artery disease (CAD) and earlier intervention was sought. Application to emergency room (ER) and/or percutaneous coronary intervention (PCI) after MPS, admission to coronary unit, stent application, non-fatal myocardial infarct (MI) and cardiac event resulting with death was accepted as pathological outcome. **Subjects & Methods:** In the study group, the results of 215 single-center assessed patients (mean age: 62 ± 2 ; 102 female, 113 male) were retrospectively analyzed for cardiac events. Patients were generally evaluated for risk of cardiac event after MPS and in two subgroups as having coronary artery bypass graft (CABG) ($n = 90$) and percutaneous coronary intervention (PCI) ($n = 125$). In the CABG group, 55 patient have normal MPS while 35 have pathologic. In 6 patients with normal group, coronary angiography (CAG) pathology was detected. In the PCI group, 47 patients had normal MPS and 78 had pathologic results. Seven of normal had pathology in the CAG. 45 patients with abnormal MPS were needed to be evaluated with KAG; and 26 of them were treated (restented or made POBA). There was a significant difference in the outcome of MPS N / P in CABG and PCI group (χ^2 : 11.6, p : 0.001). **Results:** Cardiac events were detected in 70 of 215 patients at one-year follow-up. The distribution of MPS normal/pathologic (N/P) in the cardiac event group was 11/59. In MPS normal group; four cases with CABG and seven with stent had minor cardiac events. A cardiac event resulting with death was detected in the CABG group. The odd ratio for MPS (N/P) in determining cardiac event independently of CABG and stent group is calculated as OR: $8.1 \pm 95\% \text{ CI: } 3.9-16.8$, p : 0.0001. In addition; the odd ratio for pathologic MPS in determining cardiac event is calculated as OR: $1.27 \pm 95\% \text{ CI: } 0.24-6.5$, p : 0.001 in CABG group, and as OR: $1.27, \pm 95\% \text{ CI: } 1.1-$

1.5, p : 0.01 in stent group. **Discussion:** As a result, pathologic MPS result regardless of sub parameters (reversible and/or fix defect) is found to increase the risk of cardiac event in patient with known CAD and/or with intervention before MPS. This relation is more prominent in the stent-applied group, but causes are more serious events in CABG group.

EP-19

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Endocrinology -> Endocrinology, benign I

EP-0296

The Differences in Transport Kinetics of ^{99m}Tc -Sestamibi in Preoperative SPECT/CT Parathyroid Scintigraphy in Primary and Non-primary Hyperparathyroidism on Per-lesion Basis Qualitative Analysis

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Background: Dual phase, single tracer preoperative parathyroid scintigraphy can show three types of tracer accumulation - the presence of ^{99m}Tc -Sestamibi in both phases, only in early or late phase of the study. The appearance of the tracer in particular time points of the study is relative to protein transporters for ^{99m}Tc -Sestamibi. The etiology of primary hyperparathyroidism (pHPT) and non-primary (secondary and tertiary) hyperparathyroidism (non-pHPT) is quite different but in both increased accumulation of the tracer can be observed. **Aim:** to analyze qualitatively the transport kinetics of ^{99m}Tc -Sestamibi in preoperative SPECT/CT in pHPT and non-HPT on per-lesion basis and examine differences in types of tracer accumulation. **Material and Methods:** The group of 332 patients, 240(84.3%) females (F) and 92(27.71%) men (M) referred to preoperative SPECT/CT parathyroid scintigraphy were examined. There were 242(72.89%) patients with suspicion of pHPT: 204F(84.30%) and 38M(15.70%); 78(23.49%) patients with secondary hyperparathyroidism: 30F(38.46%) and 48M(61.54%); 12(3.61%) patients with tertiary hyperparathyroidism: 6F(50%) and 6M(50%). No abnormality in ^{99m}Tc -Sestamibi SPECT/CT study was shown in 61 patients and 5 patients with pHPT and non-PTH, respectively. Further analysis was done for 525 lesions, which were found in 280(201F, 79M) aged 11-89 years (average age 56.1 years). Based on tracer accumulation in early phase (EP) and delayed phase (DP), the following types of accumulation were identified: EP(-)/DP(+) (type I), EP(+)/DP(+) (type II), EP(+)/DP(-) (type III). **Results:** From total number of 525 lesions 300(57.14%) and 225(42.86%) were found in pHPT and non-HPT, respectively. According to types of uptake type I was found in 101(58.72%) and 71(41.28%) lesions; type II in 161(53.49%) and 140(46.51%) lesions; type III 38(73.08%) and 14(26.92) lesions for pHPT and non-HPT, respectively. Statistically significant difference was found between uptake type II and III in patients with pHPT and non-HPT (p -value=0.008) **Conclusion:** The type III of tracer

accumulation which corresponds with wash-out of ^{99m}Tc -Sestamibi in preoperative SPECT/CT parathyroid scintigraphy occurs significantly rarely in secondary and tertiary hyperparathyroidism. This may illustrate the different origin of pHPT and non-pHPT. This study was supported by a grant from budget resources for science in the years 2010-2015 as a research project No. N N402 463339

EP-0297

^{18}F -Fluorocholine PET/CT in hyperparathyroidism exploration - A monocentric experience

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Purpose: Parathyroid scintigraphy is, in combination with cervical ultrasound, a valuable tool in the management of hyperparathyroidism (HPT) before mini-invasive surgical procedure. A growing number of teams reported the interest of ^{18}F -Fluorocholine Positron Emission Tomography (FCH- PET) in parathyroid exploration. The objective of our study was to evaluate the contribution of PET-FCH in the assessment of HPT through our monocentric experience. **Materials and Methods:** Our observational, retrospective, uni-centric study was conducted from January 2017 until April 2018 including all patients who underwent FCH-PET examination. The indications of the examinations, the locations of the pathological uptakes and their histological nature when known were collected. **Results:** Forty nine PET-FCH were performed in 48 patients. The mean age was 62.4 years, sex ratio F/H = 2.5, the average activity injected 164MBq. All patients had a confirmed biological hyperparathyroidism and all examinations were performed in a preoperative perspective. The indications were : an ultrasound and / or MIBI scintigraphy doubtful or non-conclusive (43%, n = 21), persistent hyperparathyroidism or recurrence after previous surgery (33%, n = 16), suspicion of pluri-glandular disease (10%, n = 5), characterization of suspected lesion diagnosed on morphological imaging technics (6%, n = 3), first-line exploration of hyperparathyroidism (6%, n = 3) or exploration of a transplanted gland (3%, n = 1). Thirty seven positive PET-FCH revealed 41 focal pathological uptakes suggesting hyperfunctional parathyroid glands; the others 12 exams were negative. Twelve patients underwent surgery and histological analysis. Surveillance was decided for 10 patients following the result of the PET scan (5 following a negative examination, 2 with suspicious lesions but not immediately operable, 2 with suspicious lesions but a willingness of the patient of first-line medical treatment, 1 with a positive examination but surgery delayed by the management of a malignant disease). Finally, 26 patients are waiting for a therapeutic decision. Histological data are available in 12 patients, with a total of 13 removed lesions. The anatomopathological study found 10 adenomas, 2 parathyroid hyperplasias and a normal sample. Sensitivity and specificity of PET-FCH were respectively 91.6% and 100%. **Conclusion:** ^{18}F -Fluorocholine PET is an effective test in the assessment of

hyperparathyroidism and preoperative assessment, especially when others imaging techniques are not contributory.

EP-0298

An Assessment of the Effectiveness of a new 'TripleSPECT+' Protocol in Parathyroid Adenoma Localisation, including consideration of Surface Rendered Processing

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Background and Aim: Localisation of parathyroid adenomas using scintigraphy can guide surgical intervention for patients with hyperparathyroidism. This study aimed to compare the effectiveness of a new 'TripleSPECT+' parathyroid protocol to the 'TriplePlanar+' protocol used previously in our department. We also aimed to assess any additional benefit to the new protocol of advanced post processing using surface rendering. **Materials and Methods:** The previous TriplePlanar+ protocol consisted of 400MBq ^{99m}Tc -MIBI intravenously, with early planar images, delayed planar images at 2 hours, with possible additional clinician directed SPECT or SPECT-CT. This was followed by thyroid planar imaging following 80MBq pertechnetate intravenously. The new TripleSPECT+ protocol consisted of a thyroid SPECT study following 40MBq pertechnetate intravenously, immediately followed by early ^{99m}Tc -MIBI SPECT after 900MBq ^{99m}Tc -MIBI injection. All patients then had delayed MIBI SPECT-CT at 2 hours. These images were then available for post processing including surface rendering if reporters felt this would be helpful. A retrospective assessment was made of reports for sequential patients before and after the introduction of the new TripleSPECT+ protocol. Reports were graded according to confidence of reported lesions into the following categories: strongly positive, weakly positive, indeterminate and negative, for parathyroid adenoma detection. **Results:** 60 sequential patients were evaluated: 30 before and 30 after the introduction of the new protocol. Of the 30 patients who underwent the TripleSPECT+ protocol, 21 had advanced post processing using surface rendering performed. Using the TriplePlanar+ protocol: (n=30, mean age: 59, 73% female), 43% were graded positive (20% strongly, 23% weakly), 3% were indeterminate and 53% were negative. Using the new TripleSPECT+ protocol: (n=30, mean age: 58, 83% female), 57% were graded positive (47% strongly, 10% weakly), 7% indeterminate and 37% as negative. With consideration of surface rendering these results would have been (n=21): 86% graded positive (67% strongly, 19% weakly), 0% indeterminate and 14% negative. **Conclusion:** In this small pilot study without the benefit of histopathological correlation, the new TripleSPECT+ protocol appears considerably more successful at localising lesions than the TriplePlanar+ protocol particularly when surface rendered images are also considered.

EP-0299

Diagnostic Performance of Radiolabelled Choline PET/CT in Detecting Hyperfunctioning Parathyroid Glands in Patients with Primary Hyperparathyroidism: A Meta-analysis from the PET and Thyroid Working Groups of the Swiss Society of Nuclear Medicine.

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Purpose: Primary hyperparathyroidism (PHPT) is a common endocrine disorder usually due to hyperfunctioning parathyroid glands (HP). Surgical removal of HP is the main treatment in PHPT, particularly in symptomatic patients. The correct detection and localization of HP is challenging and crucial as it may guide surgical treatment in patients with PHPT. To date, different imaging methods have been used to detect and localize HP in patients with PHPT and there are increasing literature data about the role of radiolabelled choline PET/CT in this setting, in particular when conventional imaging (ultrasound or ^{99m}Tc -MIBI scintigraphy) is negative or inconclusive. Therefore, we aimed to perform a meta-analysis about the diagnostic performance of radiolabelled choline PET/CT in detecting HP in patients with PHPT to provide more evidence-based data in this setting. **Methods:** A comprehensive computer literature search of studies published through April 2018 in PubMed and Cochrane library databases regarding the diagnostic performance of radiolabelled choline PET/CT in patients with PHPT was carried out. The following search algorithm was used: A) "choline" or "fluorocholine" or "F-choline" or "C-choline" or "FCH" or "CH" or "FECH" or "FMCH" and B) "PET" or "positron emission tomography" and C) "parathyroid" or "hyperparathyroidism". Pooled detection rate, sensitivity and positive predictive value (PPV) of radiolabelled choline PET/CT in detecting HP in patients with PHPT were calculated, on a per-patient and on a per-lesion based analysis. Statistical analyses were performed using StatsDirect software (Altrincham, UK). **Results:** Thirteen studies on the use of radiolabelled choline PET/CT in 486 patients with PHPT were included in the pooled analysis. The meta-analysis provided the following results on a per-patient based analysis: detection rate was 92% [95% confidence interval (95%CI): 89–95%], sensitivity 95% (95%CI: 92–97%), PPV 97% (95%CI 95–98%). On a per-lesion based analysis pooled sensitivity and PPV were 92% (95%CI: 88–96), and 92% (95%CI 89–95%), respectively. No significant heterogeneity among the selected studies was found. **Conclusions:** Radiolabelled choline PET/CT demonstrated an excellent diagnostic performance in detecting HP in patients with PHPT with negative or inconclusive conventional imaging. Large multicenter studies and cost-effectiveness analyses are needed to strengthen the role of this imaging method in this setting.

EP-0300

Pet/ct With ^{18}F -fluorocholine May Detect Parathyroid Adenomas Also In Preclinical Or Subclinical Stage

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Aim: The majority of patients with primary hyperparathyroidism are diagnosed in a preclinical or subclinical stage. Identification of pathologic parathyroid glands in primary hyperparathyroidism, traditionally based on neck ultrasound (US) and/or 99mTc-Sestamibi scintigraphy, can be very challenging. PET/CT with 18F-Fluorocholine (18F-FCH) might improve detection of pathologic parathyroid glands, thanks to its better spatial resolution and lesion-to-noise ratio. We aimed to compare the diagnostic performance of 18F-FCH with that of dual-phase dual-isotope parathyroid scintigraphy and neck US. **Methods:** Thirty-four consecutive patients with primary hyperparathyroidism were prospectively enrolled. All patients underwent high-resolution US, dual-phase dual-isotope 99mTc-Pertechnetate/99mTc-Sestamibi scintigraphy (MIBI), and 18F-FCH. Thirteen patients out of 34 had a subclinical (normocalcemic) hyperparathyroidism; 3 patients had inappropriately normal serum PTH levels with concomitant hypercalcemia. **Results:** In the whole patients' group, mean values were respectively 0,63 mL (range 0,1–1,8 mL) for parathyroid US volume, 174,2 pg/mL (66,6–615,7 pg/mL) for PTH levels and 10,5 mg/dL (9,2–12,2 mg/dL) for calcium levels; in the sub-group with sub-clinical hyperparathyroidism mean values were respectively 0,46 mL (0,1–1,8 mL) for US volume, 151,9 pg/mL (80,0–249 pg/mL) for PTH levels and 10,0 mg/dL (9,2–10,7 mg/dL) for calcium levels, while in the group with inappropriately normal serum PTH mean parathyroid volume was 1 mL, mean PTH levels 70 pg/mL, mean calcium levels 10,63 mg/dL. The detection rates in the whole group were 68% for neck US, 71% for 18F-FCH PET/CT, and 15% for MIBI. No-one of the normocalcemic hyperparathyroid patients have been identified by MIBI, while US and 18F-FCH achieved 61% and 71%, respectively. Patients with inappropriately normal serum PTH levels showed no significant differences from the whole group results (MIBI was positive in 2 patients, 18F-FCH in 3 and US in 2; among 2 histopathological confirmation, one of them was MIBI negative). In 6 out of the 13 patients with sub-clinical hyperparathyroidism a final diagnosis was achieved by cytological examination and/or surgery: 4 were FCH positive, 1 FCH PET/CT was erroneously interpreted as negative (intra-thymic parathyroid adenoma) and 1 had a doubtful result (poor target-to-background ratio). **Conclusions:** 18F-FCH PET/CT showed a great utility in pre-surgical evaluation of parathyroid glands in hyperparathyroid patients, even if the parathyroid volume is small. 18F-FCH appears particularly useful in the sub-group of patients with sub-clinical hyperparathyroidism, among which the 99mTc-Sestamibi scintigraphy showed a poor sensitivity.

EP-0301

Physiologic uptake of stellate or upper thoracic ganglia on ⁶⁸Ga-DOTATOC PET/CT

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Purpose: In ⁶⁸Ga-1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid-D-Phe¹-Tyr³-octreotide (DOTATOC) positron emission tomography/computed tomography (PET/CT), small foci of increased ⁶⁸Ga-DOTATOC uptake are easily found in the paravertebral cervicothoracic junction which correspond to the location of the bilateral stellate or upper thoracic ganglia. This retrospective study aimed to evaluate physiologic uptake in the cervicothoracic junction on ⁶⁸Ga-DOTATOC PET/CT. **Subjects & Methods:** Eighty-two patients (49 men, 33 women) who underwent ⁶⁸Ga-DOTATOC PET/CT for the evaluation of neuroendocrine tumors (n = 75) and osteomalacia (n = 7) were included. The maximum standardized uptake value (SUVmax) of the bilateral cervicothoracic junction and SUVmean of aortic arch were obtained. SUVmax of the bilateral cervicothoracic junction to blood pool ratio (CBR) was compared according to the laterality, age, and sex. **Results:** In all 82 patients (median age, 54 years; range 21–86), ⁶⁸Ga-DOTATOC uptake was noted in the bilateral sides of the cervicothoracic junction, paravertebral area between the 1st to 2nd ribs anterior to the ribs. Two focal ⁶⁸Ga-DOTATOC uptakes were seen in 78 patients and three focal ⁶⁸Ga-DOTATOC uptakes were seen in 4 patients. Of 78 patients who showing two focal ⁶⁸Ga-DOTATOC uptakes, ⁶⁸Ga-DOTATOC uptake was seen in the same level of ribs in 67, and different levels of ribs in the 11 patients. Of 67 patients, ⁶⁸Ga-DOTATOC uptake was seen close to the bilateral 2nd ribs in 49 patients, and near the bilateral 1st ribs in 18 patients. Mean CBR was 2.85 ± 1.16 (range 1.08–7.87). CBR was 2.80 ± 1.07 (range 1.05–6.20) for the right and 2.90 ± 1.39 (range 1.02–10.88) for the left one without significant difference (*p* = 0.257). There was a moderate, negative correlation between the age of the patients and CBR (*r* = -0.411, *p* < 0.001). CBR was 3.07 ± 1.24 (range 1.34–7.87) for male and 2.53 ± 0.95 (range 1.08–5.69) for female showing borderline of significant difference (*p* = 0.073). **Conclusion:** There is physiologic uptake in the paravertebral cervicothoracic junction which corresponds to the locations of the stellate or upper thoracic ganglia on ⁶⁸Ga-DOTATOC PET/CT. Imaging of the sympathetic ganglia by ⁶⁸Ga-DOTATOC PET/CT may open a new window to study the relationship between somatostatin receptor expression of the ganglia and sympathetic nervous system related disorders.

EP-0302

Added Value of Companion Targeted Ultrasound to Parathyroid Scintigraphy: Correlation with Pathologic Findings

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Introduction: With the advent of minimally invasive surgery for hyperfunctioning parathyroid tissue, pre-operative localisation has become increasingly crucial in the surgical workup. Established modalities include Tc-99m sestamibi scintigraphy (PT scintigraphy), ultrasound (US), and multiphasic computed to-

mography, all with varying utility and limitations. Planar PT scintigraphy, as a functional imaging modality and ability to screen a large field of view, is however, limited in spatial resolution without the routine use of SPECT-CT. We investigated the value of companion US, as a readily available technique without added ionising radiation, performed alongside PT scintigraphy, in improving the overall diagnostic sensitivity. **Subject & Methods:** Planar PT scintigraphy was performed and interpreted as per established guidelines. The usage of subtraction imaging with Tc-99m pertechnetate, SPECT-CT, or delayed imaging was at the discretion of the attending nuclear physician. Targeted US was performed by nuclear physicians or accredited residents prior to scintigraphy, with re-look ultrasound performed as indicated after initial planar scintigraphy to correlate with latter findings. A retrospective review of cases over a 4 year period was performed, in conjunction with known surgical and histopathological findings. **Results:** A total of 390 cases were reviewed. PT scintigraphy and companion US were performed in all cases. Subtraction imaging was performed in 130 (33.3%), and SPECT/CT in 58 (14.9%), the remaining relying on delayed scintigraphy. Of the cases reviewed, 255 (65.4%) were deemed positive by the interpreting nuclear physician, 133 (34.1%) negative, and 2 (0.5%) were equivocal. The breakdown of the key modalities for diagnosis is as follows: Scintigraphy positive, US positive; 213 (54.6%) Scintigraphy positive, US negative; 20 (5.1%) Scintigraphy negative, US positive 17 (4.4%) SPECT positive, US negative; 5 (1.3%) The remainder were negative on both modalities. Notably, 4.4% of cases were negative on scintigraphy but suspicious for hyperfunctioning parathyroid tissue on US. Of these cases, 5 went to surgery and 4 (80%) were concordant. A total of 150 patients underwent surgery with documented histological findings. Overall sensitivity of the combined PT scintigraphy/US technique was 82.6% with positive predictive value (PPV) of 96.8%. Taking into account scan negative patients who did not go to surgery, specificity was 97.0% with a negative predictive value of 82.9%. **Conclusion:** A combined PT scintigraphy with targeted US approach to identifying hyperfunctioning parathyroid tissue leads to a high PPV of 97%. The addition of targeted US can help to localise an additional 4% of lesions without requiring ionising radiation.

EP-0303

Pitfalls of using 18F-choline as a second line imaging in patients with primary hyperparathyroidism and negative conventional imaging localisation in a multiglandular disease patient subgroup

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Introduction: Primary hyperparathyroidism (PHPT) is a common endocrine disorder, characterised by parathormone (PTH) overproduction caused in 80-85% by a single parathyroid adenoma and in 10-15% by multiglandular disease (MGD): parathyroid hyperplasia or dual adenoma. Preoperative localisation is performed by nuclear medicine imaging methods in order to enable minimally invasive parathyroidectomy (MIP) in patients

with a single hyperfunctioning gland (SHG). MGD or negative imaging result in classical bilateral neck exploration. Both anatomical and functional imaging methods have a suboptimal sensitivity for detecting MGD leading to misdiagnosis and putting patients treated with MIP at risk for later recurrences. **Objectives:** Evaluation of diagnostic value of 18F-choline PET/CT as a second line imaging in patients with negative conventional imaging. To demonstrate a potential pitfall of MGD patients being falsely classified as SHG (and as such predisposed for MIP) only patients with MGD were included in the analysis. **Methods:** 104 patients prospectively enrolled in a comparison study were imaged preoperatively with conventional parathyroid scintigraphic methods (99mTc-sestaMIBI SPECT/CT, 99mTc-sestaMIBI/pertechnetate subtraction imaging and 99mTc-sestaMIBI dual-phase imaging) and 18F-choline PET/CT. Only patients with MGD were included in this analysis. Imaging results were compared against histology and postoperative Ca2+ and iPTH to calculate sensitivity and specificity for 18F-choline PET/CT and conventional methods combined. **Results:** Fifteen patients with histologically confirmed MGD (14% of the total study group) were included: 5 patients with dual adenoma and 10 patients with 33 hyperplastic glands. Per-lesion sensitivity of PET/CT was significantly higher (88%) than sensitivity of conventional imaging combined (44%), with specificity being 100% for all imaging methods. Per-patient analysis showed that 2/15 patients were negative on conventional imaging and would benefit with second line 18F-choline PET/CT which correctly established MGD. 7/15 patients were falsely classified as SHG on conventional imaging while 18F-choline PET/CT correctly classified them as MGD. In 1/15 patient both imaging methods localised only SHG. In 2/15 patients all glands were correctly localised by conventional and PET imaging. Remaining 3/15 patient were correctly classified as MGD with both methods, conventional imaging localising less glands than 18F-choline PET/CT. **Conclusion:** As demonstrated in a group of patients with MGD, choosing 18F-choline PET/CT as a second line imaging when conventional imaging is negative does improve sensitivity on a per-lesion basis, but can often falsely localize only a SHG (47% of patients in our study group) predisposing patients for MIP which can in case of sufficient intraoperative PTH reduction lead to PHPT persistence.

EP-0304

Minimally invasive parathyroidectomy in primary hyperparathyroidism: Value of preoperative localization

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Purpose: To evaluate the concordance of functional (FT) and morphological (MT) imaging techniques in the preoperative location in primary hyperparathyroidism (PHPT), to justify minimally invasive surgery (MI) and to analyze differences depend-

ing on the location of the hyperfunctioning glands. **Subjects & Methods:** We retrospectively studied 64 patients, 50 (78.1%) women, mean age 63 years (95% CI 59–66), with PHPT screened with ^{99m}Tc -MIBI scintigraphy, and subsequently operated from July 2016 to December 2017. Planar scintigraphy was acquired (15 min and 3 hours post administration of 740 MBq ^{99m}Tc -MIBI) and SPECT-CT after early imaging, as well as cervical ultrasound. Additionally, PET with ^{11}C -Methionine, CT and/or ^{99m}Tc thyroid scintigraphy when they were not conclusive. The pathological confirmation of the parathyroid lesion and the normalization of the calcemia indicated the success of the intervention. **Results:** ^{99m}Tc -MIBI was positive in 58 patients (90.6%); four more in PET, reaching a preoperative localization with FT in 62 patients (96.9%). The ultrasound localized the lesion in 58 (90.6%), two more with CT, achieving localization with MT in 60 (93.7%). In the intervention, hyperfunctioning gland-s were successfully removed in 60 patients (93.7%), 47 (78.3%) in perithyroid location, 13 (21.7%) in extrathyroid location, having noted concordance of MT and FT in 43 (91.5%) and 11 (84.6%) respectively. One was hyperplasia, the other adenomas. Considering the four not located intraoperatively, two were ectopic (MIBI, US, CT concordant) and two were false positives of MIBI by thyroid adenomas. The initial approach was MI in 47 patients (73.4%), extended in the same procedure to cervicotomy in 5: just one due to discordance in the preoperative location, the rest due to technical difficulties (two intrathyroid location of the adenoma, one due to the large size of the adenoma, and another one due to an error in the intraoperative pathological analysis). Initial cervicotomy was performed in 17 patients (26.6%), due to coexistence of thyroid pathology in 12 cases, double adenoma in 2, reoperation in 3. In 41/42 (97.6%) MI surgical procedures the lesion was successfully excised (6 in extrathyroid location, 35 perithyroid location), in the 5 extended MI (2 extrathyroid, 3 perithyroid) and in 14/17 (82.3%) cervicotomies (5 extrathyroid, 9 perithyroid). **Conclusion:** The correct preoperative location allows a minimally invasive approach in most PHPT, regardless of the perithyroid or extrathyroid location of the lesion. A multidisciplinary approach to the entire procedure is necessary.

EP-0305

Comparison of Diagnostic Sensitivity and Quantitative Indexes between ^{18}F -Fluorocholine PET/CT and ^{99m}Tc -MIBI SPECT/CT in Primary Hyperparathyroidism: A Pilot Study
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Purpose: ^{99m}Tc -MIBI has been used for parathyroid imaging. Recently, ^{18}F -fluorocholine (FCH) PET has been reported effective for parathyroid imaging. In this study, we compared visual and quantitative indexes between ^{99m}Tc -MIBI SPECT/CT and ^{18}F -FCH PET/CT. **Subjects & Methods:** Eight patients with hyperparathyroidism were prospectively enrolled and underwent SPECT/CT and PET/CT before operation. Each location of parathyroid was visually graded on both images. For positive lesions, target-to-normal ratio (TNR) and metabolic tumor volume (MTV) with reference to mean count of the lungs were analyzed. Inter-observer agreement of visual grading was assessed, and

quantitative indexes were evaluated in terms of correlation with anatomical factors and functional status of patients. **Results:** Among 8 patients, 5 lesions were diagnosed with parathyroid adenoma, and 10 lesions, with hyperplasia. Both SPECT/CT and PET/CT showed excellent inter-observer agreement ($\kappa > 0.7$). PET/CT exhibited a higher sensitivity than SPECT/CT, without statistical significance (93% vs. 73%, $P = 0.250$). MTV was smaller on PET/CT (3.45 ± 2.00 mL vs. 5.60 ± 3.50 mL, $P = 0.01$), whereas TNR exhibited no significant difference (6.45 ± 3.10 vs. 6.46 ± 2.50 , $P = 0.955$). MTV on PET/CT was correlated with pathologic volume ($r = 0.994$, $P < 0.001$) whereas MTV on SPECT/CT was correlated with preoperative PTH level ($r = 0.715$, $P = 0.046$). **Conclusion:** ^{18}F -FCH PET/CT has a high diagnostic sensitivity for hyperfunctioning parathyroid glands and close correlation with anatomical volume of lesions, whereas ^{99m}Tc -MIBI SPECT/CT is well correlated with functional status. Further study is warranted regarding diagnostic performance and functional significance of ^{18}F -FCH PET/CT.

EP-0306

Quantitative multiple-phase scintigraphy for the optimization of the gamma probe-guided parathyroidectomy using a separate-day protocol

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Introduction: solitary adenoma is the most common cause of primary hyperparathyroidism (PHPT) and minimally invasive radioguided surgery (MIRS) is up-to-date curative approach. The conventional dual-phase ^{99m}Tc -sestamibi (MIBI) scintigraphy is based on the different thyroid-parathyroid washout and MIRS is generally the most successful within a recommended narrow time window 2–3 h after preoperative MIBI administration. However, parathyroid adenoma and thyroid gland tracer uptake and washout may vary from patient to patient and these factors may have an effect on MIRS success rate. **Aim:** assessment of an additional value for determining patient specific time period between preoperative MIBI administration and gamma probe guided surgery based on multi-phase scintigraphy. **Materials and Methods:** the diagnosis of PHPT was confirmed by repeated parathyroid SPECT/CT examinations at 10, 90, 150 and 210 min after MIBI administration in 34 adult patients (9 men, 25 women). Gamma camera was calibrated so quantitative measurements of SUV (standardized uptake value) were possible. SUV values (average - SUVavg and maximum - SUVmax) were obtained by modified iterative reconstruction OSCGM (Ordered Subset Conjugate Gradient Minimization). We compared the SUV values in the volumes of interest over parathyroid adenoma (SUVadenoma) and contralateral thyroid lobe (SUVthyroid). The ratios between SUVadenoma and SUVthyroid resulted in activity washout curves. Based on differences in this washout we recommended patient specific time interval from MIBI administration to MIRS. On the day of surgery time of MIBI administration, beginning and surgery duration, parathyroid adenoma-thyroid

differences in counts per second in vivo and in vitro together with histological findings were recorded. **Results:** eutopic parathyroid adenoma was found in 23/34 cases, 11/34 were localized ectopically (5 in paraesophageal region and 6 located distally to lower thyroid pole). Early parathyroid washout was observed in 10/34 cases. Up to now 12 of 34 patients with PHPT underwent MIRS with recommended optimal time to surgery (MIBI-MIRS) from 30 to 180 min. MIRS was successful (histopathologically confirmed) in all 12 cases with surgery duration between 20–50 min (avg. 31 min). **Conclusion:** multi-phase SPECT/CT scintigraphy provides valuable SUV information for individualized approach to more efficient and faster surgery: maximizing contrast between background and parathyroid adenoma, shortening surgery duration, reducing radiation burden to surgeons and staff. We consider this method the most beneficial for patients with ectopically localized parathyroid adenomas and for those with early washout.

EP-0307

Is the second Octreotide SPECT/CT needed?

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Introduction: In most centres, an Octreotide scan with SPECT/CT is routinely performed at 4 and 24 hours following administration of ¹¹¹In-pentetreotide. It is unclear if both images are needed and which imaging time point is superior. No studies have been done to compare the octreotide uptake at the different time points. In this study we quantitatively assessed octreotide uptake by measuring SUV on both early (4 hours) and delayed (24 hours) images. **Materials and methods:** We retrospectively reviewed 54 octreotide studies (2 scans each) from 49 patients (age: 63.0±13.1, F:M=29:20) with positive lesions over 4 years. Both early and delayed images were acquired on a Sym-T SPECT-CT scanner (Siemens Medical Solutions, USA), and consisted of a static planar scan followed by SPECT/CT. Images from SPECT/CT were reconstructed using attenuation, scatter, and resolution recovery correction and quantified in Standard Uptake Value (SUV) units (HERMES HybridRecon). Maximum SUV (SUV_{max}) and peak SUV (SUV_{peak}) were measured for each lesion at each timepoint. In addition, the ratio of tumor to background (normal liver parenchyma) activity was assessed. Values were reported as Median ± IQR. **Results:** Of the 54 scans in the study, 75 lesions were assessed. The median SUV_{max} was similar between the early and delayed images (12.3 ± 18.4 versus 14.4 ± 20.7, p = 0.9). The uptake in the liver was also similar (3.5±1.4 vs. 3.3±1.8, p=0.4). There was no significant difference in the ratio of tumor/liver between the early and delayed time points (3.5 ± 3.9 vs. 3.6 ± 4.9, p=0.7). Similar results were obtained with SUV_{peak} with the similar ratio of tumor/liver uptake between the early and delayed time points (3.5 ± 3.7 vs. 3.5 ± 4.6, p=0.5). SUV_{peak} was 10.1 ± 17.3 on the early and 13.4 ± 18.8 on the delayed images (p=0.9), respectively. **Conclusion:** Although based on SNMMI procedure guidelines, octreotide imaging is to be acquired at 24 hours with imaging on 4 or 48 hours being optional, our study indicated that the target to background ratio is comparable

between the 4 hour and 24 hour images. Considering the less bowel activity on the early images, the routine acquisition at 4 hours is considered superior for abdominal tumors. The current study supports the single time-point octreotide imaging to reduce resource utilization, increasing patient's convenience and reducing radiation exposure from additional CT.

EP-20

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Endocrinology -> Endocrinology, benign II

EP-0308

Value of SPECT-CT in parathyroid scintigraphy associated to per-operative PTH

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Purpose: To show the value of associating Single-photon Emission computed tomography (SPECT-CT) images in parathyroid scintigraphy to per operative PTH in detecting and preventing failure of the surgical procedure. **Subjects and Materials:** We conducted a retrospective study in 44 patients that went into parathyroidectomy intervention and to whom a parathyroid scintigraphy including the SPECT-CT protocol was performed. The pre and per-operative PTH was measured (Ten minutes after the gland resection) to all patients. We confronted the decrease of per-operative PTH value to the results of SPECT-CT parathyroid scintigraphy. **Results:** A single parathyroid adenoma was seen in 43 patients versus a double adenoma in one patient. Pre-operative PTH was high in all patients with an average value of 403,46 pg/ml and a median value of 246 pg/ml. The average value of per-operative PTH was about 95,95pg/ml with a median of about 75pg/ml. The decrease of PTH was estimated to 50% in 42 patients. The average value of PTH decreasing was about 68,76%. **Discussion and conclusion:** Per-operative PTH is the gold standard in parathyroid adenoma surgery. It confirms the success of the ablation when the decreasing rate is estimated to 50% of the initial value in 97% of cases. In our study the results of the SPECT-CT were well correlated to the decreasing of the per-operative PTH in 42 patients. A double parathyroid adenoma (seen in SPECT-CT) was the reason of a persistent high level of per-operative PTH because of the non-excision of the second adenoma based on normal macroscopic morphology during the surgical procedure. A late decreasing rate of per-operative PTH was noticed in the other patient because of kidney failure.

EP-0309

Radioguided parathyroidectomy: Initial experience using Tc-99m pertechnetate/ Tc-99m Tetrofosmin for the diagnostic scan and Tc-99m sestamibi for radioguided parathyroidectomy in a tertiary hospital in sub Saharan Africa.

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Purpose: To highlight the use of Tc-pertechnetate/ Tc-99m Tetrofosmin in parathyroid imaging and role of Tc-99m sestamibi for radioguided parathyroidectomy in management of patients with hyperparathyroidism. **Materials and methods:** 62 patients with hyperparathyroidism who had parathyroid imaging using Tc-99m pertechnetate/ Tc-99m Tetrofosmin between January 2016 to December 2017 at Aga Khan University Hospital, Nairobi. A subset of patients in whom a parathyroid adenoma was identified had radioguided parathyroidectomy using Tc-99m sestamibi. **Results:** Parathyroid adenomas were identified in 23/62 (37%) of patients using Tc-99m pertechnetate/Tc-99m Tetrofosmin dual tracer/subtraction study. 11/23 of the patients had radioguided parathyroidectomy using Tc-99m sestamibi with an ancillary preoperative 2 hour delayed image performed. On the delayed sestamibi image, all the adenomas localized on the dual tracer study were redemonstrated. An additional adenoma was identified in one of the patients. All the parathyroid adenomas localizable on the sestamibi scan were successfully removed under gamma probe guidance with minimal invasion and reduced operating time. Success of surgery was confirmed by drop in the 24 hours serum calcium and parathyroid hormone levels and on histology of the specimens. **Conclusion:** Tc-pertechnetate/ Tc-99m Tetrofosmin is a feasible alternative where sestamibi is unavailable. Patients with Tc-99m sestamibi localizable parathyroid adenoma can have successful radioguided parathyroidectomy with minimally invasive surgery and reduced operating time.

EP-0310

Added Value of 4 Scoring System MIBI Parathyroid Scintigraphy in Renal Hyperparathyroidism

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Aim: to assess if 4 scoring system MIBI parathyroid scan can predict early tertiary transformation and possible management alteration in secondary renal hyperparathyroidism. **Materials and methods:** this study include 50 patients (male: female ratio 1:1, mean age: 52.1±11.9) with CRF and on dialysis in whom triple phase MIBI parathyroid scan were assessed using visual 4 scoring system. Every individual focal uptake were evaluated in relation to background with scores using the following characteristics (No uptake = 0, mild = 1, moderate = 2, marked = 3). This was correlated with clinical and laboratory data. **Results:** Using this new scale, Patients were classified as group with low uptake (score 0 and 1) including 23 patients and other 27 patients in group with high uptake (score 2 and 3), 18 patients elicit score 3 (marked uptake) in one or more glands predicting tertiary transformation. 27 patients showed 4 gland hyperplasia, 20 with 2 glands and 3 patients presented with 3 glands hyperplasia. Presence of generalized persistent bony pain and features of high bone turn over on whole body MIBI scan were significantly higher in patients with high uptake (92.5%) compared to 17.4% for low uptake group (P<0.001). In relation to laboratory tests, Serum parathormon level & Alkaline phosphatase were significantly elevated (683 ± 254 and 571 ± 146 respectively) in high

uptake group compared to (170 ± 105 and 134 ± 23 respectively) for patients with low uptake (P<0.001). A total 147 focal spots were detected. 90 reported as score 1 (mild uptake), 37 score 2 and 20 with markedly increased uptake (score 3), while no uptake was detected in 53 predicted site of parathyroid glands (score 0). This individual lesion analysis can help in modulation of treatment approach; as patients with low uptake can benefit from medical treatment, limited disease to 1 or 2 glands, may be subjected for limited surgical resection and preservation of the gland with least uptake to avoid recurrent hyperparathyroidism. **Conclusion:** Using the 4 score system MIBI parathyroid scintigraphy can be useful in guiding different therapeutic approaches for renal hyperparathyroidism. **Key words:** MIBI scintigraphy, scoring system, renal, secondary hyperparathyroidism.

EP-0311

¹⁸F-Choline PET/CT for preoperative localization of hyperfunctioning parathyroid adenoma

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Purpose: To evaluate the usefulness of ¹⁸F-fluorocholine PET/CT for the preoperative localization of hyperfunctioning parathyroid tissue. ¹⁸F-Fluorocholine, as a phospholipid analogue, is integrated into newly synthesized membranes of proliferating cells and its uptake is increased by upregulation of choline kinase. In parathyroid adenomata, increased phospholipid-dependent choline kinase has been shown to be related to PTH secretion. What kind of imaging can be suggested in the preoperative setting of patients with hyperparathyroidism but negative finding at conventional imaging? **Methods:** We examined a pilot group of 18 patients (15 women, 3 men; age range 41- 84 years) with biochemically proven hyperparathyroidism and inconclusive or unsatisfactory results at conventional radiological imaging modalities (ultrasonography, CT or MR of the neck) and nuclear medicine (scintigraphy with ^{99m}Tc-sestaMIBI). In each of them 2.5 MBq/Kg of ¹⁸F-fluorocholine was injected. All patients were submitted to two PET/CT scans of the neck and upper mediastinum, respectively at 5 and 60 min after injection (low-dose CT imaging: 70 mAs, 120 kV; 2 bed positions in high resolution, 6 min per bed position, Philips GEMINI Big Bore). It was performed a qualitative analysis and a semiquantitative assessment calculating the standardized uptake value maximum (SUV max) with a spherical ROI drawn on region of uptake. Reading sessions were performed separately by two experienced observers. On review and comparison of the results, disparities were resolved by consensus. **Results:** In this study, preliminary results are very promising, showing a high lesion to background ratio, also for sub-centimetric nodules, in most patients. Particularly, in 11/18 patients, ¹⁸F-fluorocholine PET/CT has a clearly positive result. In 7/18 patients our examination was not definitive. All lesions were visible at both imaging times (performed 5 and 60 min after injection) and no significant difference between SUV calculated in early and late images were found. **Conclusions:** This pilot study suggested that ¹⁸F-fluorocholine PET/CT is an accurate,

efficient imaging modality to detect and localize hyperfunctioning parathyroid tissue in most of our patients (60%) where the diagnostic performance of conventional radiology and nuclear medicine imaging methods could not carry out more certainty. This imaging modality enables surgeons to carry out targeted minimal invasive surgery, minimizing associated risks, morbidity and cost. Furthermore, SUV analysis shows irrelevant changes between early and late images, assuming the possibility of performing only early acquisition, so reducing acquisition times and patients exposure to ionizing radiation.

EP-0312

The Contribution of SPECT to Tc-99m MIBI Dual-phase Planar Parathyroid Scintigraphy

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Purpose: Technetium-99m methoxyisobutylisonitrile (MIBI) dual-phase planar parathyroid scintigraphy (DPS) is commonly used to locate the parathyroid pathologies. Although the additional value of SPECT for the recognition of parathyroid pathologies is controversial, it has been known to be associated with a higher accuracy and specificity than DPS. We evaluated the contribution of SPECT to conventional DPS in patients with primary hyperparathyroidism. **Subjects & Methods:** We reviewed our patient records between September 2017 and January 2018, retrospectively. 107 consecutive patients had biochemically primary hyperparathyroidism and DPS and SPECT studies performed for preoperative parathyroid localization. We excluded forty patients who were not operated and/or unachievable histopathological results. We studied on the final data set of 74 lesions of 67 patients (F/M:54/13, mean age:59 y±13) based on lesion localization using histopathologic results as the gold standard. In a histopathological examination, we considered patients with parathyroid adenoma/hypercellular tissues as the real positive, patients with normal parathyroid tissue or lymph nodes as the real negative. In addition, serum calcium and parathormone levels obtained before and after the operation were taken into account for all patients. **Results:** Histopathology reported 64/74 parathyroid adenomas (54 lesions as single adenoma, 10 lesions in 5 patients as double adenomas), 4/74 hypercellular parathyroid tissue (encapsulated single lesions in 4 patients), 5/74 normal parathyroid tissue (normal resected glands in 5 patients, together with the single adenoma in 2/5 of them) and 1/74 non-neoplastic lymph node without any parathyroid tissue. DPS and SPECT images revealed 52/74 and 69/74 lesions, respectively. 22/74 lesions on the DPS (3 of 22 lesions were normal parathyroid glands) and 5/74 lesions on the SPECT (3 of 22 lesions were normal glands) were not detected. Sensitivity, specificity, and accuracy values based on the lesion localization were 72.1%, 50%, 70.3% for DPS and 97.1%, 50% and 93.2% for SPECT. The lesions not detected on DPS, but on SPECT study and positive lesions on both studies had mean gland weight of 1580 mg and 650 mg ($p<0.05$) and mean gland volume of 1.31 cc and 0.33 cc ($p<0.05$), respectively. **Conclusion:** The most common cause of primary hyperparathyroidism

is single parathyroid adenoma and accuracy of the preoperative lesion localization is critical for surgical management of the patients. Our findings show that SPECT study may provide a contribution on lesion basis to DPS due to a higher capability to detect the true positive cases with a better sensitivity and accuracy.

EP-0313

Role Of ^{99m}Tc / ^{99m}Tc -MIBI Dual-trace Subtraction Scintigraphy With Subsequent SPECT - CT Preoperative Imaging Of Parathyroid Adenoma

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Parathyroidectomy is the only curable approach to symptomatic primary hyperparathyroidism (PHPT) with increased levels of parathyroid hormone (PTH) and serum calcium. Parathyroid glands are usually located at the four thyroid poles, but in some cases ectopic adenomas can be found in other extrathyroid areas, difficult to be identified. Subtraction of the images after dual-tracer ^{99m}Tc -pertechnetate/ ^{99m}Tc -MIBI application with subsequent neck and chest SPECT/CT studies are advanced nuclear medicine technology for identification of PHPT. **Aim:** The aim of this work was to assess the clinical role of combined ^{99m}Tc -pertechnetate/ ^{99m}Tc -MIBI scintigraphy using subtraction technique, followed by SPECT/CT for preoperative anatomic location of parathyroid adenomas when planning minimally invasive surgical treatment. **Patients and methods:** 76 patients (72F/4M) with symptomatic PHPT and hypercalcemia were studied. Thyroid scintigraphy with ^{99m}Tc -pertechnetate (74MBq) and parathyroid ^{99m}Tc -MIBI (740MBq) scintigraphy were performed according to the dual-tracer subtraction protocol with subsequent SPECT/CT low dose images. All scintigraphic results were compared to the pathological data and clinical follow-up. **Results:** Single hyperfunctioning positive parathyroid adenomas were imaged in 51 pts (in upper/lower thyroid poles or intrathyroid locations); multiple parathyroid foci were detected in 3 pts; additional adenomas after previously surgery or thyroidectomy were identified in 4 pts; extrathyroid adenomas were localized in 7 pts - in 4 cases with retrosternal mediastinal topography and in 3 cases with retrotracheal location. SPECT/CT studies revealed single parathyroid adenomas in 3 cases with nodular goiter. The smallest adenoma, visualized by SPECT/CT was in axial diameter of 6.1mm. Negative results were established in 8pts: in 4 cases with co-existing hyperplastic nodular goiter and in 4 of remaining pts without abnormal gland. Precise anatomic detection of hyperfunctioning parathyroid adenomas was achieved in 89.47% (68/76). **Conclusion:** Our results showed it could be summarized that preoperative combined ^{99m}Tc -pertechnetate/ ^{99m}Tc -MIBI scintigraphy using subtraction technique with subsequent SPECT/CT optimized correct surgical approach in approximately 90% of involved patients with PHPT.

EP-0314

The value of Tc-99m MIBI SPECT/CT for predicting the parathyroid pathology: Five year retrospective analysis

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Introduction: Preoperative imaging methods play an important role in determining the treatment of primary hyperparathyroidism. In this study patients who were operated at Ankara Numune Hospital with the diagnosis of primary hyperparathyroidism were included. Postoperative pathology results Preoperative SPECT/CT, ultrasonography (USG), pre and postoperative parathormone (PTH) and calcium (Ca) levels of the patients were investigated. **Methods:** Among 454 patients operated in Ankara Numune Hospital between January 2013 and January 2018, 175 patients of whom; pathology, SPECT/CT and USG reports, preoperative/postoperative PTH and Ca values could be reached were included to this study. Patients with a pathology report of “parathyroid adenoma” and “hyperplastic parathyroid gland” were accepted as “pathology positive”, those with a pathology report of “normal parathyroid tissue” were accepted as “pathology negative”. USG and SPECT/CT imaging reports were also grouped as positive and negative based on their findings. Highest PTH and Ca values seen in 3 months before surgery and lowest PTH and Ca values seen in 3 months after the surgery were recorded. **Results:** 175 patients (135 females, 40 males, mean age: 51 ± 11) were included. Mean preoperative PTH level was $533.37 (\pm 792.63)$ pg/mL. Among 175 patients, 143 were “pathology positive” and 32 were “pathology negative”. All patients showed a decrease in postoperative PTH and Ca values. In 143 patients with positive pathology; the concordance of SPECT/CT and pathology was 97% (140 pts, $p=0.07$) and the concordance of USG and pathology was 69% (99 pts). In 32 patients with negative pathology; it was seen that concordance of SPECT/CT and pathology was 12% (4 pts) and that concordance of USG and pathology was 53% (17 pts). Positive predictive value (PPV) of SPECT / CT was calculated as 83% and PPV of USG was calculated as 86%. Negative predictive value was not calculated as patients with negative SPECT/CT and USG were not operated. When all patients were investigated; of 57 (32%), patients with positive SPECT/CT and negative USG 43 (75%) were positive for pathology and 14 (25%) were reported negative for pathology. Parathyroid adenomas were shown histopathologically for 2 out of 3 patients with positive USG and negative SPECT/CT negative. **Conclusion:** In this retrospective first analysis of our five-year experience; positive predictive values of preoperative SPECT/CT and USG were similar. However, SPECT/CT is preferable over USG in patients with especially ectopic parathyroid pathology.

EP-0315

Diagnostic Performance of Dual phase Tc99m MIBI Planar Scintigraphy, SPECT/CT and Ultrasonography in detection of parathyroid adenoma in patients with primary hyperparathyroidism

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Introduction: Primary hyperparathyroidism (PHPT) is a common endocrine disease that is caused by a single adenoma in approximately 85% of cases. Surgical management is the mainstay of treatment for parathyroid adenoma (PA). Minimally inva-

sive surgical techniques achieve similar cure rates with a lower risk of complications and better cosmetic results in patients with solitary PA. Accurate preoperative localization with imaging modalities is important for identifying patients suitable for minimally invasive surgery. In this study we aimed to evaluate the diagnostic performance of ^{99m}Tc-MIBI planar scintigraphy (PS), SPECT/CT and ultrasonography (US) in patients with PHPT. **Material and Method:** Fifty-eight patients with biochemical evidence of PHPT who underwent pre-operative imaging with parathyroid scintigraphy and US for detection and localization of PA and proceeded to surgery were included in the study. All patients underwent dual phase ^{99m}Tc-MIBI parathyroid scintigraphy (early and delayed planar images and delayed SPECT/CT). Data analysis was performed to evaluate the sensitivity, specificity, and accuracy and PPV of planar images, SPECT/CT and US alone and combined US and SPECT/CT. Histopathology was used as gold standard. **Results:** Sensitivity, specificity, PPV and diagnostic accuracy for detection of PA, 80,4%, 42,8%, 91,1% and 75,8% for PS; 80,4%, 57,7%, 91,1% and 77,5% for delayed SPECT/CT; 88,2%, 85,7%, 97,8% and 87,9% for US and 94,1%, 71,4%, 96% and 91,3% for SPECT/CT+US. Combined US and SPECT/CT has been shown to increase sensitivity and diagnostic accuracy. The overall sensitivity of PS and SPECT/CT didn't vary however additional information which is helpful for planning minimally invasive surgery gained from tomographic images. **Conclusion:** The combined use of US and SPECT/CT has incremental value in accurately localizing PA over either technique alone. In the preoperative assessment of patients with PHPT, combination of imaging methods allows selection of patients who would be suitable for minimally invasive surgery.

EP-21

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Endocrinology -> Thyroid, benign I

EP-0316

Determination of the Thyroid Volume with SPECT - A Monte Carlo Study

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Introduction: The thyroid volume is important for dose planning when treating thyrotoxicosis with ¹³¹I. Volume determination is often based on planar scintigraphy with ^{99m}Tc pertechnetate, but several studies have shown better results using SPECT. For volume calculations, automatic segmentation methods are advantageous, and threshold methods are commonly used. The threshold percentage should preferably be determined in a patient-like geometry with a known thyroid volume. The aim of this study was to use SPECT Monte Carlo simulations of different versions of the digital anthropomorphic XCAT phantom to optimize a threshold level for measurement of the thyroid volume. **Method:** Realistic uptake of ^{99m}Tc pertechnetate in the thyroid, salivary glands and background were sampled from 10 patient SPECT images. The thyroid uptake was divided into 3 groups;

low, medium and high, and the corresponding average values were applied to 22 versions of the XCAT phantom (11 men and 11 women, whereof 4 child phantoms corresponding to 5 and 10 years of age). The thyroid volumes were varied between 15 and 25 cm³ in the adult phantoms. Monte Carlo simulations with SIMIND were performed and 10 Poisson noise realisations with a clinically realistic noise level were generated for each low-noise SPECT simulation. The images were reconstructed with OSEM (5 iterations, 10 subsets) and corrected for attenuation, scatter and distance-dependent resolution. Images both with and without post-filtering (Butterworth, 0.6 cm⁻¹, P = 7) were used. The optimal threshold, as percentage of the maximum thyroid voxel value, for each reconstruction was calculated and the average was used as a global threshold. Bias and uncertainties in volumes were then calculated based on this threshold. **Results:** The optimal threshold without filtering was 21.1% if the 5-year phantoms were included and 20.7% without. Corresponding results with filtering were 31.5% and 30.1%, respectively. The total standard deviation for the volume for unfiltered images was 1.7 cm³ including the 5-year phantoms and 1.8 cm³ without. Corresponding results for filtered images were 2.1 cm³ and 1.7 cm³. For filtered, but not for unfiltered images, bias was found to be correlated to the thyroid volume. **Discussion:** The thyroid is a small organ and scintigraphic methods have relatively low spatial resolution. Some uncertainties in the calculated volume must therefore be tolerated. The above-described correlation between size and bias indicates that unfiltered images are safer to use, especially for deviating uptakes. Further work is needed to study other types of filters and segmentation methods.

EP-0317

Correction of radiation induced stunning (CRIS) in pre-therapeutic radioiodine-131 uptake test of patients suffering from goiter

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Aim: Thyroid stunning (TS), defined as a reduced intrathyroidal uptake of radioiodine-131 after previous diagnostic amounts of radioiodine-131, was first reported in 1951 but the underlying reasons for this phenomenon are still surrounded by controversies. Possible explanations are a decrease of viable thyroid cells caused by exposure of β -radiation as well as an unknown dose dependant cellular inhibiting effect of the β -radiation on iodide transport mechanism. In a recent study we could demonstrate a significant dependence of TS upon pre-therapeutic administered radiation dose [Gy] in patients suffering from goiter undergoing a radioiodine-131 uptake test (RIUT) prior to radioiodine therapy (RIT). Therefore, the aim of this study was to correct this effect of radiation induced stunning (CRIS) mathematically in order to improve accuracy of RIUT. **Material and Methods:** A retrospective monocentric analysis of 135 patients (median age 70 (35–95), 91 female) suffering from goiter undergoing a RIT without any additional thyreostatic medication was performed. Depending on the Marinelli equation and our previously obtained results which indicate a significant decrease of intra-ther-

apeutic radioiodine-131 uptake (EMU) ($p < 0.05$) depending on pre-therapeutic administered radiation dose of 21% per Gray a CRIS-modification of the Marinelli equation was conducted. The calculation of required activity of radioiodine-131 to obtain an intra-therapeutic target dose of 150 Gy was re-evaluated in all 135 patients using CRIS. **Results:** The median thyroid volume was 55 ml (19–477ml) and the median administered activity in RIUT was 2.95 MBq (range: 1.46–6.84MBq) resulting in a median dose caused by this activity of 0.35 Gy (0.03–1.96Gy). Median EMU in RIUT and in RIT was 32 % (10–70 %) and 31 % (16–61 %) respectively. Therefore the mean ratio of RIT and RIUT EMU was 1.01 (0.57–2.04). A calculation using the pre-therapeutic calculated activity for a target dose of 150 Gy, intratherapeutic EMU and effective halflife resulted in a mean target doses of 152 Gy (59–385Gy). A retrospective recalculation of the target dose using the CRIS modified activity revealed a mean dose of 149 Gy but with a significant smaller range of 83–187Gy. The mean ratio of RIT and CHRIS-modified EMU was 0.99 (0.55–1.91). **Conclusion:** By the use of the CRIS modification of the marinelli equation intra-therapeutic intrathyroidal uptake can be predicted with significantly higher accuracy, leading to an improvement of RIT in patients suffering from goiter. However, whether CRIS is also leading to a higher success rate of RIT has to be evaluated in further studies.

EP-0318

Efficacy of ^{99m}Tc-DTPA SPECT/CT in Diagnosing Orbitopathy in Graves' Disease

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Purpose: The most frequently used methods of assessing Graves' orbitopathy (GO) include: Clinical Activity Score (CAS), ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI). There exists another, slightly forgotten, imaging method: single-photon emission computed tomography (SPECT) with the use of diethylenetriaminepentaacetic acid tagged with ^{99m}Tc (^{99m}Tc-DTPA). These days it is possible to conduct a SPECT examination fused with a CT scan (SPECT/CT), which increases the diagnostic value of the investigation. **Aim:** The aim of this paper is to evaluate the usefulness of ^{99m}Tc-DTPA SPECT/CT in diagnosing Graves orbitopathy, as compared with other methods. **Subjects & Methods:** Twenty-three patients with suspected active (infiltrative-edematous) Graves' orbitopathy were included in the study. Each patient underwent a CAS, an MRI, and a SPECT/CT. **Results:** The obtained results were analysed statistically, with the assumed statistical significance of $p < 0.05$. The SPECT/CT and MRI were found to have the highest sensitivity: 0.93 each. The SPECT/CT had the highest specificity: 0.89. MRI and CAS had lower values: 0.78 and 0.56, respectively. The occurrence of an active form of GO had no impact on the exacerbation of exophthalmos or the thickness of the oculomotor muscles. **Conclusion:** The ^{99m}Tc-DTPA SPECT/CT method provides a very good tool for assessing the active form of GO and can, alongside the MRI scan, be used as a referential diagnostic procedure in GO.

EP-22

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Endocrinology -> Thyroid, benign II

EP-0319

Incidence of Hashimoto's Thyroiditis in Women of Reproductive Age

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Aim: Hashimoto's thyroiditis (HT) with the increased level of thyroglobulin antibodies (antiTg) and/or thyroid peroxidase antibodies (antiTPO) is the most frequent autoimmune thyroid disease. HT represents a risk for the development of hypothyroidism, especially during pregnancy, when thyroid gland has to increase the synthesis of thyroid hormones by 25-50%. Furthermore, in some reports, even euthyroid HT was associated with the increased risk of pregnancy loss. Currently there is no consensus on universal screening for HT in women of reproductive age. Therefore, the aim of our study was to evaluate the incidence of HT in women of reproductive age, who had no previous diagnosis of thyroid disease. **Materials & Methods:** In this prospective clinical study we included 306 consecutive female volunteers in reproductive age. Women with the known thyroid disease were not included in the study. In every participant, thyroid ultrasound was performed using a 7.5-MHz linear transducer. Thyroid volume was calculated by the ellipsoid model (width × length × thickness × $\pi/6$ for each lobe). Level of thyrotropin (TSH), antiTg and antiTPO was measured. **Results:** Out of 306 women, 19 (6.2%) had increased level of antiTg, 13 (4.3%) had increased level of antiTPO, and 20 (6.5%) had increased level of both antiTg and antiTPO. Thus, 17% of women had HT. The median age of 306 study participants was 27 years (19-56 years). With respect to age, women with the increased level of antiTg and/or antiTPO did not differ from the women with the normal level of antiTg and/or antiTPO (31 (21-49) and 27 (19-56) years, respectively, $p=0.155$). The median thyroid volume in 306 women was 7.5 mL (range, 2.5-16.6 mL). Thyroid volume was significantly larger in women with the increased level of antiTg and/or antiTPO than in women with the normal level of antiTg and/or antiTPO (8.7 ± 2.7 and 7.3 ± 2.5 mL, respectively, $p<0.001$). The median TSH level in 306 women was 1.61 mIU/L (0.32-116.9 mIU/L). Level of TSH was significantly higher in women with the increased level of antiTg and/or antiTPO than in women with the normal level of antiTg and/or antiTPO (6.0 ± 18.9 and 1.7 ± 0.9 mIU/L, respectively, $p<0.001$). **Conclusion:** Our results show that 17% of women in reproductive age without previously known thyroid disease actually have HT. Since HT may be associated with adverse effects on pregnancy, screening strategy in groups at risk should be considered.

EP-0320

Radioiodine Therapy (I-131) for Hyperthyroidism: Our experience

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Aim: The purpose of our study was to evaluate the therapeutic response of radioiodine (RAI) therapy in patients with hyperthyroidism caused by different etiologies (Graves disease, toxic adenoma and toxic multinodular goiter). **Materials and methods:** A retrospective study was conducted on a cohort of 180 patients (132 women, 48 men; age: 56.7 ± 14.5 years) who received RAI treatment, between January 2011 and February 2017. Ninety-three (93) patients were diagnosed with Graves disease, 51 with toxic adenoma and 36 with toxic multinodular goiter. The administered activity ranged between 370 and 740MBq, according to the clinical situation. A clinical examination and a serum assessment of TSH, FT4 and anti-thyroid antibodies were made at baseline at 3, 6 and 12 months after RAI therapy. **Results:** The treatment of hyperthyroidism had a global success rate of 89%, with 160 of 180 patients achieving euthyroidism or hypothyroidism. 11% of the patients (20/180) had residual hyperthyroidism after the treatment, and this number was more significant in the group of patients with Graves disease (15/93 - 16%). The rate of residual hyperthyroidism in toxic adenoma and toxic multinodular goiter patients was 6% (3/51 and 2/36, respectively). There was no significant difference in the response rate to different doses of RAI treatment groups or gender. **Conclusion:** RAI treatment is an effective modality for definitive treatment of hyperthyroidism. The success rate was 89%, which is acceptable according to the references from larger studies (80-100%). Response rate was related to etiology (lower in Graves disease) but was not related to RAI dosage etiology or gender.

EP-23

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Neurology -> Dementia

EP-0321

Value of Tc99m-ECD Perfusión Brain SPECT CT in the Diagnosis of Alzheimer Disease

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Purpose: The real value of Brain Perfusion SPECT CT, which seems to be a very useful tool in the diagnosis of Alzheimer disease, is still unknown, as most published data are obtained with brain perfusion SPECT only. The aim of our study is to investigate the diagnostic value of Brain Perfusion SPECT CT (BP SPECT CT), taking the Amyloid (F18) Brain PET CT as a gold standard. **Materials and Methods:** We study 32 patients who performed amyloid brain PET CT with an atypical or difficult diagnosis of Alzheimer disease. All patients had 20 minutes PET acquisition

time, 90 minutes after the I.V. injection of 370 MBq of Florbetaben (F18), and a BP SPECT CT, that's were acquired between 30 and 60 minutes after the injection of 370 MBq of Tc99m-ECD, maximum accepted time between both studies, is 6 months Interval, 3 patiens who had not BP SPECT CT were excluded. The presence of unilateral or bilateral temporal or temporoparietal hyperperfusion was considered as a positive SPECT CT scan for Alzheimer disease. **Results:** Twelve patients had positive PET and SPECT CT scans (41.4%) Fifteen patients had negative PET and SPECT CT scans (51.7%) Two patients had a positive SPECT CT and a negative PET scan (6.9%). The sensitivity of Brain SPECT CT is 100% with a specificity of 88.2%. **Conclusion:** Our results suggest that brain perfusion SPECT CT is very good tool, which correlates with the findings of amyloid brain PET CT the diagnosis Alzheimer disease with a 100% sensitivity and 82.2% specificity.

EP-0322

A Complete Analysis in Dementia: Visual and Voxel based Quantitative Analysis on Brain SPECT Scan

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Background: It has been recognized that olfaction is impaired in demented patients. This study aims to investigate olfactory impairment in Dementia in a comprehensive scheme including visual and quantitative assessment of brain SPECT scan as well as analysis the results of odor test. **Materials and Methods:** 19 patients with (age range 40 -78 yrs., mean age = 61, SD = 9.7) (11 male and 8 female) clinically diagnosed as Dementia were recruited in this study. Different examinations were gathered for all of the participants. Memory was assessed by Wechsler memory test, as well as olfactory function was examined by a definite odor test. SPECT scan was performed for all of the participants in order to assess perfusion changes. Cervical carotid artery was examined by Ultrasound in order to measure intima layer thickness. Quantitative analysis was used for comparing each individual SPECT scan with a group of control including 20 subjects using SPM package. Finally regions with significant hypo perfusion were anatomically labelled through automated anatomical labelling (AAL) toolbox which run under SPM. AAL includes 116 different brain regions. **Results:** Based on odor test, 9 were abnormal while 10 were normal. An experienced physician recognized 2 normal SPECT scan while 17 abnormal. In SPECT SPM analysis, regions with significant decrease perfusion was obtained separately for each patient. Different clusters were characterized by location, size of the cluster and T values which can reveal more detailed information about the degree of severity and its anatomical region. **Conclusion:** The obtained results indicate that there is no statistically significant relationship between an odor test and dementia, Wechsler memory test and dementia, an odor test and Wechsler memory test, an odor test and intima layer thickness, dementia and intima layer thickness (p-value < 0.5).

EP-0323

¹⁸F-Flutemetamol Cerebral PET/CT: Our Initial Experience

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Purpose: to report the introduction of the new PET tracer ¹⁸F-Flutemetamol (Vizamyl) in the routinary workflow of our nuclear medicine department and to evaluate its feasibility. **Subject and methods:** 15 dementia patients, 8 females and 7 males (mean age 68 years, range 49-74) have been studied with PET/CT using the new tracer ¹⁸F-Flutemetamol from November 2016 to February 2018. All of them had a clinical diagnosis of dementia and had already been submitted to ¹⁸F-FDG Cerebral PET/CT in the attempt to characterize the type of neurodegenerative condition. Stringent inclusion criteria were followed: age lower than 75 years, objective cognitive decline, inconclusive clinical and instrumental examination (MRI and FDG-PET). In all patients the assessment of the amyloid load was necessary to improve the diagnostic accuracy or to modify the patient management. The selection of the patients was decided by consensus during multidisciplinary meetings among geriatric physicians, neurologists, neuroradiologists and nuclear medicine physicians. After 6 hour fasting condition patients were injected e.v. with 185 MBq of ¹⁸F-Flutemetamol. PET/CT images were acquired 90 min post injection by a Siemens Biograph mCT 64-4 R tomograph, using list mode acquisition for 20 minutes. Low dose CT was coregistered for attenuation correction and anatomical localization. The interpretation of images was performed by two experienced nuclear medicine physicians on Vizamyl PET/CT examinations using the specific criteria on Vizamyl PET. **Results:** 12 patients (80%) presented a positive scan (presence of cerebral amyloid) and 3 (20%) a negative one (absence of cerebral amyloid). The clinical value of PET amyloid scan was discussed for each patient in the multidisciplinary meeting. In the 3 negative cases it has been possible to exclude Alzheimer Disease (AD). In 6 positive patients with a clinical diagnosis of Mild Cognitive Impairment (MCI) it has been possible to conclude for MCI due to Alzheimer disease. In 1 positive patient with age < 50 years AD early onset was confirmed. In the remaining 5 positive patients adequate follow up was decided to reach a final diagnosis. The concordance on Vizamyl PET interpretation between the two nuclear medicine physicians was almost 93,5% (only in one case interpretation was reached by consensus). **Conclusion:** ¹⁸F-Flutemetamol cerebral PET/CT is a feasible a very useful examination, well tolerated by the patients. An accurate selection of patients and a multidisciplinary approach are essential.

EP-0324

Role Of Tc99m-hmpao Regional Cerebral Blood Flow Spect-ct In The Diagnosis Of Primary Progressive Aphasia.

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Objectives: The aim of this study was to assess the clinical utility of Tc99m-HMPAO regional cerebral blood flow single photon emission computed tomography (RCBF SPECT-CT) in the diagnosis of Primary Progressive Aphasia (PPA). **Methods:** We review 30 Tc99m-HMPAO RCBF SPECT-CT studies, that were performed in our department to confirm PPA after a clinical evaluation of this patients with neuropsychological tests in the dementia unit (DU). We use the neuropsychological tests results, as a reference diagnostic test for statistical analysis, and compare them with the RCBF SPECT-CT results. **Results:** In our 30 patients with clinical PPA diagnosis, 24 presented brain blood perfusion abnormalities compatible with PPA, and 6 were not compatible with PPA. 22 of the 24 RCBF SPECT CT studies which were compatible with PPA, were diagnosed with PPA in the UD clinical evaluation, and the other 2 patients had another diagnosis. 2 of the 6 RCBF SPECT-CT studies which were not compatible with PPA, had PPA diagnosis in the UD through neuropsychological tests. The other 4 patients presented other diagnosis according to DU. Comparing the results of RCBF SPECT-CT and the neuropsychological tests results, the RCBF SPECT-CT had a sensitivity of 92% and specificity of 67%, a positive predictive value of 92% and a negative predictive value of 67%, to diagnose PPA. **Conclusions:** The Tc99m-HMPAO regional cerebral blood flow SPECT CT provided high levels of sensitivity and specificity, in diagnosis of primary progressive aphasia, and it is a very useful tool in the management of this patients, since it allows to make an early diagnosis in a pathology of insidious evolution.

EP-24

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Neurology -> Movement disorders

EP-0325

Differential diagnosis among early-stage degenerative parkinsonisms by discriminant analysis: FDG-PET voxel based study

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Aim: The aim of our study was to assess by means of a statistical discriminant analysis the specific metabolic patterns of different degenerative parkinsonisms at early onset, as assessed by a voxel based approach, in order to correctly assign each patient to a specific form of parkinsonism. **Methods:** we retrospectively enrolled 77 patients with a clinical diagnosis of degenerative parkinsonism confirmed by a follow-up of at least 5 years (8 Parkinson Disease (PD; mean age 65), 19 Multiple System Atrophy (MSA; mean age 69), 26 Progressive Supranuclear Palsy (PSP; mean age 69), 11 Cortico-Basal Syndrome (CBS; mean age 69), 13 Lewy Body Dementia (LBD; mean age 73). All patients had

undergone a [¹⁸F] FDG PET within 1 year from onset of symptoms. FDG-PET scans were spatially normalized in MNI brain atlas space with a specific FDG template using a statistical parametric mapping software (SPM12). Two-sample t-test was used to compare each group of degenerative parkinsonism with a database of 123 controls group obtained from the AIMN Italian Normative database. Age and gender were used as nuisance variables; non-corrected $p < 0.001$ was considered statistically significant. Clusters resulted to be significantly hypometabolic on SPM analysis were identified and located on MNI atlas. T-values and clusters extent (K_v) of the cortical and sub-cortical regions involved in each degenerative parkinsonism were used to carry out a statistical discriminant analysis among the different degenerative parkinsonism subtypes. **Results:** discriminant analysis classified as belonging to the PSP group patients with significantly hypometabolism clusters within the frontal cortex, caudates and mid-brain. The regions of hypometabolism with significant T-value that best allocated patients to the MSA group were putamen and cerebellum. Cortical asymmetrical hypometabolism in frontal areas identified patients with CBS whereas the presence of hypometabolism in occipital cortex identified patients as LBD (Wilk's lambda 0.40, $p < 0.0001$). No specific pattern of hypometabolism was observed comparing PD with control subjects. **Conclusions:** in this study the distribution of the regions of FDG hypometabolism in different atypical parkinsonisms is consistent with previous data of the literature. However, our data suggest that even on very early stage of disease (1 year from symptoms onset) a specific distribution of hypometabolism as assessed by a voxel based approach is able to correctly classify patients into a specific degenerative parkinsonism subgroup.

EP-0326

123i-mibg Imaging For Parkinson'S Disease: The Diagnostic Value Of The Early Heart-to-mediastinum Count Ratio.

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Aim: Parkinsonism is a common syndrome, but early diagnosis of Parkinson's disease (PD) is challenging, as the symptoms of different types of neurodegenerative diseases frequently overlap, especially in the diagnosis of earlier stages onset. The delayed (4 h after the injection) Iodine-123-Metaiodobenzylguanidine (¹²³I-mIBG) scintigraphy can help in early differential diagnosis. Early imaging is also reported more and more often as effective for diagnosis, reducing the burden of delayed imaging. Recent studies on the Lewy Body Dementia reported optimal thresholds of 2.0-2.2 for early heart to mediastinum ratio (He/Me), and 2.27 for late heart to mediastinum ratio (Hl/MI) as physiological ratio. Purpose of this study is to tune the threshold for early H/M ratio obtaining a diagnostic accuracy analogous to the better consolidated practice of delayed imaging in PD patients. **Materials and Methods:** Forty-three patients (mean age 65.8±9.2 years) presenting Parkinsonism syndrome of recent onset (Hoehn e Yahr < 1.5) were enrolled and underwent ¹²³I-mIBG scintigraphy

in our Nuclear Medicine Unit. Images were acquired after 15 and 240 minutes from the injection of 150–185 MBq of ^{123}I -mIBG with a dual-head gamma camera (Infinia, GE Healthcare, Milwaukee, USA), using LEHR collimator. The early and late H/M were evaluated by drawing Polygonal Region-of-Interests on the heart and on the upper half of the mediastinum. Correlation between He/Me and HI/MI were investigated with Spearman correlation coefficient and related test. Differences between He/Me and HI/MI were investigated through the Wilcoxon rank-sum test. Simple linear regression was used to assess calibration. Optimal threshold and overall predictive performance were determined by Receiver Operating Characteristic (ROC) curve, classifying tentatively patients having a HI/MI lower than 1.6 as suffering from PD. **Results:** He/Me was not significantly different from HI/MI (p -value=0.835). The ROC curve highlights that He/Me is highly reliable, in fact ROC curve analysis showed an AUC of 0.935 (95%CI: 0.845–1.000). The He/Me optimal threshold was 1.66, with sensitivity, specificity, and diagnostic accuracy of 95.5%, 85.7, and 90.7%, respectively. **Conclusion:** The He/Me threshold can be tuned effectively and is almost as accurate as the most frequently used delayed ^{123}I -mIBG imaging. This can reduce the burden of delayed imaging, while preserving an acceptable diagnostic accuracy allowing time and economic saving, and improving patient comfort.

EP-0327

Does the severity of nigrostriatal degeneration in the early symptomatic phase of Parkinson's disease predict medium-term cognitive decline?

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Purpose: Development of dementia is associated with reduced life expectancy in Parkinson's disease (PD). This study tested the severity of nigrostriatal degeneration according to I-123-FP-CIT SPECT during the early symptomatic phase of the disease with respect to medium-term prediction of cognitive decline. **Methods:** The analysis included all PD patients of the Parkinson's Progression Marker Initiative with (i) clinical diagnosis of PD since ≤ 2 years, (ii) reduced striatal dopamine transporter availability according to visual inspection of FP-CIT SPECT at screening/baseline (i.e., SWEDDs were excluded), (iii) normal cognition at baseline, and (iv) clinical evaluation of cognitive status at 36 months follow-up ($n=74$, 58.6 ± 10.3 y, 36 female). The group was subdivided into 'more pronounced' and 'less pronounced' nigrostriatal degeneration using the median of the putaminal FP-CIT specific binding ratio as cut-off (hottest voxel method, whole brain w/o striatum, thalamus and brainstem as reference region, minimum of both hemispheres). The chi-square test was used to test the hypothesis that the fraction of patients who had experienced cognitive decline to MCI or dementia at the 36 months follow-up ('decliner') was larger in patients with more pronounced nigrostriatal degeneration. **Results:** 10 of the 74 patients (13.5%) had experienced cognitive decline at the 36 months follow-up (all to MCI). There was a tendency towards

a higher fraction of decliners in the patient group with more pronounced nigrostriatal degeneration (18.9% versus 8.1%, one-sided $p=0.087$). Age did not differ between patients with more pronounced and less pronounced nigrostriatal degeneration (59.8 ± 9.2 y versus 57.3 ± 11.3 y, $p=0.302$). **Conclusion:** These findings suggest that more severe nigrostriatal degeneration in the early symptomatic phase of PD is a risk factor for medium-term cognitive decline.

EP-0328

Corticobasal Syndrome variants: Is functional nuclear imaging with FDG-PET or SPECT patterns capable of predicting clinical features?

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Purpose / introduction - Corticobasal Syndrome (CBS) is an atypical parkinsonian syndrome recognized as a cognitive disorder associated with several cortical features, caused by multiple pathologies, including Corticobasal Degeneration (CBD) and Alzheimer's disease (AD). Accurate antemortem diagnosis is challenging. We aimed to compare the clinical features of patients with probable CBS according to different individual brain functional patterns, exploring the potential role of metabolic imaging as a biomarker of different underlying pathologies. **Subjects & methods** - Sixteen patients with clinical diagnosis of probable CBS were submitted to brain FDG-PET (14 patients) or SPECT with $^{99\text{m}}\text{Tc}$ -ECD (2 patients). They were first investigated concerning their movement disorders profile and cognitive symptoms. According to their functional brain patterns, we distributed them into an "AD pattern" group (CBS likely related to AD) and a "non-AD pattern" group (CBS likely unrelated to AD). Both groups were compared concerning their clinical features, movement disorder profiles, and some of them tested for the presence of brain amyloid. **Results** - Four patients presented with typical AD patterns and the remaining 12 presented non-AD patterns with a wide variety of possible etiologies in the metabolic images. Dystonia demonstrated a significant difference between groups as 100% of individuals with this feature presented a non-AD pattern ($p=0,019$). Myoclonus showed a tendency to be related to the AD group ($p=0,069$) and apraxia of speech (31,8%) to the non-AD group, as 100% had a non-AD pattern ($p=0,181$). There were significant differences between the AD and non-AD groups on Addenbrooke's Cognitive Examination-Revised ($p=0,001$) and Mini-Mental Score Examination (MMSE) ($p=0,035$), both lower in the AD pattern group, and Hoehn and Yahr scale (HY) ($p=0,015$), worse in the non-AD group. Three patients were submitted to $^{11\text{C}}$ -PiB-PET and tested positive for brain amyloid, two of them in the AD group. **Discussion/conclusion** - Dystonia and apraxia of speech were most closely related to a non-AD and myoclonus to an AD brain functional pattern in patients with CBS. Individuals with an AD pattern presented with lower ACE-R and MMSE and higher HY scores. Also, amyloid positivity in three individuals indicates that some of these patients may be in the Alzheimer's disease continuum. Molecular

brain imaging shows a potential to predict the different CBS variants while depicting their specific resting-state functional brain patterns.

EP-0329

Investigation of Iodine-123 loflupane SPECT standardised uptake values (SUVs)

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Aim: To investigate the use of standardised uptake values (SUVs) for quantification of Iodine-123 loflupane SPECT uptake within the striatum. **Introduction:** I-123 loflupane imaging is a standard clinical investigation of striatal dopamine transporters. It is used clinically to investigate Parkinsonian Syndromes and dementia with Lewy bodies. I-123 loflupane uptake is routinely assessed using semi-quantitative striatal-occipital specific binding ratios (SBRs). Semi-quantification has been shown to be useful in supporting the visual interpretation of I-123 loflupane SPECT studies [1]. In this preliminary investigation we demonstrate the SUV calibration using an anthropomorphic striatal phantom and determine SUVs for a group of retrospective patients (normal n=10, abnormal n=10, categorised by imaging report). The SUVs determined were compared to striatal-occipital SBRs derived from BRASS (Hermes, Sweden). **Materials and Methods:** An anthropomorphic striatal phantom filled with I-123 iodide was imaged on a Siemens Symbia SPECT/CT system (Siemens, Germany). The images were reconstructed using iterative reconstruction (with attenuation and scatter correction and resolution recovery applied). From the phantom data, an SUV correction factor (kBq/cnts) was computed using Hermes SUV-SPECT software. A group of 20 patients referred for I-123 loflupane SPECT were retrospectively analysed. The group were of a similar age (63-76yrs) with 13 male and 7 female patients. To allow SUVs to be determined the patient's height, weight, activity and residual activity measurement were recorded. Images were reconstructed using Hermes SUV-SPECT Neurology reconstruction with our SUV correction factor applied. SUVmean, SUVmax and SUVpeak were determined for the striatal regions using a standard VOI technique. Striatal-occipital SBRs were also determined for each patient. **Results:** The results (mean $\pm$ standard deviation) for the striatum (normal vs. abnormal) are as follows SUVmean 6.75 ± 0.82 vs. 4.56 ± 0.59 , SUVmax 11.98 ± 1.57 vs. 7.82 ± 1.18 and SUVpeak 10.05 ± 1.34 vs. 6.66 ± 1.05 . The SUVmean, SUVmax & SUVpeak values all showed a statistically significant ($p < 0.01$) difference between normal and abnormal groups. All three SUV metrics showed good correlation when compared with striatal-occipital SBRs (SUVmean $r^2 = 0.70$, SUVmax $r^2 = 0.67$ and SUVpeak $r^2 = 0.69$). **Conclusion:** This initial investigation has demonstrated that SUVs can be used to differentiate between normal and abnormal I-123 loflupane SPECT uptake and show good agreement with current semi-quantitative methods. Further work is merited with a larger patient group. **References:** Therese A. Söderlund et al, "Value of Semi-quantitative Analysis for Clinical Reporting of ^{123}I -2- β -Carbomethoxy-3- β -(4-Iodophenyl)-N-(3-Fluoropropyl) Nortropane SPECT Studies", J Nucl Med 2013; 54:714-722.

EP-25

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Neurology -> Neurodegeneration

EP-0330

Correlating Scintigraphic quantitative indices with Clinical grading scales in early Parkinson's disease identification & Staging

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Dopamine transporter imaging studies deranged nigral dopaminergic projections to striatum in Parkinson's disease (PD). Modified Hoehn & Yahr staging (MHY), Unified Parkinson's disease rating scales (UPDRS) are clinical grading systems routinely used in PD staging. This prospective study aims to compare quantitative scintigraphic and clinical rating scales in identifying PD and study association between uptake, quantitation & clinical stage. **Materials & Methods:** 74 suspected PD (58: 16 M : F, mean age 60.3 ± 13.4 yrs) prior to initiating medications enrolled. Patients classified as stage 0 to III as per MHY. 25 mCi Tc Trodat was injected and 4 hours later brain SPECTCT was performed and images reconstructed. Visual & semiquantitative analysis was done by drawing ROIs on dorsal striatum & occipital cortex. Ratios of specific to non specific striatal TRODAT - 1 binding, putamen to caudate ratio (P/C ratio) calculated. Asymmetric index (ASI) determined. McNemar, ANOVA test and Kruskalwallis test was applied and, correlation coefficient was determined. **Results:** MHY staging 0, I & II included 8, 47, 19 pts respectively. Average duration of presenting complaints 12.246 ± 7.670 , median 10. Images acquired in GE OPTIMA NM 640. SPECT showed contralateral striatum more affected than ipsilateral. TRODAT uptake found to be progressively reduced with advancing PD. TS showed sensitivity, specificity, accuracy, NPV, PPV of 90.9, 87.5, 86.5, 95.2 & 45.5 % respectively. There is statistically significant agreement between TS and clinical rating scales in early PD but not in later stages. Scintigraphic indices had negative correlation with UPDRS. Specific uptake of ipsi, contralateral striatum and contralateral putamen ratio decreases with increasing UPDRS score. ASI has positive correlation with UPDRS (Cor Coeff 0.806) & increases with increasing UPDRS score i.e disease duration. Average value of ipsi, contralateral striatal specific uptake, contralateral P/C to caudate ratio progressively reduced with increasing MHY stage. **Discussion:** TS has high sensitivity & specificity in early PD identification. Longer duration of symptoms show reduced uptake & higher ASI. With advanced clinical rating, SPECT quantitation values showed downward trend. Significant difference in ASI observed in all MHY stages. Pairwise comparison was done for all stages for every quantitative index. ASI of striatal binding of trodat is important than clinical rating scale to diagnosis all stages of PD with ease. **Conclusion:** Tc-Trodat SPECT is simple, robust, highly sensitive, specific & accurate for identifying and staging PD. Striatal uptake reduces progressively with advanced PD, while asymmetric Trodat binding increases.

EP-26

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Neurology -> other Neurology (i.e.: neuroinflammation, epilepsy, headache)

EP-0331

Cerebral hybrid FDG PET/MRI in patients addressed for chronic fatigue syndrome with suspected macrophagic myofasciitis

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Introduction: Macrophagic myofasciitis (MMF) is a rare inflammatory disorder defined by arthromyalgias and chronic fatigue syndrome as well as cognitive impairment in patients with history of intramuscular injections of aluminum hydroxide-containing vaccines^{1,2}. A specific spatial pattern of cerebral glucose hypometabolism with 18F-FDG-PET/CT was shown in patients with histopathologic features of MMF at muscular site of vaccine injection³. **Method:** Patients with chronic fatigue syndrome and suspected MMF were addressed for cerebral imaging in our institution. All patients underwent hybrid PET/MRI (Siemens Biograph mMR®) 30 min. after intra-venous injection of 18F-FDG (mean 190±65 MBq). MRI sequences. Imaging results were consecutively analyzed. **Results:** We included 23 patients, mean age was 42. In 14 patients, glucose cerebral metabolism was lower in the occipital, lateral temporal and parietal lobes as well as hippocampus and cerebellum. In contrast, frontal cortex and basal ganglia were not affected. This pattern was only seen partially in 8 patients. Finally, one patient showed only light hypometabolism which was considered to be related to a mild cognitive impairment. The performed MRI sequences did not show anatomic anomaly related to the PET results. In 10 (?) patients spectroscopy was performed and showed. Additionally 7 patients underwent cerebral blood flow sequences. **Conclusion:** Hybrid 18F-FDG PET/MRI might be a potential non-invasive imaging tool for patients with chronic fatigue syndrome associated with MMF. Larger studies including a comparison to normal database are needed. **1.** Gherardi RK, Coquet M, Cherin P, et al. Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. *Brain : a journal of neurology*. Sep 2001;124(Pt 9):1821-1831. **2.** Authier FJ, Sauvat S, Champey J, Drogou I, Coquet M, Gherardi RK. Chronic fatigue syndrome in patients with macrophagic myofasciitis. *Arthritis and rheumatism*. Feb 2003;48(2):569-570. **3.** Van Der Gucht A, Aoun-Sebaiti M, Kouv P, et al. FDG-PET/CT Brain Findings in a Patient With Macrophagic Myofasciitis. *Nuclear medicine and molecular imaging*. Mar 2016;50(1):80-84.

EP-0332

Functional imaging inpatients with drug-resistant focal epilepsy.

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Aim: Interictal [18F]fluorodeoxyglucose-positron emission tomography (FDG-PET) is useful in the presurgical evaluation of patients with drug-resistant focal epilepsy. Interictal [18F]fluorodeoxyglucose-positron emission tomography (FDG-PET) is useful in the presurgical evaluation of patients with drug-resistant focal epilepsy. Hypometabolism overlies the seizure-onset zone (SOZ) with a sensitivity of 86-90% in temporal lobe epilepsy (TLE) and of 45-60% in extra-TLE. We aimed at clarifying its relationship with ictal high-frequency oscillation (iHFOs) and arterial spin labeling (ASL), an emerging non-invasive magnetic resonance imaging (MRI) perfusion technique. **Materials and Methods:** Twelve consecutive patients with cortical epilepsy for pre-surgical evaluation underwent a standardized assessment including video-electroencephalography (EEG) monitoring, structural MRI with ASL sequences and FDG-PET. We studied the correlation between epileptogenicity maps and FDG-PET and ASL. **Results and conclusion:** Of the 12 patients [7 women and 5 men; mean age 23]. The frequency band of iHFOs was on average 81-139 Hz (lowest, 30-60 Hz; highest, 160-210 Hz) and localized the epileptogenic zone. PET scan identifies hypometabolism FDG-PET interictal hypometabolism only in cases of temporal lobe epilepsy (TLE) and cortical dysplasia, whereas it was normal in extra-temporal epilepsy. ASL-MRI abnormalities (hypoperfusion) were seen in 7 patients with TLE and in two of 3 patients with extra-TLE. Conclusion: This finding suggests that interictal FDG-PET and ictal HFOs may share common underlying pathophysiologic mechanisms of ictogenesis in temporal lobe epilepsy. Interictal ASL is a non-invasive method that may help to localize the epileptogenic in extra-TLE zone showing hypoperfusion in FCD.

EP-0333

Assessment of Brain Perfusion Disorders in Patients with Dizziness: Thorough Qualitative and Voxel based Quantitative Analysis on Functional SPECT Neuroimaging

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Background: Due to limited studies of perfusion impairment in patients with dizziness, measuring the level of perfusion impairment in patients and determining the areas involved in white matter and gray matter is very important. This study evaluates the prevalence of perfusion disorders in patients with dizziness. Furthermore the current study investigates whether there is an association between brain perfusion defects and dizziness severity. **Materials and Methods:** 34 patients suffering from dizziness, whose disease was confirmed by an expert neurologist were participated in this study. Age range is 28 to 79 with mean age about 54 yrs. and SD. 13.44 yrs. All the patients underwent brain SPECT scan. The severity of perfusion defects and number of affected areas were determined by visual assessment done by an expert nuclear medicine physician's. All the SPECT data were compared statistically with our control group includes 20 subjects, in order to determine significantly hypo perfused area of the brain in dizziness patients. Finally significant hypo perfused area was anatomically labelled using automated anatomical labelling (AAL), which covers 116 different brain re-

gions. All this quantitative analysis was accomplished through using SPM software package. **Results:** Obtained results reveal that there was a significant relationship between dizziness and thickness of the carotid artery as well as a significant relationship between the thickness of the carotid artery and the number of affected areas in the brain. In addition to visual analysis, quantitative details were provided through SPM program including information about clusters with significant perfusion reduction characterized by location, size of the cluster and T values were obtained. Group analysis of the brain scan data in SPM software indicated a significant decrease in perfusion in temporal lobe including: fusiform right, Para hippocampal right, and middle temporal left. Furthermore, significant hypo perfused area in brain SPECT were mapping on brain MRI which facilitates more accurate localization. **Conclusions:** Quantitative analysis of the brain SPECT scan can reveal more detailed information about the extent of perfusion deficits and its anatomical region. Based on findings, increment of the thickness of the carotid artery causes to reduce brain perfusion in white matter and gray matter. It subsequently reduces cell metabolism which probably can lead to dizziness in patients. Although further studies with higher number of participants are needed to elucidate the problem with more details.

EP-27

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Non oncology study -> Other clinical studies ->
Gastroenterology, benign

EP-0334

67-gallium Citrate Oral Scintigraphy Evaluation In Crohn Disease: A Novel Inflammatory Highlighter?

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Purpose: The management plan for a patient with Crohn's Disease should take into account evaluation and identification of activity, site and behavior of disease. Endoscopy and radiology are complementary techniques, however repeated use over the time it's little tolerated. The aim of this report was to assess activity, site and extension of Crohn's Disease using ⁶⁷Gallium citrate oral Scintigraphy [GCS]. **Methods:** In this prospective analytical cross sectional study, we describe a pilot with 6 consecutive cases of Crohn's Disease [CD] and 3 control patients in follow up which were studied with GSC and colonoscopy. The patients were underwent a digestive transit studies with ⁶⁷gallium citrate (300uCi-11,1MBq) after oral ingestion. Anterior abdomen images were performed at 1, 3, 6, 24, 48 and 72 hours. All patients with CD were classified for activity clinical (CDAI), phenotype (Montreal Classification) and endoscopic score (SES-CD). **Results:** Of six patients with Crohn's Disease (4 women, 2 man; mean age, 36 years) in treatment with Anti-TNFs (4 clinical remission; 2 activity disease) all of them showed some degree of activity thought GCS and only two confirmed by

colonoscopy. The segment more affected was right colon (5/6). Terminal ileum was marked in two cases (2/6). Colonic extension was two segments in 50%. **Discussion:** The endogenous ⁶⁷Gallium citrate has been used to evaluation of inflammatory and/or infectious diseases with variables results. We decided use the oral form in inflammatory intestinal disease with interesting results. Inaccessible regions to standard endoscopic techniques remain a challenge and the new tools assessments are necessary to evolve management for Crohn's Disease. GSC evaluation showed activities areas in colon and ileum in patients with both clinical activities and remission, sometimes with normal endoscopy. **Conclusion:** The new findings in GCS evaluation revealed activities areas in patients with clinical and endoscopic remission. GSC per chance can be used to assess efficacy of anti-TNF therapies and has a potential for guided biopsy by colonoscopy.

EP-0335

Drug conciliation for gastric emptying scintigraphy : a "digest" for transdisciplinary interaction !

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Gastric emptying scintigraphy (GES) is the gold standard modality for gastroparesis diagnosis. Patients are often polymedicated, still, it has been described many drugs can significantly interact with gastric emptying, and bias the GES interpretation. According to the recommendations from the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine, patients should stop taking these medications 2 days prior to the scan. Given to the fact that these medications and their administration were rarely considered for GES interpretation, and in order to optimize the diagnosis, a drug conciliation (DC) was performed. This study aimed at evaluating the impact of DC on GES. **Materials and methods:** A literature review of drugs interactions with GES has been established. Jointly with the gastroenterologists, the exam indication was specified for each patient (initial diagnosis or therapy monitoring). Medications were investigated crossing three different sources (the patient himself, the computed drug history file at the Hospital, and the patient's pharmacy). The patient was phone-called by the radiopharmacists the week before the exam. Any drug likely to interfere with GES was analyzed and categorized. The patient was told to interrupt non-vital, GES-interfering drugs 2 days before the exam. At the patient's arrival on the day of the exam, a pharmaceutical interview with the patient focused on drug intake on the last two days and the information was immediately forwarded to the nuclear physician. The indication accuracy, the pharmaceutical time spent, the number and the severity of each potential drug interaction with GES, the patient's compliance with his treatment recommendations, and the information collided in the medical report, were the main indicators used for evaluation. **Results and discussion:** 45 patients performing GES were followed-up. 91% were multi-medicated including at least 1 drug influencing gastric emptying. Interviews with the patient and the gastroenterologist were helpful to precise the GES indication and adapt the recommendations consistently.

88% of these patients followed the given instructions regarding drug interruption, and 100% of the medical reports included the medications listed from DC, required to the gastroenterologist for interpretation. Nuclear physicians, gastroenterologists, and patients were all satisfied of drug conciliation and radiopharmaceutical involvement in the process. Conclusion. Pharmacological treatment conciliation is a way to improve information and communication on patients' medications. This study also illustrates how a transdisciplinary team can effectively improve practices for the patient's care sake.

EP-0336

The role of oropharyngo-esophageal scintigraphy in patients with neurodegenerative diseases candidates to speech therapy

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Aim: to investigate the role of oropharyngo-esophageal scintigraphy (OPES) in patients with neurological diseases classified by the "Dysphagia Outcome and Severity Scale" (DOSS) and candidates to speech therapy. **Methods:** We enrolled 33 patients (15 women and 18 men, mean age 59 years, range: 24-87) complaining of dysphagia with diagnosis of amyotrophic lateral sclerosis (14/33), multiple sclerosis (9/33), Parkinson's disease (4/33), spinocerebellar ataxia (2/33), neonatal brain disease (2/33) and ataxic syndrome (2/33). All patients underwent OPES using a standardized procedure (5 ml semiliquid bolus labeled with 37 MBq of 99mTc-nanocolloid; dynamic acquisition for 60 seconds). Images were acquired with patients face in an 80° projection in front of gamma-camera. ROIs on the oral cavity, pharynx, esophagus and stomach were drawn to collect data about Oral, Pharyngeal and Esophageal Transit Time (OTT, PTT and ETT respectively), Esophagus-Gastric Transit Time (EGTT), Oral, Pharyngeal and Esophageal Retention Index (ORI, PRI, and ERI respectively) and Esophageal Emptying Rate (EER). Patients were divided into 2 groups: DOSS1 (moderate, mild/moderate and mild dysphagia) which included 19/33 patients, DOSS2 (normal or slight compromised swallowing) which included 14/33 patients. Cohen's test was applied to compare OPES results with DOSS groups. **Results:** ORI was pathological in 8/19 pts of DOSS1 and non-pathological in the remnant, while it was non-pathological in all 14 pts of DOSS2, showing fair agreement ($k=0.38$). PRI resulted pathological in 11/19 pts of DOSS1 and non-pathological in the remnant while it was pathological in 3/14 pts DOSS2 and non-pathological in the remnant, showing fair agreement ($k=0.34$). ERI resulted pathological in 17/19 pts of DOSS1 and non-pathological in the remnant while it was pathological in 7/14 pts of DOSS2 and non-pathological in the remnant, showing moderate agreement ($k=0.41$). EER resulted pathological in 15/19 pts of DOSS1 and non-pathological in

the remnant while it was pathological in 7/14 pts DOSS2 and non-pathological in the remnant, showing fair agreement with DOSS ($k=0.29$). OTT, PTT, ETT and EGTT showed no agreement with DOSS. **Conclusion:** Dysphagia is a relevant problem in neurological patients. OPES is a simple and well tolerated procedure that provides information on all the swallowing act until the stomach is filled. The evaluation of each segment, not only oral and pharynx, is fundamental because it is related with DOSS and integrates the clinical evaluation, helping the physiatrist in the choice of the speech therapy.

EP-0337

Utility of Salivary Gland Scintigraphy in the Diagnosis of Sjögren Syndrome

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Objective: To analyze usefulness of (99m)Tc-pertechnetate salivary gland scintigraphy in patients with of Sjögren's syndrome suspicion. **Materials and methods:** We retrospectively analyzed 74 studies carried out during the last two years (10 men and 64 women with ages between 19-75 years). Seventeen studies were excluded due to lack of follow-up. A dynamic study was performed for 30 minutes, administering a citrus stimulus in the middle of the exploration. Images were processed by drawing ROIs in parotid and submandibular glands and making activity / time curves. Uptake and elimination phases were visually evaluated. **Results:** 35 of the 57 patients were Sjögren's Syndrome diagnosed, 33 of them had a positive result on the scintigraphy (VP). Of the 22 patients in whom disease was discarded, 18 had a negative study (VN). Sensitivity and specificity values in our sample were 94% and 82% respectively, obtaining a PPV of 89% and a NPV of 90%. 56.8% of the patients presented affection of both the uptake and the elimination phase of the radio-tracer, 37.8% showed only uptake phase affection and 5.4% only elimination phase affection. The pattern of global damage (parotid and submandibular) was the most common (73% of the studies), followed by the exclusive damage of the submandibular (19%) and the parotid (8%) glands. **Conclusions:** Salivary gland scintigraphy is a useful non-invasive method for the diagnosis of Sjögren's syndrome, with a high sensitivity and specificity. The most frequent alteration observed was affection of all the glands and in both phases of the study (uptake and elimination).

EP-0338

Utility of the salivary gland scintigraphy in the diagnosis of Sjögren's disease in relation to antibodies

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Objective: To analyze usefulness of salivary gland scintigraphy in patients with Sjögren's syndrome suspicion in relation

to reference antibodies. **Materials and methods:** We retrospectively analyzed, 74 studies carried out during the last two years (10 men and 64 women), with ages between 19–75 years. Seventeen studies were excluded due to lack of follow-up. A dynamic study was performed for 30 minutes, administering a citrus stimulus in the middle of the exploration. Images were processed by drawing ROIs in parotid and submandibular glands and making activity / time curves. Uptake and elimination phases were visually evaluated. Antibodies were collected in all patients, considering positive the presence of anti-Ro antibodies, anti-La antibodies, or the combination of both positive rheumatoid factor and positive ANAS at titers $\geq 1:320$. **Results:** 30 of the 57 patients had a diagnosis of Sjögren's Syndrome based on antibody criteria, 25 of them had also obtained a positive result on the scintigraphy (VP). Of the 27 patients who had negative antibodies, 15 had a negative scintigraphy (VN) study too. Considering the positivity of antibodies as the gold standard for the diagnosis of Sjögren's syndrome, the sensitivity value of the scintigraphy in our sample was 83%. **Conclusions:** Salivary gland scintigraphy is a useful diagnostic tool in the diagnosis of Sjögren's syndrome, considering the positivity of antibodies as the gold standard for the diagnosis of that disease.

EP-28

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Non oncology study -> Other clinical studies ->
Hematology, benign

EP-0339

Wandering spleen on FDG PET/CT

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Intoduction: Wandering spleen is a rare condition with a reported incidence of less than 0.5%. In patients with wandering spleen it is characterized by ectopic localization of spleen anywhere in the abdomen or pelvis because of the laxity of splenic ligaments. It can be congenital or acquired with a high incidence of splenic torsion and infarction. Herein we presented FDG PET/CT findings of a patient diagnosed with incidentally detected wandering spleen. **Method:** A 61 year-old female diagnosed with breast cancer was referred to FDG PET/CT for evaluating the response to treatment. **Results:** Mild FDG uptake (SUVmax:1.5) was seen in the primary lesion area in the upper outer quadrant of the right breast on FDG PET/CT images. Interestingly, the spleen was not located in the left upper quadrant without history of splenectomy. A mild hypermetabolic soft tissue density mass with hilum was observed in the mid abdomen and this mass was evaluated in favor of spleen. On repeating PET/CT scan the spleen was observed in totally different localization rather than normal and previously observed PET/CT position but no change was detected in other findings. **Discussion:** Wandering spleen can lead to torsion and splenic infarct. The standart treatment procedure of

wandering spleen is splenopexy unless torsion of the pedicle. Wandering spleen should be kept in mind when spleen was not located in its original position and mild hypermetabolic soft tissue mass with hilum was seen in the lower abdomen and pelvis.

EP-29

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Non oncology study -> Other clinical studies -> Uro-nephrology, benign

EP-0340

Optimization Of The Method For Calculating The Rate Of Glomerular Filtration Of The Kidneys In Patients With Hydronephrosis Using Reniography With ^{131}I -Hypuran

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Aim: Optimization of the mathematical method for calculating the rate of glomerular filtration (GF) of the kidneys, taking into account the developed correction amplitude coefficient, using the renography with ^{131}I -Hypuran. **Material and method:** Renography with ^{131}I -Hypuran was used to study 125 patients (73 women and 52 men) aged 28 to 65 year. The control group is represented at the expense of the same patients, who calculated the rate of GF of the kidneys using a renoscintigraphy with $^{99\text{m}}\text{Tc}$ -DTPA. Calculation the rate of GF of the kidneys was carried out according to the formula of standardized volume of distribution of radiopharmaceuticals (RF) using the developed design correction amplitude coefficient of curve of renography.

Results: According to the results of the study, all patients with hydronephrosis were divided into four cohorts, depending on the amplitude of the scintigraphic curve. cohort (n = 18) had an amplitude of the renographic curve of less than 30 imp/sec, cohort (n = 37) - 31-60 imp/sec, cohort (n = 43) - 61-80 imp/sec, IV cohort (n = 27) - 81-100 imp/sec. According to our calculations, the corrective amplitude coefficient for cohort was 1.0, for cohorts - 1.5, for cohorts - 2.0, for IV cohorts - 2.5. Thus, the mean rate of GF according to the radionuclide method, taking into account the amplitude coefficient, was equal to 37.2 ± 1.65 ml/min, II cohorts 49.4 ± 1.81 ml/min, III cohorts 65.7 ± 2.03 ml/min, IV cohort 81.3 ± 2.11 ml/min. In comparison, according to calculations of renoscintigraphy with $^{99\text{m}}\text{Tc}$ -DTPA, the mean rate of GF in I cohort was 36.2 ± 1.43 ml/min, II cohorts 51.1 ± 1.53 ml/min, III cohorts 67.2 ± 1.77 ml/min, IV cohort 82.6 ± 2.03 ml/min. The difference between rate of GF indices calculated using the applied methods of calculation was not significant ($p > 0.05$). **Conclusion:** Radionuclide method of calculating rate of GF, taking into account the correction amplitude coefficient, can be used to monitor changes in the filtration processes of the kidneys in controlling the quality of treatment for patients with hydronephrosis, using a simple and more economical method - renography with ^{131}I -Hipuran, which is relevant for many developing countries.

EP-0341**Assessment of the Relationship Between the Visual and Quantitative Findings of Dynamic Renal Scintigraphy in Patients with Renal Ectopic and Fusion Anomalies**

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Purpose: We aimed to investigate the correlation between visual and quantitative findings of Tc-99m diethylenetriamine penta-acetic acid (DTPA) dynamic renal scintigraphy in patients with renal ectopic and fusion anomalies. **Subjects and Methods:** We screened medical records of DTPA dynamic renal scintigraphy images performed in our department between 2015 and 2018, retrospectively for the presence of the renal anomalies. The study subjects comprised thirty-six kidneys (18 components of 9 patients with a horseshoe kidney, 2 patients with a cross ectopic kidney, and 16 patients with a pelvic ectopic kidney) of twenty-seven patients (F/M: 11/16, mean age: 35 years $\pm$ 16). Renal perfusion and excretion phases (renal input function (RIF) as normal/decreased) and excretion phase (renal output function (ROF) as normal/non-obstructive/obstructive) were visually assessed. The quantitative analysis of the RIF was evaluated by the split renal function (SRF), the maximum radioactivity count (Cmax), the time-to-peak of the renogram curve (Tmax), and the renal retention index (RRI), wherever the quantitative analysis of the ROF is assessed by the clearance half-time (T1/2), and the normalized residual activity before furosemide (NORA-BF) and after furosemide (NORA-AF) (F+20 protocol). We statistically surveyed the correlations between the visual and quantitative findings. Spearman's or Pearson's correlation test was used depending on whether the data follow a normal distribution or not. **Results:** There was a strong linear correlation between RIF and SRF evaluations ($r=0.76$). Correlations between RIF and Cmax, Tmax, RRI were not statistically significant ($p>0.05$). Our findings revealed a negative linear correlation between ROF and T1/2 ($\rho=-0.73$), between ROF and NORA-BF ($r=-0.46$), and between ROF and NORA-AF ($r=-0.57$). The distribution of the mean values of SRF in groups with normal and decreased RIF were $50.4\%\pm 7.1$ and $26.1\%\pm 14.6$, respectively ($p<0.001$). The distribution of mean values of ROF quantitative parameters according to normal, non-obstructive and obstructive groups as follows: T1/2 (normal: $8.7\text{ min}\pm 7.5$, non-obstructive: $23.4\text{ min}\pm 7.4$, $p<0.001$), NORA-BF (normal: 0.5 ± 0.2 , non-obstructive: 1.8 ± 1.2 , and obstructive: 1.7 ± 0.4 , $p<0.05$) and NORA-AF (normal: 0.3 ± 0.2 , non-obstructive: 0.6 ± 0.5 , and obstructive: 1.8 ± 0.4 , $p<0.001$). **Conclusion:** This study supports the utility of SRF in evaluating RIF in patients with renal ectopic and fusion anomalies. Findings of this study suggest that it may be useful to consider the quantitative parameters in the discrimination of obstructive/non-obstructive patterns for evaluation of the excretion phase in the anomalous kidney.

EP-0342**Evaluation of Renal Split Function by Scintigraphy and Geometric Mean Calculation**

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Introduction: The split renal function is routinely assessed by renal scintigraphy (renal scan), especially for living kidney donors and patients with suspected renal obstruction. Despite that attenuation artifact due to the difference in kidney positioning could be partially corrected by geometric mean (GM); renal scans are routinely acquired on posterior images. Dual-headed cameras have become routine equipment and enable dynamic GM for renal scan. In this study we assessed the split function by imaging kidneys both anteriorly and posteriorly on dual head gamma cameras. The split function calculated by geometric mean was obtained and was compared to the results from routine (posterior only) image measurements. **Materials and Methods:** We reviewed renal scans with ^{99m}Tc -MAG or ^{99m}Tc -DTPA from 20 patients (age: 66.4 ± 19.3 , F:M=14) from Jan. 23, 2018 to April 23, 2018 who had both anterior and posterior images acquired on dual head ECAM cameras. Split renal function using posterior images were retrieved from the clinical workup, and GM images were processed subsequently. The region of interest of each kidney and the background was drawn by a reader blinded to clinical data on Hermes hybridViewer V2.6, in a similar manner as clinical routinely. The split function of the right and left kidney calculated from the posterior and geometric means were compared. Continuous variables were presented as mean $\pm$ standard-deviation. **Results:** Of 20 patients with renal scans, 14 had normal positioning kidneys (group 1). Abnormal positioning kidneys (group 2) were observed in pelvic kidney (2), horseshoe kidney (1), malrotated kidney (1), and the kidney with adjacent tumors (2). The mean split function of the right kidney was $54\pm 11\%$ from GM, compared to $52\pm 11\%$ from posterior for group 1, and $43\pm 11\%$ from GM, compared to $37\pm 16\%$ from posterior for group 2. The difference in right or left kidney split function was $2.6\pm 1.6\%$ for group 1 and $8.7\pm 4.8\%$ for group 2, respectively. **Conclusion:** This preliminary data showed that geometric mean could improve the diagnostic accuracy in split renal function, with the change of 2-3% in normal positioning kidneys and 8-9% in abnormal positioning kidneys. Considering no additional radiation exposure or additional imaging time for the geometric method, it should be used in the routine assessment of renal split function.

EP-30**e-Poster Area**

Clinical -> Diagnostic study -> Adult study -> Oncology study -> General oncology -> External beam radiation therapy planning

EP-0343**Dose painting in prostate cancer with simultaneous ^{11}C -Choline PET and Multiparametric MR**

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Purpose: To evaluate a PET/MR protocol to identify tumor lesions in the prostate from avid ^{11}C -Choline and its correlation with high anatomical resolution MR-T2 images and Diffusion

Weighted Imaging (DWI) to define a new biological target volume (BTV) for radiotherapy planning treatment (RP). **Subjects & Methods:** Eight patients with prostate cancer (PC) diagnosed by biopsy underwent simultaneous PET and multi-parametric (mp-MR) protocol with ^{11}C -Choline located in the prostate and RP simulations. For all patients, a standard plan of IMRT (sIMRT) was designed with a dose of 70 Gy to the planning target volume (PTV) from CT images and two IMRT plans with a simultaneous integrated boost (SIB-IMRT) to deliver 74.76 and 77 Gy to the BTV and 70 Gy to the rest of the PTV from PET/MR images, in order to escalate therapeutic doses in tumor lesion detected. **Results:** A total of 14 lesions were detected, mean lesion size $\pm$ standard deviation 4.33 ± 3.13 cm³ (range 1.3 - 11.10 cm³), involving peripheral (PZ) and central zone (CZ) in prostate gland. MR-T2 images fused with PET images were useful to delimit lesions located in the PZ. For CZ lesions, MR-T2 images had to be analyzed together with PET and DWI images. On the other hand, DWI sequence showed a great potential in the BTV marking, mainly in the prostate CZ. For identification of the prostatic capsule (PC) and seminal vesicles (SV), the use of high resolution MR-T2 images provided a precise definition of the CTV, the difference percentage size was -12% for PC and -20% for SV as compared with computed tomography (CT). Changes in dose levels in organ at risk (OARs) after increasing selective dose developed in the lesion are not significant when compared to sIMRT, by clinical criteria. **Conclusions:** This work shows that ^{11}C -Choline PET/MR protocol localized in the prostate can be used to define tumor lesions in radiotherapy planning treatment. The combination of PET and MR multiparametric images achieve the best delineation of the tumor and OARs, decreasing the volume to be irradiated up to 20% compared to the planning with CT images. The adoption of SIB-IMRT strategy within the defined areas can deliver escalating therapeutic doses without increasing toxicity in the OARs. High doses in prostate tumors may significantly improve the therapeutic response of patients by preventing relapses after the first year of treatment.

EP-31

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> General oncology -> Radioguided surgery

EP-0344

Our Performance In Sentinel Lymph Node Biopsy (SLNB) After Neoadjuvant Chemotherapy In Patients With Locally Advanced Breast Cancer (LABC) Diagnosis

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Aim: We evaluated our performance in SLNB after neo-adyuvant chemotherapy (A-NAC) in patients diagnosed with LABC, obtaining the detection rate and false negatives of the technique and analyzing the response to treatment (tumor and lymph node) and the evolution of the disease. **Material and method:**

Retrospective study (January/2012-January/2018). The inclusion criteria were: consecutive patients, diagnosed with LABC (TNM-AJCC-7th-Edition); scheduled for NAC; with radiological evaluation to the treatment, (RECIST 1.1 criteria); submitted, A-NAC, to mastectomy/lumpectomy, SLNB and axillary lymphadenectomy (LDN); we evaluated the pathological response (Miller & Payne criteria) and we performed a follow-up of the response to treatment (at least 12 months A-NAC). **Results:** Of 422 patients, 34 patients met the inclusion criteria, (average age: 48.8 years), 2 with bilateral involvement, in total 36 breasts. The initial T staging was: cT1: 5(14%); cT2: 19(53%); cT3: 7(19%); cT4a: 4(11%); cT4b: 1(3%). The initial N staging was: cN(0): 4(11%) and cN(+): 32(89%). We performed fine-needle aspiration biopsy (FNAB) for all cN(+) patients. The results were 23(72%) FNAB(+) and 9(28%) FNAB(-). Histological subtypes included: infiltrating ductal carcinoma (IDC): 31 (86%), infiltrating lobular carcinoma (ILC): 2 (6%), IDC+Ductal Carcinoma in-situ (DCIS): 1(3%), HG-DCIS: 1(3%) and Mucinous Carcinoma: 1(3%). The prognostic biomarkers status were: Luminal(A): 3(8%), luminal(B): 15(42%), triple negative: 6(17%) and Her2: 11(31%). A-NAC the responses of the target lesions by MRI were: 9(28%) complete responses (CR) 22(61%); partial responses (PR) 3(8%); stable diseases (SD) and 2(6%) progressions (PG). A-NAC and post-surgery outcomes SLNB were: 19(53%) SLNB(+): 14PR; 1CR; 2SD and 2PG. 13(36%) were SLNB(-): 5PR; 7CR; 1SD and 4(11%) did not present tracer migration (NM): 3 were PR, (1 was LDN(+), relapse later and then died) and 1 CR. However, in this group, we found that no lymph node histological changes were attributable to the treatment (according to Miller & Payne criteria: type A and B responses). The LDN results were: 11(31%) LDN(+) whose were: 7(19%) SLNB(+); 1(3%) SLNB(-) and 3(8%) NM. 25(69%) were LDN (-): 12(33%) SLNB(+), where the SLNs were the only infiltrated lymph nodes. 12(33%) SLNB(-) and 1(3%) NM, (with lymph nodes pathological response Miller & Payne type A). Only 8% of cN(+) A-NAC patients presented lymph node response to pN(0). None SLNB(-) presented progression including the false negative. The 2 PG after therapy remain stable. **Conclusions:** In our series, the SLNB detection rate was 89%, probably related to the absence of lymph nodes changes attributable to the therapy. We obtained 3% of false negatives and none of the SLNB(-) presented progression.

EP-0345

Reproducibility of Sentinel Lymph Node Scintigraphy

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Purpose/introduction: In some tumors, sentinel lymph node (SLN) biopsy has been reported as a safe and accurate method for screening lymph node malignancy involvement. Defined as the first node to receive the seeding of lymph-borne metastatic cells, sentinel lymph node can be easily identified by scintigraphic techniques (SLNS). Although this intraoperative technique guides the surgeon to the sentinel node, scintigraphic images provide important preoperative information about the

exact location of the target. Because some doubts existed about the accuracy of the SNLS identification in the clinical practice, we aimed to assess the reproducibility of SLNS technique in our department. **Subjects & methods:** Patients who repeated SLNS between 19-01-2004 and 24-04-2017 due to surgery re-schedule were selected. The paired SLNS were retrospectively categorized in one of three groups by two blind readers: group 1 - overlapping lymphatic drainage, group 2 - partially overlapping lymphatic drainage, characterized by the identification of the same SLN, but with different drainage pathways, and group 3 - non-overlapping lymphatic drainage, defined by the identification of different SLN in both scintigraphic studies. **Results:** Thirty patients repeated SLNS in the selected time period. Two patients did not completed one of the two scintigraphic studies and one was submitted to surgery between the two SLNS, and thus were excluded. Our sample consisted of 13 melanoma patients, 12 with unilateral breast cancer and 2 with vulvar carcinoma (20 women, 7 men, average age: 68.3 ± 10.8 years). The time period between studies was 15.5 ± 14.8 days (minimum 1 day and maximum 77 days). In 26 patients (96%), there was a completely overlapping lymphatic drainage (group 1). No patient was included in group 2. Only one patient with breast cancer had a non-overlapping lymphatic drainage (4%). In this patient, the axillary SLN faintly identified in the first study was not seen in the second SLNS, performed 42 days later. Histopathology confirmed diffuse infiltration of the axillary pathway and SNL. **Discussion/conclusion:** In our sample, SLNS was highly reproducible. The only observed difference in the paired studies seemed to be caused by disease progression (metastatic infiltration of axillary SLN), and not inherent to the technique.

EP-0346

Sentinel Lymph Node Biopsy (SLNB) In Vulvar Cancer. 10 Years Of Experience In The Balearic Islands

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Aim: Utility of Sentinel Lymph Node Biopsy (SLNB) procedure in early-stage of Vulvar Cancer patients and evaluation of results, recurrences and morbidity in a follow-up time of 10 years.

Materials & Methods: From 2008 until 2018, 40 patients with vulvar cancer and SLNB were reviewed. The day before the intervention, ^{99m}Tc-Nanocol (4mCi) was injected peritumorally in all patients. Dynamic and planar lymphoscintigraphy of the inguinal region, obtaining anterior and lateral projections, were performed. During the surgery procedure inguofemoral lymph nodes were checked with a gamma probe detecting the SLNs. Intraoperative histopathologic assessment of these SLNs were performed. **Results:** Median age of patients was 72 years. Final histology determined: 37 squamous cell carcinoma, 1 carcinosarcoma, 1 apocrine hidroadenocarcinoma and 1 unknown. Migration rate was 97.5%, with a total of 129 SLNs removed (median 3.2/patient). Tumor location: 3 out of 25 with lateral lesions had bilateral drainage and 2 out of 15 with middle line lesions had unilateral drainage. On lymphoscintigraphy, 16 out

of 40 had bilateral drainage: 9 SLN negative (1 with left blockage drainage) and 7 SLN positive; 24 out of 40 had unilateral drainage: 21 SLN negative (1 false negative) and 3 SLN positive. Of the total SLN positive (10/129), in 8 of them an inguofemoral lymphadenectomy was performed. We had just 1 case of false negative, having positive lymphadenopathies next to the SLN(-). In 12 out of 40 patients appeared postsurgical complications, with 4 lymphedemas. During a median follow-up of 4 years, we identified recurrences in 6 out of 10 patients with SLN positive (40% mortality) and in 7 out of 30 patients with SLN negative (16% mortality). **Conclusion:** SLNB in Vulvar Cancer is the technique of choice for a correct staging and locoregional therapy (detection rate nearly 100%). It is important to have a correct clinical lymph node staging before the surgery in order to avoid potential blockage drainages which could induce false negative SLN. In our experience, the positivity of SLN had no relation with a higher recurrence rate, but it has a relation with the mortality (40% in positive SLN). Total lymphedema rate was 10%, with only one case of early lymphedema associated with a positive SLN, without lymphadenectomy. In our follow-up time, any patient with negative SLN developed lymphedema.

EP-0347

Visualization of sentinel lymph nodes in head and neck tumors

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Aim: The aim of the study was to evaluate the diagnostic efficiency of the new radiopharmaceutical ^{99m}Tc-Alotech for the detection of sentinel lymph nodes (SLN) in patients with head and neck tumors. **Materials and methods:** The study included 21 patients treated in the Department of Head and Neck tumors of the Tomsk National Research Medical Center of the Russian Academy of Sciences. ^{99m}Tc-Alotech was injected in the sub-mucosal layer along the perimeter of the tumor for visualization of sentinel lymph nodes in 2-4 points (20 MBq in each injection). Single-photon emission computed tomography (SPECT) of the neck area was performed on a gamma camera (E.CAM 180, Siemens) 3 and 18 hours after injection of radiopharmaceutical. Evaluation of examination results was carried out visually and by calculating of the inclusion's intensity of the radiopharmaceutical in sentinel lymph nodes in comparison with the place of introduction. Results of the SPECT and CT examinations were combined for improvement of a topographic localization. Intraoperative detection of sentinel lymph nodes was performed using gamma probe Gamma Finder II® (USA) by careful measurement of gamma radiation level in the projection of lymphatic collectors. **Results:** Sentinel lymph nodes were detected in all patients during the SPECT and intraoperative radiometry, sensitivity of the method was 100%. 1 sentinel lymph node was visualized in 18 (85.7%) patients, 2 SLNs were located bilaterally in 3 (14.3%). Sentinel lymph node was located in the III level of the neck in 76.2% cases. The intensity of inclusion of ^{99m}Tc-Alotech in the SLN at 18 hours after injection was $8.3 \pm 7.5\%$ in SPECT ex-

amination, $12.7 \pm 8.8\%$ - in radiometry. There were no metastatic invasion in sentinel lymph nodes and other lymph nodes of the neck area during the histological evaluation, specificity of the method was 100%. Multimodal technique with combining of SPECT and CT results allowed to surgeons to focus on the sentinel lymph node anatomical location. **Conclusions:** The use of the ^{99m}Tc -Alotech radiopharmaceutical in patients with head and neck tumors makes it possible to detect sentinel lymph nodes with sensitivity and specificity of 100%. ^{99m}Tc -Alotech is characterized by a high level of accumulation in the SLN with improvement of visualization and reduction the operation time.

EP-0348

First results from ex-vivo experience in Radioguided Surgery Technique with Beta- Radiation in meningioma and neuroendocrine patients

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Introduction: Radioguided surgery (RGS) is a technique aimed at assisting the surgeon to reach a complete resection of the tumour, while minimizing the amount of healthy tissue removed. RGS with beta- radioisotopes, as ^{90}Y , is a novel approach focused on developing a new probe which, detecting electrons and operating with low background, provides a clearer delineation of the margins of lesions with low radiation exposition for surgeons. **Aim:** To validate this RGS procedure, tests on ex-vivo specimens of tumors expressing somatostatin receptors as brain meningioma and gastro-entero-pancreatic neuroendocrine tumors (GEP NET) were performed. **Materials and Methods:** We studied these tumors due to the high uptake of a beta- emitting radiotracer already in use in clinical practice as ^{90}Y -DOTATOC. Patients were enrolled according to the tumour Standard Uptake Value ($\text{SUV} > 2$) and the expected Tumour to Non-tumour Ratio ($\text{TNR} > 10$) estimated from ^{68}Ga -DOTATOC PET/CT images. So far, after giving written informed consent, 4 meningioma and 4 GEP NET patients, received ^{68}Ga -DOTATOC/PET, MR or CT scan, two weeks prior to surgery. Twenty-four hours before surgery, meningioma pts received a median activity of 4.5 mCi; NET pts received 5 mCi of ^{90}Y -DOTATOC. **Results:** Surgery was performed as clinical and radiological indicated. Tumors and the around tissues were sectioned in different samples and were examined with the beta- detecting probe to assess the sensitivity of millimeter-sized tumour remnants. All the tumor samples showed high counts of radioactivity, with difference from surrounding healthy tissues. The radioactivity in the tumour samples was between 4.5 and 17x greater than the background activity. 11 surgical removed NET lesions identified on CT (8 lesions) or ^{68}Ga -DOTATOC PET/CT (11 lesions) were found to have foci of elevated activity at RGS. The abdomen CT missed

1 peripheral nodule and 2 nodules at the hepatic hilum but the complementary evaluation of ^{68}Ga -DOTATOC PET/CT increased the overall accuracy. **Conclusions:** These first ex-vivo RGS tests showed that through this probe we can discriminate very strongly between tumor and nearby healthy tissues by the administration of low activities of ^{90}Y -DOTATOC. We are planning to complete the trial in NET patients, as it is well known that a complete surgery could better the prognosis of this disease. Further developments of the probe could increase its sensitivity, in order to reduce the dose for a given administered activity. The association of CT/MR and ^{68}Ga -DOTATOC PET/CT in NET and meningioma patients remains mandatory to obtain a minimal invasive surgery.

EP-0349

Evaluation of Selective Sentinel Lymph Node Biopsy in Breast Cancer Patients without Axillary Involvement Candidates to Neoadjuvant Chemotherapy: a Prospective Study

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Purpose: Sentinel node biopsy (SNB) is still a controversial issue in patients undergoing neoadjuvant chemotherapy. The aim of this study is to evaluate the results of the sentinel lymph node biopsy (SLNB) after a neoadjuvant chemotherapy in breast cancer patients without axillary involvement at diagnosis, after six years applying a validated and implemented procedure. **Subjects and methods:** Prospective study from April 2011 to March 2017 with 85 women included (mean age: 48 y) with breast infiltrating carcinoma treated with neoadjuvant chemotherapy (anthracyclines plus taxanes) for conservative purposes. Axillary status was established by clinical examination and ultrasound (fine needle aspiration were performed for indeterminate or suspicious axillary lymph nodes). Afterwards neoadjuvant chemotherapy, lymphoscintigraphy was performed after the periareolar injection of 37 MBq ^{99m}Tc labelled nanocolloid. The sentinel node was analysed by HE staining and immunohistochemistry. Axillary lymphadenectomy was performed when the sentinel node was positive for disease. Clinical and radiological follow-up was carried out for an average of 42 months. **Results:** The most frequent presentation was an unifocal tumor, invasive ductal carcinoma grade III, Luminal B molecular subtype with positive Her2Neu, Ki67 ≥ 20 and initial stage IIA. The lumpectomy was performed in 89.4% of the total cases. The detection rate of the lymphoscintigraphy was 98.84%. The sentinel node was positive in 23.5% and negative at 76.5%. The false negative rate for intraoperative SLNB was 8.45%. The mean number of axillary sentinel node removed was 2.2 (1-4). In the axillary lymph node dissection there was infiltration of other lymph nodes only in

46.7 % of the cases. The complete response after neoadjuvant chemotherapy occurred in 36.5% of the cases. 52.3% of the negative SLNB did not present a complete response. No cases of axillary recurrence with negative SLNB have been reported. 15% of patients with positive SLNB and 6.2% with negative SLNB presented disease progression. Local recurrence occurred in 5.9% of patients. The mean, from the intervention to the onset of progression, was 25 months. **Conclusions:** SLNB is a safe technique to define axillary status in patients with breast cancer without axillary involvement at diagnosis and candidates for neoadjuvant chemotherapy. No cases of axillary relapse with negative sentinel node were reported.

EP-0350

Subcentimeter solitary pulmonary nodule and ground glass opacity. Usefulness of Radioguided Video-Assisted Thoracic Surgeon

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Introduction: The detection of incidental subcentimeter solitary nodule and ground glass opacity is a common and rising CT finding and sometimes it's difficult to have a definitive diagnosis with transbronchial or percutaneous CT-guided biopsy. The video assisted thoracic surgery (VATS) is the preferred procedure for diagnosis but it can be a challenge to locate these small lesions and the use of isotopes can help in its detection. The principal aim of this study is to evaluate the usefulness of radioguided VATS in our center. Twelve patients (one patient with two nodules) with indeterminate solitary pulmonary nodule underwent radioguided VATS in our Hospital. CT-guided injection of 74MBq ^{99m}Tc -MAA in 0,2ml was performed the day of the VATS. After the injection SPECT/CT images were performed to confirm the correct injection of the radiotracer. An intraoperative thoracoscopic gamma probe was used to locate and resect the pulmonary region with the nodule within. Histology was checked in order to complete or upgrade the surgery. **Results:** Thirteen nodules were resected with radioguided VATS. The success rate was 100%. Mean size was 10,8mm (range 7-20mm). All nodules were resected by atypical segmentectomy. In five cases the procedure ended in lobectomy (38,4%), in one ended in anatomical segmentectomy (7,7%) and in the other seven there was no surgery upgrade (53,9%). Histological examination revealed two benign lesions (15,4%), one metastatic nodule (7,7%) and ten primary lung tumors (76,9%). Perioperative complication or mortality was reported. **Conclusion:** Radioguided VATS is a safe procedure that helps the surgeon detecting small pulmonary nodules, with a high successful rate of resection. It also minimizes the percentage of resected lung for diagnosis and therapy.

EP-0351

Use of ^{99m}Tc -EDDA/HYNIC-TOC (Tektrotyd) for Radioguided Surgery of Gastroenteropancreatic Neuroendocrine Tumors: A Feasibility Study

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Purpose: Surgical resection of primary tumor and involved lymph nodes in patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) has a significant prognostic impact. Aim of this study was to evaluate feasibility of radioguided surgical nodal staging using ^{99m}Tc -EDDA/HYNIC-TOC (Tektrotyd®) in GEP-NETs. **Subjects and methods:** Patients with histologically proven GEP-NET eligible to radical or palliative surgery showing avid tumor uptake on ^{99m}Tc -EDDA/HYNIC-TOC scintigraphy and SPECT/CT were prospectively enrolled. Approximately 4h before surgery, 185 MBq of ^{99m}Tc -EDDA/HYNIC-TOC were i.v. administered. Intraoperative localization of primary tumor and radioactive lymph nodes was performed using a hand-held gamma-probe set on ^{99m}Tc energy peak. Radioactive lymph nodes were localized and excised before proceeding to regional lymphadenectomy. Extra-regional lymphatic basins were also investigated. Resected specimens were re-evaluated *ex vivo* with the gamma-probe after macroscopic lymph node isolation. **Results:** Since February 2017, five GEP-NET patients were enrolled (3 pts had G1-G2 ileal NET, 1 pt G2 rectal NET and 1 pt gastric NEC). All primary lesions seen on pre-operative scintigraphy were successfully localized with gamma-probe and completely excised. Mean *in-vivo* tumor count-rate was 399 counts-per-second/cps (range 80-496). Histological examination confirmed pre-operative diagnosis in all cases. A total of 107 lymph nodes was resected (mean number per patient 21, range 14-40), including 35 radioactive lymph nodes (mean number 7, range 3-12). Mean *in-vivo* nodal count-rate was 185 cps (range 14-722). 20/35 radioactive lymph nodes were metastatic at histologic examination (mean number 4, range 1-11). No metastatic involvement of "cold" lymph nodes was reported. Notably, *ex-vivo* count-rate of metastatic lymph nodes showed no significant variation from *in-vivo* gamma-probe evaluation, whereas non-involved nodes showed generally a sharp decrease in *ex-vivo* count-rate. In one patient, radioguided nodal evaluation determined the localization of a metastatic node in a extra-regional district. Median follow-up after surgery was 11 months (range 5-13). Clinical and instrumental follow-up evaluation showed stable disease in every patient, with no evidence of nodal disease recurrence. **Conclusions:** This pilot study confirmed feasibility of radioguided nodal staging in GEP-NET patients. The use of ^{99m}Tc -EDDA/HYNIC-TOC allowed manageable surgical scheduling, limiting radiation exposure of patients and medical staff. Moreover, this procedure can be performed using a standard gamma-probe routinely used for sentinel lymph node biopsy. Preliminary results on false-negative rate suggest that this could represent a reliable approach for surgical nodal staging with a clinical impact on prognosis.

EP-0352

The value of SPECT/CT in detection of sentinel lymph node in melanoma patients

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Introduction: Lymph node status is one of the most important prognostic factors for recurrence and survival in malignant melanoma patients. Sentinel lymph node (SN) biopsy is a standard procedure in staging regional lymph nodes in early stage disease. SPECT/CT is hybrid imaging technique that can improve visualization and localization of SN. The aim of this prospective study was to assess the contribution and additional value of SPECT/CT imaging in detection and biopsy of the SN in malignant melanoma patients. **Method:** 87 patients with malignant melanoma were included in prospective study conducted from December 2010 to September 2015. After intradermal administration of radiocolloid particles all patients underwent planar scintigraphy according to usual protocol and SPECT/CT immediately after the last planar imaging. **Result:** SPECT/CT showed statistically higher number of sentinel lymph nodes in relation to the number of sentinel nodes detected by planar scintigraphy. SPECT/CT detected 229 sentinel nodes (average 2.62 per patient), 17.5 % more than planar scintigraphy in 37.9% of patients. Identification and localization of sentinel lymph nodes was more accurate by SPECT/CT imaging than planar scintigraphy. We noted identical findings of SPECT/CT and planar scintigraphy in 52.9% of patients. In 39.1% of patients planar scintigraphy and SPECT/CT findings were inconsistent in number of sentinel nodes and in 20.7% of patients in the drainage areas, SPECT/CT detected new drainage areas that could not be recognized by scintigraphic analysis alone. The planar scintigraphy shows more than one drainage area in 25 patients and SPECT/CT in 33 patients. Fifteen patients had metastases in sentinel lymph nodes, 14 only in sentinel lymph nodes. There were no false negative results. In 2 patients sentinel lymph node with metastasis were visualized only with SPECT/CT. The positive impact of SPECT/CT on patient management was observed in 42.5% of patients. **Conclusion:** SPECT/CT has significant advantages over planar scintigraphy in the detection of sentinel lymph node. We recommend SPECT/CT to be a part of the standard protocol for sentinel lymph node detection and biopsy in all melanoma patients.

EP-0353

The Use Of A Targeted Sentinel Node Radiopharmaceutical Can Reduce Imaging Time In Patients With Malignant Melanoma

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Tc-99m tilmanocept is a new radiopharmaceutical which has been developed to specifically target the mannose receptors (CD206) on macrophages present in the lymph nodes. Unlike colloids (such as Tc-99m nanocoll) which depend on filtration to perform sentinel node localisation, tilmanocept is a small molecule that passes through the lymphatic channels from the injection site and then targets the lymph node macrophages. As sentinel node localisation is effectively a destructive process direct comparison of 2 Tc-99m labelled agents within a single

patient is not feasible. Therefore the results of 55 Tc-99m Tilmanocept studies in patients undergoing sentinel lymph node biopsy (SLNB) for melanoma were retrospectively compared with 55 site (arm, leg, trunk, head and neck) matched controls performed using Tc-99m nanocoll within the same department and using the same activity, same injection techniques, same referral and surgical team. To determine if there was a reduced need for imaging time such that the sentinel node(s) are identified more rapidly with tilmanocept the time of injection and completion of study were noted from the electronic patient record (EPR) for each patient. Overall the mean time from injection of tilmanocept to localisation of the sentinel node and completion of the study was 60 +/- 24 min for tilmanocept compared to 97 +/-41 min for nanocoll (p=0.00). For the 16 axial sentinel nodes (trunk, head and neck) the mean time to study completion was 76 +/- 20 min for tilmanocept and 117 +/-69 min for nanocoll (p=0.03). For the 39 appendicular (limb) sentinel node sites the mean time for tilmanocept was 55 +/- 23 min and for nanocoll 88 +/-16 min (p=0.00). A similar number of sentinel nodes were seen with each agent (2.1 for tilmanocept vs 1.5 for nanocoll (n.s)) Tilmanocept can indeed reduce imaging time by a mean of 37 minutes when compared to nanocoll. This time saving is seen with both appendicular and axial site sentinel nodes and had cost efficiency implications not just for nuclear medicine camera time, but for the sentinel node patient pathway as a whole which our unit is reviewing in the light of these findings.

EP-0354

Radio-guided lung lesion localization: introducing a fluoroscopy system in a SPECT/CT scan

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Purpose: Video-assisted thoracoscopic surgery (VATS) is the procedure of choice for surgical biopsy and removal of peripheral lung nodules. Nevertheless, the use of VATS can be difficult in the case of small, non solid, or deep lung nodules. The purpose of this study was to report our experience in the use of radiotracer localization and resection of small, indistinct, or non palpable pulmonary lesions. We developed an innovative technique installing a fluoroscopy system on a SPECT/CT scan that allowed to perform CT-guided injection of radiotracer directly on SPECT/CT. **Materials and Methods:** Patients were selected for the radiotracer procedure in presence of difficulties in locating nodules with VATS. 0.2 mL of 99Tc-MAA (human serum albumin macroaggregates labelled with 15 MBq eluted 99Tc) and 0.3 mL nonionic iodinated contrast was injected in or near the nodule under CT-guide. All CT-guided radiotracer injections were confirmed with SPECT/CT. During the VATS procedure, an endoscopic gamma detecting probe was introduced to scan the lung surface. The area of major radioactivity, which matched with the area of the nodule, was resected. **Results:** Between January 2016 and February 2018, 32 patients (19 male and 13 females), median age of 63 years (range, 27-83 years) underwent CT-guided radiotracer injection. The mean nodule size was 11

mm (range, 4 to 24 mm). The mean distance of the nodule to the nearest pleural surface, as measured in CT, was 18 mm (range, 0 to 65 mm). CT nodules morphology characteristics were: 14 nodules ground glass, 11 solid and 7 partly solid. No significant adverse events occurred. 31 patients had successful localization of the nodules and in one case a diffuse extravasation of the tracer occurred. In this patient the surgery was not performed. In one patient the surgeons decided for an open thoracotomy after unsuccessfully VATS. Overall, lobectomy was performed in 2 patients, segmentectomy in 1, and wedge resection in 28 patients. No mortality occurred. The pathological diagnosis was 15 (49%) primary lung cancer, 7 (22%) metastases and 9 (29%) benign lesions. **Conclusions:** Radiotracer localization of pulmonary lesions is a feasible procedure with a high rate of success. In our knowledge we are the first group who developed and successfully used fluoroscopy system in a SPECT/CT scan.

EP-0355

Concordance between conventional scintigraphy and the freehand SPECT optical gammacamera in the preoperative evaluation of the sentinel lymph node biopsy in breast cancer

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Purpose: To evaluate the accuracy of the freehand SPECT gammacamera in the sentinel lymph node biopsy (SLNB) in breast cancer by determining the concordance of the number and position of sentinel lymph nodes (SLN) between preoperative conventional scintigraphy (CS) and the freehand SPECT optical gammacamera (fhSPECT). **Subjects & Methods:** A prospective study of 21 patients with breast cancer, all suitable for SLNB procedures was held, involving a peritumoral injection of 37–148 MBq (1–4 mCi) of ^{99m}Tc -albumine nanocolloids. Images with both CS and the fhSPECT system were done immediately and 2 hours after the injection (the CS required taking anterior, lateral and/or oblique images, while the fhSPECT system involved a scanning process over the region of interest from multiple different directions and angles). Then, we compared both techniques' detection results of both the SLN's location by imaging and the exact position mark through gammaprobe of the SLN projected in skin. **Results:** Patients mean age was 60.2 years old (range 41–85). Tumor location: left breast - 38%; right breast - 62%, with this quadrant localizations: UIQ - 36%, UOQ - 31%, LIQ - 24%, LOQ - 9%. Average tumor size: 18.46 mm. Tumor histology was: IDC (invasive ductal carcinoma): 80%, DCIS (ductal carcinoma in situ): 9%, Mucinous carcinoma: 5% and ILC (invasive lobular carcinoma): 5%. Imaging localization of the SLN between both techniques had a 95% concordance (CS did not reveal SLN image localization in 1 patient). Skin marking had a 77% concordance (even though fhSPECT shows a more precision in depth and direction, differences in 5 patients were due to discrepancy between the fhSPECT's optical image and the gammaprobe counting, probably due to operator dependent factors). **Conclusion:** The high image concordance demonstrates that the preoperative scan with the freehand

SPECT gammacamera is a valid tool for SLN localization, since it offers a good optical and 3D image. It is crucial to perform the scanning process in a meticulous and reproducible manner, since the appropriate training and the experience degree of the operator are the key factors in the generation of high quality reconstructed 3D images.

EP-0356

Impact of the implementation of radioguided ^{125}I seed localization technique on the surgical specimen volume of non-palpable breast lesions.

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Introduction/ Purpose: The improvement in the sensitivity of imaging techniques and the increase of the screening mammography programs have led to localize more non-palpable breast lesions which need to be localized accurately for their optimal excision. To evaluate the variability of the Surgical Specimen Volume (SSV) related to the Tumor Volume (TV) with the implementation of radioguided ^{125}I seed localization technique (RSL). **Subjects and method:** 184 patients with non-palpable breast lesions treated with RSL technique from 2014 to 2017 were considered for the study. The SSV, TV (by radiological image calculated sphere), the Optimal Resection Volume (ORV: one centimeter more than TV radio sphere) and the Resection Ratio (RR: SSV/ORV healthy parenchyma exceed) were calculated. Mean age was 56,7. **Results:** TV in 2014: $2,77\text{cm}^3(\pm 1,38)$; in 2015: $2,59\text{cm}^3(\pm 1,61)$; $2,47\text{cm}^3(\pm 1,10)$ in 2016 and $2,58\text{cm}^3(\pm 1,49)$ in 2017. ORV was $6,96\text{cm}^3(\pm 1,38)$ in 2014; $6,77\text{cm}^3(\pm 1,61)$ in 2015; $6,67\text{cm}^3(\pm 1,10)$ in 2016 and $6,77\text{cm}^3(\pm 1,49)$. SSV in 2014 was $42,27\text{cm}^3(\pm 28,66)$, while in 2015 del $38,74\text{cm}^3(\pm 22,21)$; $26,18\text{cm}^3(\pm 18,81)$ in 2016 and $34,90\text{cm}^3(\pm 29,98)$ in 2017. The estimated RR was 5,91 in 2014; 5,68 in 2015; 4,02 in 2016 and 5,31 in 2017. A decrease on the ratio is objectified through the years. RR was analyzed among the patients with marginal or failed seed localization, been the ratio in this case slightly higher 5,99. The rate of affected margins (if distance to tumor was considered $<1\text{mm}$) was the following: 7,3% in 2014; 5,3% in 2015, 17,1% in 2016 and 6,5% in 2017. **Conclusion:** Non-palpable lesions ought to be completely removed without increasing the resection of healthy tissue/parenchyma.

EP-0357

Sentinel Lymph Node Detection And Biopsy In Gynecological Tumors. Our Experience

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Objective: To evaluate the detection rate and false negative (FN) cases of ^{99m}Tc -Nanocolloidal albumin planar lymphoscintigraphy, SPECT/TC images and intraoperative detection of the sentinel lymph node (SLN) with the use of a gamma probe in endo-

metrial, cervical and vulvar carcinomas. **Methods:** We studied 39 patients with histological confirmation of vulva (7), cervical (12) and endometrial (20) cancer. Sentinel lymph node scintigraphy with ^{99m}Tc - Nanocolloidal albumin was performed to all patients previous to the surgery. For vulvar carcinoma, 111MBq of the tracer were administered intradermally around the tumor or scar, for cervical and endometrial cancer 148MBq of the tracer were injected in the four quadrants of the cervix. Planar images were acquired 30min post-injection as well as planar and SPECT/TC images 2-3 hours post injection. An exhaustive search was performed with a gamma probe during the surgery. A bilateral lymphadenectomy was performed in all patients. We considered FN those cases with a favorable SNL detection with negative histologic findings but metastasis in other lymph nodes in the lymphadenectomy. **Results:** In endometrial adenocarcinomas (20), 1.25 ± 1.16 SD SLN were detected in the lymphoscintigraphy. In the surgery, 1.85 ± 1.87 SLN were detected. The lymphoscintigraphy did not detect SLN in 7 cases, whereas in the surgery SLN was not found in 5 cases (detection rate 70%). In this group of patients one FN was obtained. Cervical cancer (12) showed 1.66 ± 1.15 SLN in the lymphoscintigraphy. In the surgery 1.91 ± 0.9 SLN were detected. 11 out of 12 patients had a successful SNL detection (91.67% detection rate). In this group FN was not found. Vulvar tumors (7) showed 2 ± 1.73 SLN in the lymphoscintigraphy. In surgery, 1.85 ± 1.46 SLN were detected. 4 patients had a successful SLN detection (71.43% detection rate). In this group one FN was obtained. Overall, 8 out of 39 patients presented nodal metastases (20.51%). Of these, 4 had positive SLN, 7 failed in the detection and 2 were FN. **Conclusion:** In our experience, selective SLN biopsy in gynecological tumors has a lower detection rate (70% -90%) than in other types of tumors, with a False Negative rate similar to other research groups. It is necessary to include a greater number of patients to qualify such technique. Taking into consideration that cervical tumors results are more promising than the others it could be approved, acquiring greater experience, as an adequate lymph node staging technique.

EP-0358

Sentinel Lymph Node Biopsy In Melanoma: Results Of Survival

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Aim: To analyze our experience and the results of sentinel lymph node biopsy (SLNB) in melanoma and to identify the predictive factors of positive SLNB, metastatic risk and survival time. **Materials and Methods:** It is an observational and retrospective study of patients with melanoma stage I-II, who underwent SLNB according to the NCCN criteria, between December 1999 and December 2017. We obtained demographic, histological data (Breslow thickness, mitotic index, lymphovascular invasion, regression and ulceration), migration and anatomopathological results of the sentinel lymph node (SN), metastatic risk and survival time. **Results:** 133 patients

were included (mean age at diagnosis: 51.7 ± 15.7 years, 56.2% of women and mean follow-up: 78.3 ± 50.1 months). The definitive study of the SN was positive in 24% patients. 19 patients died (14.3%) and 26 patients (19.7%) developed metastases. Related factors statistically significant, with a positive result of SN were: age (48.9 ± 15.3 vs 60.4 ± 13.5 years, $p < 0.001$), male sex (22/66 vs 10/70 cases, $p = 0.005$), Breslow (3.6 ± 2.2 vs 1.9 ± 1.5 mm, $p < 0.01$) and ulceration (13/25 vs 15/60 cases, $p = 0.016$). A positive result of SN was related to a higher percentage of metastases (50% vs 10% cases, $p < 0.0019$), shorter overall survival time (54.7 ± 38.1 vs 85.9 ± 51.3 months, $p < 0.001$) and disease-free interval (25.8 ± 29.9 vs 51.9 ± 50.6 months, $p < 0.001$). Survival analysis shows statistically significant differences in: age (62.0 ± 14.0 vs 50.1 ± 15.3 years, $p = 0.002$), Breslow thickness (3.3 ± 1.8 vs 2.2 ± 1.8 mm, $p = 0.009$), ulceration (9/13 vs 19/72 patients, $p = 0.002$), regression (2/2 vs 9/43 patients, $p = 0.011$), positive result of SN (10/19 vs 22/114 patients, $p < 0.002$) and development of metastases (13/19 vs 13/113 patients, $p < 0.001$), the latter being the main predictor of mortality in the multivariate analysis (OR: 9.4, $p < 0.001$). **Conclusions:** In our study, age at diagnosis, Breslow thickness, melanoma ulceration and positive SN are the main factors associated with the development of metastases and lead to a lower survival time.

EP-0359

Importance of ROLL technique in the location of lesions with difficult surgical access in oncology patients.

Preliminary results

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Purpose: To analyze the value of ROLL (Radioguided occult lesion localization) technique as a guide for the location and excision of lesions with suspected malignancy in patients with a neoplastic history. **Subjects and Methods:** We have retrospectively evaluated the surgeries performed using the ROLL technique in our service. Nine interventions have been carried out. The patients (6 women and 3 men), aged 16 to 48 years, had a history of papillary thyroid carcinoma (5), medullary thyroid carcinoma (1), infiltrating ductal breast carcinoma (1), ductal breast carcinoma and urothelial tumor (1), and right femoral fusocellular sarcoma (1). All of them presented, in their follow-up, small lesions (9-16 mm) with difficult surgical approach, suspicious of recurrence or metastasis. The tracer injection was intralesional guided by ultrasound 3-4 hours prior to surgery. The administered dose was of 0.2 mCi of ^{99m}Tc albumin macroaggregates (MAA- ^{99m}Tc) in a volume of 0.05 ml. The scintigraphy technique consisted of planar and SPECT/TC images. Surgical location was performed by means of a gamma detection probe (Europrobe 3.2 System model). The correct placing of the tracer on the lesions was confirmed, as well as the absence of skin contamination in the scintigraphic study. In one patient, methylene **dye was used as an aid in the surgery.** **Results:** In all cases, radiodirected removal of the lesions was achieved through minimally invasive surgeries.

No post-surgical complications were observed. The lesions were located in the surgical site in 7 (3 paratracheal, 3 laterocervical and 1 axillary) and in the path of tumor dissemination in 2 (right iliac and left supraclavicular). The histopathological result in 7/9 cases was lymph node metastasis, in 1 case of granumalotous scar tissue and 1 case of follicular hyperplasia. **Conclusions:** ROLL technique is a useful and relatively simple method that allows the definitive removal and diagnosis of lesions of difficult surgical access, with low morbidity.

EP-0360

Sentinel Lymph Node Biopsy in Patients with Breast Cancer: Detection and Rate of Recurrence in 5-7 Years, according to Method of Radiotracer Administration

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Introduction: The controversy between different ways of radiopharmaceutical administration in sentinel lymph node (SLN) biopsies in breast cancer still persists. We compare intratumoral and periareolar injections and analyze detection and the nodal and extranodal relapse with a minimal 5-year follow up. **Methods:** 269 women, age 25-86 years (55±11), mean tumor size 15.52±10.93 mm, 89 palpable tumor-179 no-palpable tumor. Histologic type, 203 (75.8%) invasive carcinoma and 65 (24.2%) other type, histologic grade I (26.3%), II (45%) and III (28.7%), immunohistochemical profile (IHC), 183 (72%) luminal, 53 (21%) HER2+ (luminal B-HER2, HER2 pure) and 16 (6.3%) triple-negative. We classify the patients in two groups according to the method of radiotracer administration, 174 (64.7%) intratumoral (IT), without periareolar re-injection, and 95(35.3%) periareolar (PA). After the administration of 2 mCi of ^{99m}Tc-nanocolloid, we performed planar scintigraphy (PS), surgical detection with gamma probe and intraoperative pathological analysis of the SLN. We evaluated the detection and percentage of lymph nodes and extranodal relapse. **Results:** SLN global detection 249/269 (92.6%), 164/174(94.25%) IT and 85/95(89.47%)PA (NS). There were no significant differences between the IT and PA injection according to age, tumor location, IHC, histologic type, tumor size or histologic grade. Global mean of lymph nodes detected with PS was 1.36 ± 0.82 versus removed 1.69 ± 1.11. When the administration was intratumoral, there was involvement of the SLN in 37% (57), versus 24.7% (21) in periareolar (NS). Migration to extra-axillary territories was 11% (18) when the administration was IT, compared to 7% (6) in PA administration (NS). Only 2 patients (0.8%) had lymph node relapse (2PA) and 11 extra-lymph node relapse (7 IT, 4 PA) (9.6%): 1 local relapse, 5 bone, 1 lung, 1 liver, 2 lung and liver, and 1 local, bone and liver. **Conclusions:** Both IT (deep) and PA (superficial) administration present high percentages of detection, each procedure being effective. We found a minimum number of nodal and extra-nodal relapses without significant relationship with the way of the radiopharmaceutical administration in our group of patients. The evaluation of a larger number of patients and a longer follow-up will be necessary.

EP-0361

Usefulness Of Sentinel Lymph Node Biopsy In Patients With Breast Cancer After Neoadjuvant Therapy With Positive Axilla

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Objectives: Demonstrate a detection and false negative (FN) rate similar to the obtained in patients with negative axilla to evaluate the possibility of avoiding lymph nodes dissection in patients who received neoadjuvant chemotherapy (NAC) with positive axilla based on fine needle aspiration biopsy (FNAB) or coarse-needle biopsies (CNB) who presented good therapeutic response. **Material & Methods:** Patient data were obtained during October 2015-November 2017, attended by the center's gynecology and nuclear medicine service, Observational, cross-sectional study with Inclusion Criteria: -Diagnosed of breast infiltrating carcinoma. - Clinically and / or ultrasonically suspected axillary lymph nodes, with positive axillary FNAB / BAG for metastatic involvement (cN1) - Receiving Primary Systemic Therapy with Neoadjuvant Chemotherapy - Having responded to the NAC in the axilla so that the clinical-radiological evaluation (Ultrasound - Magnetic Resonance) was negative afterwards, in which breast surgery, Sentinel lymph node biopsy and complete axillary lymph nodes dissection were performed. The age of the patients, number of sentinel lymph nodes removed, number of positive sentinel lymph nodes, and number of nodes excised in lymph node dissection and how many were positive and evaluated histologically with hematoxylin-eosin. Chi-square statistical analysis was performed between the data obtained by the sentinel lymph node biopsy and the pathology results between these and those of lymphadenectomy. **Results:** In 49 patients, an average age of 54 years was obtained, 93.3% ductal histological type. Detection rate of 89.7%, FN rate: 5.6%, 24 patients positive in sentinel lymph node biopsy and 20 negative in surgery, 21 had positive lymphadenectomy and 24 negative in it, 1.6 nodes obtained scintigraphically, 1.7 nodes obtained in surgery, no scintigraphic detection in 6 patients, of whom 4 had MT in LA and 2 negative in lymphadenectomy, correlation between the results obtained in the sentinel lymph node biopsy and the lymphadenectomy p = <0.001 (95%). Histological response up to 90% to chemotherapy. **Conclusions:** High detection rate, low false negative rate of sentinel lymph node biopsy and good correlation between the positive results of the same and the number of nodes with those of lymphadenectomy. In all cases where the sentinel lymph node was negative, good response to the NAC was noted.

EP-0362

Sentinel Lymph Node Biopsy In Genitourinary Tumors: Review Of Our Experience

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Aim: To analyze our experience in the application of sentinel lymph node biopsy (SLNB) in patients with genitourinary tu-

mors (penile cancer and vulva cancer). **Method:** Retrospective study from March 2016 to January 2018 that includes 11 patients (8 men and 3 women) with squamous-type genitourinary primary tumor (10/11 cases) and 1/11 vulvar epidermoid type, in bilateral early stage cT1-3 cN0; age range 54-91 years (median 67 years). Two cases with vulvar melanoma were ruled out due to its histology. All patients underwent an extension study (ultrasound and / or abdominal CT scan), including ganglionar fine-needle aspiration biopsy (FNAB) in case of radiological doubt, prior to the lymphoscintigraphy study with ⁹⁹Tc-nanocolloid, to locate the sentinel lymph node (SLN). In the case of positive SLN, a deferred lymphadenectomy was performed (unilateral or bilateral as appropriate). Lymph node visualization was analyzed in the scintigraphy, number of extracted nodes, need for lymphadenectomy and lymph node or visceral recurrence within a maximum interval of 22 months (median follow-up: 13 months). **Results:** The SLN was detected in 100% of the patients. The lymphoscintigraphy showed superficial inguinal drainage with more than one hypercaptant focus in all the patients, being the exeresis carried out in the operating room of those considered sentinels, with a maximum of 3 unilaterally lymph nodes, without significant residual activity. 10/11 patients were bilateral pN0 (90.9%) without recurrence or distant disease at present. One patient (pN3) with penile cancer underwent bilateral lymphadenectomy, receiving chemotherapy, although he developed stage IV pulmonary carcinoma, dying 18 months after SLNB. **Conclusions:** Despite the small number of patients studied, the SLNB has offered, to those patients with genitourinary tumors at stage cN0, lower morbidity and mortality, being useful for lymph node staging; presenting a median of 13 months as a current period free of disease in 90.9% of them.

EP-32

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> General oncology -> Therapy
response assessment

EP-0363

Deauville score evaluation of PET2 positive patients included in the H10 trial

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Introduction: The H10 Intergroup (LYSA/EORTC/FIL) trial has demonstrated the efficiency of a PET response-adapted treatment strategy in limited stage Hodgkin lymphoma: when interim PET (iPET) is positive after two cycles of ABVD, switching to BEACOPPesc + INRT (experimental arm) significantly improved the compared to ABVD+INRT (standard arm). However, in H10 iPET was scored according to International Harmonization Project criteria (IHP) with mediastinal blood pool activity or surrounding background as reference for PET positivity. These results were reanalysed using the Deauville scale (DS) and the liver reference for positivity (DS_l≥4). **Methods:** PET/CT from iPET positive patients (IHP criteria based) included by LYSA centers in the ABVD and BEACOPP arms of the H10 were scored using the DS. Progression free survival (PFS) of Deauville scale 4-5 (DS 4-5) and DS 1-3 patients were compared between standard and experimental arms with Kaplan-Meier curves, Cox model and log-rank test. **Results:** From the ABVD arm, 71/108 (67%) iPET positive scans were available for review in the data base and 79/111 (69%) from the BEACOPPesc arm. Baseline characteristics of these two groups did not differ significantly from the whole trial population. Only 41% (29/71) and 54% (43/79) of the patients classified iPET positive in the trial in the ABVD and BEACOPPesc arms were scored positive (DS 4 or DS 5) by Deauville scoring. These percentages did not differ statistically between the two arms. According to IHP criteria, the 5y-PFS was 73% in the ABVD group vs. 90% in the BEACOPPesc group (p=0.0021, HR=2.47 (CI 95% 1.15-5.28)), in accordance to the published results of the whole trial. According to Deauville criteria, for patients scored DS 4-5, the 5y-PFS was 50% in the ABVD arm vs 86% in the BEACOPPesc group (p=0.0023, HR=3.75 (CI 95% 1.47-9.52)). By contrast, for patients scored DS 1-3, in the ABVD arm (6/42 DS 1, 8/42 DS 2, 28/42 DS 3) patients the 5-y PFS was 88% and 94% in the BEACOPPesc arm (6/36 DS 1, 9/36 DS 2, 21/36 DS 3). **Conclusion:** Among the H10 PET2 positive patients, only half of them were classified DS 4-5. These patients scored DS 4-5 are more likely to benefit from the BEACOPP as compared to iPET DS 1-3. This further supports the effectiveness of iPET response adapted intensification in early stage HL and the use of Deauville criteria for iPET2 reporting.

EP-0364

Value of 18F-FDG PET/CT in the initial staging, interim therapeutic and prognostic evaluation of mucosa-associated lymphoid tissue lymphoma

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Objective: This study assessed the value of ^{18}F -fluorodeoxyglucose (FDG) PET/CT in the initial staging, interim therapeutic and prognostic evaluation of mucosa-associated lymphoid tissue (MALT) lymphoma. **Methods:** Thirty-six MALT lymphoma patients (20 males, 16 females; average age 61.7 years) confirmed by pathology from January 2008 to January 2018. ^{18}F -FDG PET/CT were performed before chemotherapy and radiotherapy for initial staging. 17 gastric MALT lymphoma patients and 19 extragastric MALT lymphoma patients were included. PET/CT was performed in 17 of the MALT lymphoma patients after 4 courses of chemotherapy. Patients were evaluated by observers using Deauville 5-PS to two groups: positive group (≥ 4) and negative group (< 4). The results of ^{18}F -FDG PET/CT, gender, age, B symptoms, Ann Arbor staging, international prognostic index (IPI), HP positive or HCV positive and Ki-67 score were correlated to progression-free survival (PFS) using Kaplan-Meier survival analysis. **Results:** 31 of 36 patients were detected FDG-positive lesions with sensitivity of 86.1%. The sensitivity of FDG-PET/CT for the detection in Ann Arbor stage I patients was 54.5%. In Ann Arbor stage II–IV patients, the results of ^{18}F -FDG PET/CT combined with bone marrow biopsy in accordance with the results of clinical staging. The accuracy of PET/CT in staging of gastric MALT lymphoma patients was 52.9%, which was significantly lower than that of extragastric MALT lymphoma patients (89.5%, $P=0.025$). After interim therapeutic evaluation, ^{18}F -FDG PET/CT imaging changed the therapeutic regimen of 7 patients. FDG-PET/CT findings were strongly correlated with PFS ($\chi^2=4.16$, $P=0.041$). The 2-year PFS estimates for FDG-negative vs. positive patients were 85.7% vs. 27.8%. PFS in patients with low expression of Ki-67 were significantly longer than those in patients with high Ki-67 expression ($\chi^2=14.91$, $P=0.037$). **Conclusion:** In Ann Arbor stage II–IV MALT patients, the results of ^{18}F -FDG PET/CT combined with bone marrow biopsy can improve the accuracy in staging. The accuracy of PET/CT in staging of extragastric MALT lymphoma was significantly higher than that of gastric MALT lymphoma patients. ^{18}F -FDG PET/CT and Ki-67 score can provide effective information on the prognostic evaluation for MALT lymphoma patients.

EP-0365

Lesion-based Comparison Between Ra-223 Uptake And The Change In Tc-99m HMDP Uptake After Ra-223 Therapy

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Introduction: Ra-223 dichloride is used for the treatment of bone metastasis in castration-resistant prostate cancer (CRPC). Dosimetry of Ra-223 is probably important to predict treatment effect because the tumoricidal effect of Ra-223 is likely to be dose related. Ra-223 imaging is challenging due to the properties of the radionuclide, although we reported the technique of Ra-223 SPECT acquisition in order to perform semi-quantitative analysis of Ra-223 uptake. The aim of this study was to evaluate whether Ra-223 uptake is correlated with the change in Tc-99m HMDP uptake after Ra-223 therapy on a per-lesion basis. **Subjects & Methods:** Six CRPC patients who underwent Ra-223

SPECT were retrospectively evaluated. The Ra-223 SPECT was performed 2 h after the first injection of Ra-223 dichloride using high-energy general-purpose collimators for 30 min. With a reference of CT images, lesion-to-background ratio (LBRa) was calculated for metastatic lesions showing increased Ra-223 SPECT uptake two times greater than uptake in the normal spine (i.e. Ra-positive lesions). Tc-99m HMDP SPECT/CT was performed 1 month before and 1 month after Ra-223 therapy. Using attenuation and scatter corrections, and resolution recovery, standardized uptake value (SUV) of HMDP uptake was measured for the Ra-positive lesions. Since SUV of 7 in bone SPECT/CT is reported to be an appropriate threshold to discriminate between benign and metastatic bone diseases, we placed a tumor volume of interest with a fixed threshold of SUV > 7 . Then, we measured metabolic bone volume (MBV) and lesional bone uptake (LBU) that is calculated as the product of mean SUV by MBV. Percent changes in MBV (%dMBV) and LBU (%dLBU) over Ra-223 therapy were calculated, and these metrics were compared with LBRa for each lesion. **Results:** There were 18 Ra-positive bone metastases with the median LBRa of 2.47 (range, 1.74 - 5.68) in the 6 CRPC patients. The median %dMBV and %dLBU were -44.9% (range, -3.9% - -87.2%) and -60.2% (range, -16.7% - -91.9%), respectively. There were significant inverse correlation between LBRa and %dLBU ($r = -0.55$, $p = 0.019$), whereas there were no significant difference between LBRa and %dMBV ($r = -0.35$, $p = 0.156$). **Conclusion:** Lesion-based Ra-223 uptake analysis appears to be useful for predicting the volumetric and metabolic changes in Tc-99m HMDP uptake after Ra-223 therapy.

EP-0366

Role of Interim and End of treatment PET/CT for Response Assessment and Prediction of Relapse in Post-transplant Lymphoproliferative Disorder

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Background: Post-transplant lymphoproliferative disorder (PTLD) is a rare iatrogenic complication after solid organ transplantation (SOT) associated with significant morbidity and mortality. Fluorine-18 fluorodeoxyglucose positron emission tomography (^{18}F FDG-PET) and in particular ^{18}F FDG-PET with computed tomography (CT) have an established and central role in diagnosis, staging and response evaluation of lymphoproliferative diseases. In PTLD however, only studies in small patient groups or case reports have been published and little is known about the performance of interim PET (iPET) and end of treatment (EOT) PET with regards to relapse prediction and outcome. The aim of this study is to evaluate the role of iPET and EOT PET to predict relapse and survival in PTLD patients. **Methods:** We performed a single-center retrospective study of 41 patients diagnosed with PTLD after SOT between 2008 and 2017. All patients received uniform treatment with reduction of immunosuppression and risk stratified sequential treatment according to the PTLD-1 trial. Interim PET and EOT PET studies were scored according to the Deauville criteria by two nuclear medicine physicians blinded to other results. Any non-physiological FDG-uptake with Deauville score greater than 3 was con-

sidered as PET-positive while Deauville 1, 2 or 3 corresponded to complete metabolic response as has been previously reported in other lymphoma studies. **Results:** Median follow-up was 42 months (range 1–108). iPET was available in 39/41 patients (2 patients showed progression on CT for which treatment escalation was performed), and EOT PET in 37/41 patients (3 patients died during treatment and 1 patient received only four cycles of Rituximab). Based on iPET, 13 out of 39 (33%) patients had a complete metabolic response, 14 (36%) had a partial metabolic response and 12 (31%) were progressive. EOT PET was negative in 31 (84%) and positive in 6 (16%) patients. All patients with negative iPET remained negative at EOT PET, while 17 patients with positive iPET had a complete remission after 8 cycles of therapy. The positive (PPV) and negative predictive value (NPV) for PTLT recurrence were 19 % and 85 % for iPET and 17 % and 87 % for EOT PET respectively. **Conclusion:** A negative EOT PET in PTLT patients after SOT identifies a subgroup with low risk of disease recurrence. Similarly, iPET has a high NPV but low PPV, and further research is needed to evaluate the prognostic or predictive role of iPET in PTLT patients.

EP-0367

Relationship between maximal standardized uptake value on FDG-PET and PD-L1 expression in clear cell renal cell carcinoma

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Kidney cancer, in particular clear cell renal cell carcinoma (CCRCC), is often lethal, and is characterized by insensitivity to chemotherapy and radiation therapy. Recent evidence suggests that CCRCC may be susceptible to treatment with immune checkpoint inhibitors that target the PD-1/PD-L1 pathway, but identifying patients that are likely to respond to such therapy remains a challenge. The purpose of the present study was to evaluate the utility of FDG-PET imaging to infer PD-L1 expression in CCRCC. **Methods:** PD-L1 expression was evaluated by immunohistochemistry (IHC) in tumor samples from a retrospective cohort of 74 patients with CCRCC who also underwent 18-F FDG-PET/CT imaging. PD-L1 IHC scores were compared with FDG SUVmax values, with CCRCC clinical characteristics, and with IHC scores for glucose metabolism-related enzymes, GLUT1, HK2, and TIGAR. The impact of PD-L1 expression on patient survival was evaluated by Kaplan-Meier survival analysis. **Results:** Higher PD-L1 expression significantly correlated with increased FDG SUVmax ($P < 0.01$), higher CT value ($P < 0.01$), poor tumor differentiation ($P < 0.01$), and presence of lymph node metastasis ($P < 0.01$). Increased PD-L1 IHC scores correlated with increased GLUT1 and TIGAR IHC expression scores ($P = 0.03$, $P < 0.01$, respectively). Survival analysis indicates that CCRCC patients with high tumor PD-L1 expression experienced significantly poorer 5-year survival than patients with low tumor PD-L1 expression (log-rank test P -value < 0.05). ROC analysis of optimal cutoffs for combined SUVmax and CT values to predict PD-L1 low, medium, and high expressing tumors was 0%, 11.1%, and 53.8%, respectively. **Conclusion:** Higher CCRCC PD-L1 expression correlates with increased FDG SUVmax, indicating elevated tumor glucose

metabolism; this is corroborated by positive correlation of PD-L1 expression with expression of GLUT1 and TIGAR. In conclusion, FDG SUVmax, especially in combination with CT values, can be used to predict PD-L1 expression in CCRCC tissue. This indicates that non-invasive imaging FDG-PET/CT techniques may assist in identifying CCRCC patients likely to respond to immune checkpoint inhibition, and could be useful to monitor tumor response to immunotherapy. **Key Words:** Clear Cell Renal Cell Carcinoma; FDG-PET; immune checkpoint inhibitor; PD-1; PD-L1

EP-0368

Evaluation of early response to chemotherapy in patients with non-small-cell lung cancer by comparison of PET-CT based EORTC and PERCIST criteria and comparison within both criterias using SUV normalized also for body weight

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Aim: 1)To compare (assess the concordance/discordance) PET based EORTC (European Organization for Research and Treatment of Cancer) criteria and PERCIST 1.0(Positron Emission Tomography Response Criteria In Solid Tumours) criteria for the early evaluation of response to chemotherapy in patients with Non-small cell lung carcinoma(NSCLC). 2)Comparison of both PET based criteria- EORTC and PERCIST to assess concordance/discordance within both criteria using SUV normalized also for body weight. **Material & Methods:** 32 biopsy proven patients of NSCLC who underwent ¹⁸F-FDG PET-CT scan at baseline and post 2-4 cycles of standard chemotherapy were included in this study. The chemotherapeutic responses were evaluated according to the EORTC and PERCIST 1.0 criteria. The patients with discordant results were followed up with further clinical/imaging (CT/MRI/PET-CT) results. For both EORTC and PERCIST, the calculations were repeated using SUV based on body weight instead of body surface area in EORTC and lean body mass in PERCIST. Concordance among these protocols was assessed using Cohen's κ coefficient. Progression-free survival (PFS) was calculated using the Kaplan-Meier test. **Results:** EORTC and PERCIST 1.0 classifications were discordant in 3/32 patients (9.4 %), resulting in better concordance ($\kappa=0.808$, $P = 0.00$). Three patients with discordant results had PMR(Partial metabolic response) on EORTC and SMD(Stable metabolic disease) on PERCIST1.0. On follow up of these patients with discordant results showed progressive disease after 7, 10 and 14 months on CT or PET-CT. No difference in response assessments between PERCIST (SUVpeak (bw)) & EORTC(SUVmax(bw)) and PERCIST(SULpeak) & EORTC(-SUVmax(bsa)). Good concordance between PERCIST_5 (five lesions) and PERCIST_1(one lesion) classifications with discordant results in 3 patients (9.4 %), resulting in better concordance ($\kappa=0.808$, $P = 0.00$). According to both the EORTC criteria and PERCIST 1.0, patients with a PMR and SMD had a significantly longer PFS than PMD ($P<0.0001$) for EORTC and ($P<0.0001$) for PERCIST 1.0. **Conclusion:** 1) Good concordance between PET based EORTC and PERCIST 1.0 criteria with only few cases with

discordant results which were not statistically significant. 2) For early response assessment, comparison of both PET based criteria- EORTC and PERCIST using SUV normalized also for body weight show similar results as standard criteria using SUV normalized for body surface area (bsa) in EORTC and lean body mass (lbm) in PERCIST. 3) The percent changes of FDG uptake on PERCIST from baseline to after chemotherapy had a high correlation whether a single hottest lesion or 5 hottest lesions anywhere in the body were measured.

EP-0369

¹⁸F-FDG-PET/CT for treatment response assessment in classical Hodgkin Lymphoma (cHL) under immunomodulatory PD-1 blocked (nivolumab) therapy

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Introduction: The intersection between immune surveillance and tumor has led to broad therapeutic advances that are now being studied in all cancer types. Reed-Sternberg cells in classical Hodgkin-lymphoma (cHL) overexpress PD-1 ligands. Therefore Nivolumab, PD-1 inhibiting IgG4 antibody, was recently approved by the US FDA for relapsed/refractory (RR) cHL. Will ¹⁸F-FDG-PET/CT maintain its excellent accuracy based on SUVmax changes in response assessment also under immunomodulatory therapy? **Methods:** Nine cHL patients (7 males, 2 females, mean age 34 year; range 19-75 year) were treated with Nivolumab in a compassionate program between February 2016 and December 2017. Nivolumab was administered intravenously 3mg/kg every two weeks with no-end of therapy, until disease progression or unacceptable toxicity occurred. All patients underwent ¹⁸F-FDG-PET/CT before first nivolumab administration ("baseline" PET0), at 2nd and 6th month into therapy (PET1 and PET2 respectively), and if nivolumab wasn't interrupted earlier, at 12th month (PET3). Maximum Standardized Uptake Value (SUVmax), Metabolic Tumor Volume (MTV) and Total Lesion Glycolysis (TLG) were recorded for all ¹⁸F-FDG-PET scans and separately evaluated for data analysis. Relatively to PET0, patients achieving at any time Deauville Criteria (DC) 1-3 or >50% reduction of SUVmax or MTV or TLG were classified as "PET responders". Hematologic clinical evaluation at 6th month into therapy and/or biopsy served as reference standard. **Results:** Six months into therapy, 7 of 9 patients (77.7%) had clinical hematologic remission but SUVmax values confirmed only 4/7 responders (2 complete, 2 partial response) showing 3 "pseudo-progression": SUVmax evaluation resulted in 100% sensitivity but low specificity and wasn't statistically significant (p=0.38). MTV and TLG values had more than 50% reduction between PET1 and PET2 in all clinical responders, showing 100% specificity and sensitivity, p=0.04. MTV at PET0 was also statistically significant for responders vs refractory (mean MTV 79.5 vs 453, respectively. p=0.04). After PET2 also patients with "pseudo-progression" continued nivolumab and then PET3 SUVmax confirmed clinical response. In contrast, clinical progression (2/9 patients) was confirmed by increasing

SUVmax, MTV and TLG values between PET1 and PET2. Overall 5 of 9 patients had treatment related "Non-specific" FDG uptake referred to inflammation (pulmonary, gastric and thyroid). **Conclusions:** ¹⁸F-FDG-PET/CT response assessment under immunomodulatory treatment is different from conventional chemotherapies, showing not only slower metabolic response but also pseudo-progression. FDG-PET may result more accurate considering MTV and TLG changes, in particularly between PET1 and PET2. More studies are warranted to decide the right timing for ¹⁸F-FDG-PET/CT for RR cHL under anti-PD1.

EP-0370

Does ¹⁸F-FDG PET-CT have a predictive role in locally advanced non-small-cell lung cancer (NSCLC) patients treated with a novel multimodal approach?

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Introduction: The standard care in patients with locally advanced non-small-cell lung cancer (LA-NSCLC) is definitive concurrent chemo-radiotherapy (CCRT), but prognosis remains poor. Multimodal approaches, including low-dose fractionated radiotherapy concurrent to induction-chemotherapy (IC-LDRT) and surgery, have been proposed to improve prognosis. Aim: to evaluate whether early metabolic response assessed by ¹⁸F-FDG PET-CT could predict clinical outcome in LA-NSCLC patients treated with multimodal approach: IC-LDRT, CCRT and surgery. **Methods:** 58 LA-NSCLC patients (44M, age=65±8.2years, stage IIIa-IIIb), all treated with IC-LDRT (2 cycles of chemotherapy, 40Gy twice daily) were retrospectively evaluated. ¹⁸F-FDG PET-CT was performed at baseline and after IC-LDRT (early PET-CT). Metabolic response was evaluated according to EORTC criteria; patients were classified as responders (complete/partial response) or non-responders (stable/progression disease). Kaplan-Meier and univariate analysis were used to assess progression-free survival (PFS) and its relationship with clinical factors. **Results:** Based on metabolic response and clinical evaluation after IC-LDRT, 19/58 patients underwent best supportive care (progression and/or poor conditions). The remaining 39 patients were treated with multimodal approach: 7 directly surgery, 13 conventional CCRT (total dose=50.4Gy), 19 CCRT plus surgery. In these 39 patients, the two-years loco-regional, distant and global PFS rates were 58%, 42%, 32%, respectively. The median loco-regional, distant and global PFS times were 33, 24, 17 months, respectively. Patients treated with surgery (n=26) had better distant and global PFS (p=0.03) than those treated with IC-LDRT and CCRT (n=13). At early PET-CT, 22/39 patients were metabolic responders, 17/39 non-responders. Early metabol-

ic responders had better loco-regional, distant and global PFS than non-responders ($p=0.008$, $p=0.02$, $p=0.03$, respectively). At univariate analysis, both lymph-nodal SUV at early PET-CT and early metabolic response were predictive factors for loco-regional PFS ($p=0.006$, $p=0.04$, respectively); age was predictive for distant PFS ($p=0.01$). **Conclusion:** Our data suggest that metabolic response, evaluated after IC-LDRT, provides useful information in almost 50% of LA-NSCLC patients allowing to modify the subsequent treatment: some of them directly to surgery, others to palliative therapies. Moreover, early metabolic response allows to identify patients with poor prognosis for whom tailored and intensified treatments are needed. Early PET parameters (metabolic response and activity of lymph-nodes) are the only predictive factors for loco-regional PFS; in particular prognosis seems to depend on residual activity of lymph-nodes rather than of primary cancer. Finally, the multimodal approach (including IC-LDRT and surgery) could be a promising treatment, especially because surgery seems to influence the distant metastases development; further investigation is warranted to confirm these results.

EP-0371

Prediction of response to Immune Checkpoint Inhibitor Therapy by FDG PET

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The purpose of this study was to determine the clinical usefulness of PET-CT in evaluating the response to Immune Checkpoint Inhibitor Therapy (ICT) in patients with metastatic melanoma or lung cancer. We compared the results with the standard evaluation made with CT-scan. **Methods:** We prospectively collected data from 11 patients with metastases (5 with melanoma and 6 with lung cancer). All patients underwent 18F-FDG-PET imaging at baseline and 4 months after ICT treatment. FDG-PET response was assessed by three criteria: Total Lesion Glycolysis (TLG), EORTC criteria and PET Response Criteria in Solid Tumors (PERCIST). We compared these results with those obtained by diagnostic CT imaging with Response Evaluation Criteria in Solid Tumors (RECIST 1.1). We used the SUL peak (Standard Uptake Lean Body Mass) to assess the study by the PERCIST criteria. Then, we measured the SUVmax to assess the response following the EORTC criteria. TLG was calculated as: $TLG = \text{mean SUV} \times \text{MTV} (\text{cm}^3)$. ROC analysis and Spearman's test were calculated to define the response to therapy: SUL peak, SUVmax and TLG were compared to percentage change in the sum of the longitudinal diameter (SLD) in target lesion from a CT scans. **Results:** TLG showed the strongest correlation to SLD ($R = 0.936$, $p = 0.003$), compared to SUV max ($R = 0.827$, $p = 0.009$) and SUL peak ($R = 0.818$, $p = 0.010$). Two-tailed p -values < 0.05 were considered statistically significant. To predict progression on CT-scans, ROC analysis showed the best results for TLG in comparison with the other criteria: area under the curve (AUCs) resulted between 0.78 and 1.0. TLG had

the highest value of 1.0 (95% - confidence interval (CI): 0.71-1). **Conclusion:** The present study demonstrates that to evaluate ICT response in patients with metastatic cancer, criteria based on TLG allow to obtain better results than those obtained by PERCIST and EORTC criteria.

EP-0372

FDG avid adverse reactions to immune therapy are strong predictors of survival in patients with metastasized malignant melanoma

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Introduction: Immune therapy has revolutionized treatment options in patients with malignant melanoma. Combination of two and now three different checkpoint inhibitors leads to a plethora of adverse events (AE) - eg therapy induced thyroiditis, hypophysitis, hepatitis. This being the main cause for treatment discontinuation, recent data nevertheless hinted at a better survival of patients with therapy induced AE. The aim of this retrospective analysis was to look into disease specific survival (DSS) in patients with immune therapy that developed AE and in particular to compare with visibility of these AE in serial FDG-PET/CT scans. **Methods:** 103 patients with metastasized malignant melanoma, that were treated with checkpoint inhibitors at our interdisciplinary center and received serial FDG-PET/CT scanning for therapy monitoring were included in this study (344 scans in total, 2-10 scans per patient, av. 2,9 per pt). All clinical recordings and questionnaires for serious AE (grade 3-4 CTCAE) were consulted, all FDG-PET/CT scans were independently evaluated for FDG-avid therapy related events. **Results:** A total of 122 serious AE were documented in 64 pts (62% of all pts, 1-5 reactions per pt), 38 pts had FDG avid lesions through inflammatory uptake that was unequivocally classified as therapy associated. DSS was only slightly longer in all patients with AE (37,1 vs 33,9 months) yet mortality between those patients without AE and with FDG-non avid AE was almost the same (53,9% vs 53,8%) and significantly lower in pts with FDG avid AE (28,9%). **Conclusion:** In combinational immune therapy more than 60% of the pts develop AE. FDG avidity of these therapy induced reactions predict survival better than the general assessment of grade 3-4 events according to CTCAE.

EP-0373

Response Evaluation and Prognosis Prediction Using FDG PET in Lymphoma with Low FDG-Avidity

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Purpose: FDG PET is established as a standard imaging modality for initial staging and treatment response evaluation in FDG-avid lymphoma. However, the role of PET in lymphoma with low FDG-avidity is still limited and hasn't been thoroughly evaluated yet. The purpose of this study was to investigate the efficacies of PET indexes in low FDG-avid lymphomas in response evaluation

and prediction of prognosis. **Subjects and Methods:** Total 42 patients with low FDG-avid lymphoma were retrospectively enrolled. Low FDG-avidity was defined as SUVmax with 5 or under, which is based on mean FDG uptake of liver with 2 standard deviations. FDG PET/CT scans were performed at baseline and end-of-treatment (EOT). Response at the EOT was determined by Lugano classification and progression-free survival (PFS) was determined by follow-up data. Maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) with margin threshold of 50, 70% of the SUVmax were measured in the single hottest lesion (Target A) or 5 hottest lesions (Target B), and their efficacies regarding response evaluation and prediction of PFS was evaluated. **Results:** On EOT PET, SUVmax of Target B was the most significant value to determine treatment response ($P = 0.0005$). MTV of Target B was also significant ($P = 0.0294$ and 0.0074 for MTV_{50%} and MTV_{70%}). SUVmax of difference (%Δ) from baseline PET was significant, while TLG and MTV per se were not. In predicting PFS, all tested parameters of EOT were significant ($P < 0.05$ for all). SUVmax of Target A and B on EOT PET were the most significant indexes for predicting final response ($P = 0.0020$ and < 0.0001 , respectively). **Conclusion:** FDG PET can be used as an effective tool even in lymphoma with low FDG-avidity. SUVmax, TLG and MTV from multiple lesions have shown to be effective quantitative indexes for evaluating treatment response and predicting PFS.

EP-0374

Comparisons of PERCIST results among 4 kinds of methods in diagnosing therapeutic effect of NSCLC- Gradient Segmentation method, Adaptive threshold method, Syngo.via and GT-PET-

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Purpose: PERCIST is important criteria for determining the therapeutic effect of solid cancer using FDG-PET. Although the criterion is simple, the result might be affected by the tumor segmentation methods because of various soft-wares are available. This study was done to evaluate the difference of four kinds of methods in diagnosing therapeutic effect in NSCLC by PERCIST criteria. **Methods:** We analyzed 43 FDG-PETCT images of non-small cell cancer (NSCLC) respectively using 4 kinds of soft-wares. FDG-PET/CT examinations were done in all patients in both before and after chemo-therapy. The tumor segmentation was done using the threshold method by referencing liver count when we use Syngo.via or GI-PET. In addition, both the Gradient Segmentation method and the Adaptive threshold method were done using MIM Maestro and IntelliSpace Portal. We used PERCIST criteria for diagnosing the therapeutic effects by referencing the change of SUL peak in each case. We evaluated the concordant rate of diagnosing result, namely Complete metabolic response (CMR), Partial metabolic response (PMR), Stable metabolic disease (SMD) and Progressive metabolic disease (PMD), among the four kinds of methods. **Results:** Among 43 cases, the cases diagnosed as PMR were 20 by Syngo via, 23

by Gradient segmentation, 19 by Adaptive threshold method, 16 by GT-PET in numbers respectively. Similarly, the numbers of cases diagnosed as SMD were 16, 14, 16, 17, those diagnosed as PMD were 7, 6, 7, 6 and those diagnosed as CMR were 0,0,1,4 respectively. By PERCIST criteria, 21 cases were categorized as PMR by more than 2 methods. 15 cases were SMD, 6 cases were PMD and only one case was CMR. Overall concordant rate of 4 methods was 31 of 43 cases (69.8%). In PMR, the concordant rate was 13/21 cases (61.9%). Similarly, the concordant rate was 86.7% (13/15) in SMD, 66.7% (4/6) in PMD and 0% (0/1) in CMR. **Conclusion:** In diagnosing therapeutic effect of NSCLC by PERCIST criteria using various methods, the different results were noted in higher incidence and the discordance rate was about 30%. Particularly, the discordance was remarkable in PMR. Combined analysis using more than 2 different methods will be required in diagnosing the therapeutic effect in NSCLC.

EP-0375

Intra-patient SUL repeatability of background on 18F-FDG PET/CT

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Purpose: The standardized uptake value normalized to lean body mass (SUL) of background is often used as reference to assess tumor treatment response on 18F-FDG PET/CT. Our objective was to find the preferred background through assessing the repeatability of different background SUL. **Methods:** Patients who have had two scans within one week were selected. Background SULs from aortic blood pool (ABP), liver and muscle were recorded. Intraclass correlation coefficients (ICCs) and Bland-Altman plots were used to evaluate the degree of repeatability between two scans. Then the intra-patient difference in SULs and factors which included blood glucose level (BGL), tracer uptake period and dose were calculated as relative changes between the two scans. Finally, a linear regression model was used for analyzing all of the relative changes to identify which factor had correlation with SULs variability. **Results:** Fourteen non-diabetes patients were included. In the case of SULmax, the ICC for ABP, liver and muscle were 0.73, 0.36 and 0.39, respectively. Similar results were 0.69, 0.40 and 0.76 for SULmean in ABP, liver and muscle. From the Bland-Altman plots, we can obtain the same result as the repeatability from ICC. A linear regression analysis indicated there were strong positive correlations between differences of L-SULmax, L-SULmean and M-SULmean and that of BGL ($b=0.631$, 0.731 and 0.668 respectively, $p<0.05$ altogether). There were no correlations between differences of ABP-SULmax, ABP-SULmean and M-SULmax and that of BGL, and between differences of all background SULs and that of tracer dose and weight ($p>0.05$ altogether). Only M-SULmean difference had positive correlation with that of 18F-FDG uptake period ($b=0.483$, $p<0.05$) after linear regression analysis. The effect of BGL was more significant on L-SULmean than that on M-SULmean ($b=0.731$ and 0.668 respectively). For M-SULmean, the effect of BGL was more significant than that of 18F-FDG uptake period ($b=0.668$ and 0.483 respectively).

Conclusion: L-SULs are less consistent than those of ABP-SULs and M-SULs. Activity within ABP should be the preferred background for sequential patient evaluation.

EP-0376

Are ^{18}F -FCH PET/CT semiquantitative parameters reliable for predicting ^{223}Ra -Dichloride therapy response in metastatic castration resistant prostate cancer patients?

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Aim: To date there is not consensus about the most reliable diagnostic method in treatment response assessment in patients with metastatic castration-resistant prostate cancer (mCRPC) underwent ^{223}Ra -Dichloride Therapy. $^{99\text{mTc}}$ -diphosphonate whole-body bone scintigraphy and whole-body CT scan are generally used to evaluate treatment efficacy. However, it has been postulated that fluorine-18 fluorocholine (^{18}F -FCH) PET/CT may be also a useful tool in the response evaluation. The purpose of our study was to investigate whether ^{18}F -FCH PET/CT semiquantitative parameters are reliable to monitor response to ^{223}Ra -Dichloride therapy in mCRPC patients. **Materials & Methods:** In a period of 21 months, 24 consecutive patients (mean age 71.3 years, range 57–82) with mCRPC referred to our Nuclear Medicine Department and enrolled to underwent ^{223}Ra -Dichloride Therapy. 10/24 patients, who met the following selection criteria, were used for the analysis: 1) matched the approved inclusion criteria for the treatment; 2) completed all six scheduled ^{223}Ra -Dichloride doses (55 kBq/kg, 4 weeks intervals); 3) performed ^{18}F -FCH PET/CT both at baseline and 2 months after the end of treatment. Baseline and post-therapy ^{18}F -FCH PET/CT were performed with the same device in our Department. A total of 30 lesions (the 3 most metabolically active metastases for each patient at baseline and post-therapy ^{18}F -FCH PET/CT) were monitored and used for the semiquantitative analysis. We assessed the following semiquantitative parameters: maximum Standard Uptake Value (SUVmax), mean Standard Uptake Value (SUVmean), minimum Standard Uptake Value (SUVmin), Metabolically Active Tumor Volume (MATV) and Total Lesion Activity (TLA). Student's T-Test was used to evaluate whether a statistically significant difference existed between baseline and post-therapy ^{18}F -FCH PET/CT semiquantitative parameters. $P > 0.05$ was considered statistical significant. **Results:** In baseline and post-therapy semiquantitative evaluation, mean SUVmax changed from 7.10 to 5.7; mean SUVmean from 4.25 to 3.22; mean SUVmin from 3.19 to 2.38; mean MATV from 19.66 to 26.98; mean TLA from 76170.06 to 79014.27. Student's T-Test showed a statistically significant difference for SUVmax ($t = 2.042$; $p = 0.05$), SUVmean ($t = 2.164$; $p = 0.04$) and SUVmin ($t = 2.749$; $p = 0.01$). No statistically significant difference was found for MATV and TLA. **Conclusion:** Our experience demonstrates that ^{18}F -FCH PET/CT, thanks to the semiquantitative evaluation, have an important role in the assessment of ^{223}Ra -Dichloride treatment response. In particular among the PET/CT parameters considered in our study, the most significant ones were SUVmax, SUVmean and SUVmin. A greater number of patients

would be necessary to confirm these preliminary data and to evaluate the prognostic significance of these semiquantitative parameters.

EP-0377

Role of FDG PET in Posttreatment Surveillance of Melanoma: Census Survey in A Tertiary Cancer Center

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Purpose: In malignant melanoma, recurrence is often observed in distant areas from the primary site. While FDG PET is a sensitive imaging for detecting malignant lesions, the role of FDG PET in posttreatment surveillance period has not been investigated sufficiently. The aim of this study was to evaluate the value of PET during posttreatment surveillance in melanoma. **Methods:** A total of 76 melanoma patients who underwent FDG PET during surveillance period after completion of the first treatment were retrospectively enrolled. PET scans were grouped according to the purpose and clinical situations; routine surveillance (without symptom or sign) or evaluating clinical suspicion (symptom or image finding suggesting recurrence). Final diagnosis of recurrence was determined by complete clinical evaluation or long-term follow-up. In each situation, the diagnostic role of FDG PET was assessed. **Results:** A total of 143 scans of 76 patients were analyzed; 51 (36%) for clinical suspicion and 92 (64%) for routine surveillance. In clinical suspicion group, sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of PET were 78%, 100%, 53% and 100%, respectively. Sensitivity was higher than that of any other single imaging modality, and PET correctly diagnosed non-recurrence in 10 cases (20%). In routine surveillance group, 16 cases (17%) presented recurrence, all of which was correctly diagnosed on PET. NPV and PPV were 100% and 76%, respectively. In subgroup analysis, sensitivity and NPV were higher in low-risk group (stage I-IIA) than in high-risk group (stage IIB-IV), while specificity and PPV were higher in high-risk group. Although in asymptomatic low-risk group, PET correctly diagnosed recurrence on 10 cases with PPV of 71%. **Conclusion:** In conclusion, FDG PET is an effective diagnostic tool in posttreatment surveillance of melanoma in case of suspicious recurrence by clinical symptoms, signs, and/or other image findings. Even in cases without clinical suspicion, melanoma recurs in a considerable proportion of patients, which can be sensitively diagnosed on PET. Thus, cost-effectiveness of surveillance PET needs to be evaluated, particularly in high-risk patients.

EP-0378

Usefulness of ^{18}F -FDG PET-CT (FDG-PET) in advanced malignant melanoma (MM) submitted to pembrolizumab therapy (Pmab) - a retrospective evaluation

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Purpose: To analyse the usefulness of FDG-PET in the evaluation of response to Pmab in MM. **Subjects/Methods:** From

the 584 patients (pts) with MM submitted to FDG-PET in our department (Jan14-April18), 45 underwent Pmab. Of these, we retrospectively analyzed 21 who performed at least one FDG-PET pre- and post-Pmab. Mean age at the time of first Pmab administration was 65 years (44–87), 14 females, 7 males. The mean number of Pmab cycles/pt was 10 (1–27). Ten pts discontinued Pmab: 5 temporarily (3 for side effect control and 2 for radiotherapy), 5 permanently, due to disease progression. Five pts died. After first Pmab administration, 1.3 FDG-PET/pt were performed (1–3). FDG-PET was performed 78,6 days (mean) pre-Pmab and repeated 109,6 days (mean) after first Pmab administration. FDG-PET response criteria: - favorable response: disease stability: number/size/metabolic activity of lesions with overlapping characteristics; partial response: partial decrease in the number and/or size and/or metabolic activity of lesions (no increase in any of these parameters should be observed); complete response: disappearance of all lesions. - progression: increased number and/or size and/or metabolic activity of lesions, not related to Pmab. - uncertain response: suspected pseudo-progression: increased metabolic activity of known lesions and/or appearance of small lesions related to Pmab; mixed changes: changes in the number and/or size and/or metabolic activity of the lesions that do not fit into the other categories mentioned above. We also evaluated possible side effects of Pmab. **Results:** In the first evaluation, 5 favorable responses (3 partial responses, 1 stabilization, 1 complete response), 10 progressions and 6 uncertain responses (3 suspected pseudo-progression, 3 mixed changes) were found. Of the 3 studies classified as pseudo-progressions, one pt was re-evaluated by FDG-PET, confirming disease progression; one pt had clinical progression of disease; the remainder is waiting for re-evaluation. Of the 3 studies with mixed changes, one was re-evaluated twice, showing partial response followed by complete response; one patient died; and the remainder will be re-evaluated. FDG-PET suggested Pmab side effects in 3 patients (gastritis, thyroiditis and hypophysitis), not confirmed by clinical, laboratory and imaging evaluations. **Conclusion:** Despite all the disadvantages of a retrospective study in a small number of patients, FDG-PET correctly identified disease progression under Pmab. Caution should be taken in patients with FDG-PET pattern of pseudo-progression, since 2/3 of them had disease progression. Pmab was successful in disease control in 24% of patients, with 9,5% (2/21) showing complete response during FDG-PET follow-up.

EP-0379

A Systematic Review On Response Evaluation With Positron Emission Tomography / Computed Tomography
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Introduction: Response evaluation with PET/CT has potential in personalizing cancer therapy and evaluating treatment response. PET/CT is a powerful assessor due to its ability to differentiate between anatomical and physiological response, but designing clinical studies is challenging; there is no consensus

on which response criteria to follow, which time points to choose for scans, and how to establish rules for differentiating between responders and non-responders. **Aim:** To create an overview of study designs used for response evaluation with PET/CT and basic methodological characteristics. **Materials and Methods:** PubMed/MEDLINE and Web of Science were systematically searched for original articles on response evaluation in cancer, published in 2015 and employing at least one baseline and one post-baseline PET/CT scan. **Results:** We could identify 124 studies, 61% being prospective and the remaining 39% retrospective. Fifty-two percent were prognostic, 28% accuracy studies, and 11% a mix of these. Further 8% were descriptive response-curve studies and 1% a mix of a prognostic and a response-curve study. No RCTs could be found. Most studies used one fixed time point for imaging and evaluated one pre-defined rule for response evaluation. The median sample size was 39 (range: 5–354). Seventeen medical areas were represented, the largest group being lymphomas (N=20, 16%); PET time points varied hugely in this group. **Conclusion:** From a methodological point of view, we expected to see descriptive response-curve, accuracy, and prognostic studies as well as RCTs of which there were none. Overwhelming 90% of the studies were either accuracy and/or prognostic studies. Overall, comparative elements like inclusion of alternative tracers or modalities, several follow-up time points, variation in parameters (SUVmax, SUVmean, SUVpeak, SUL, MTV) and summary measures (absolute or relative) were less frequent than desirable. There was a noticeable gap between the kind of studies currently used for response evaluation and the kind we would suggest to ensure establishment of efficient response evaluation schemes based on PET/CT.

EP-0380

Response evaluation with ¹⁸F-FDG PET/CT in metastatic breast cancer patients treated with Palbociclib: first experience in a clinical setting

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Introduction: CDK4/6 inhibitor (Palbociclib), an anti-proliferative agent, has been recently approved in metastatic breast cancer (BC) patients to control the disease. ¹⁸F-FDG PET/CT is widely used to evaluate tumor response to treatments. To our knowledge, no clinical data are available on the use of ¹⁸F-FDG PET/CT to evaluate response to Palbociclib in BC patients. **Aim of study:** to evaluate the potential role of ¹⁸F-FDG PET/CT in this clinical setting. **Methods:** Twelve metastatic BC patients (mean age 61.5±10.5years; 5/12 with bone lesions, 4/12 with visceral lesions, 3/12 with bone and visceral lesions) treated with Palbociclib (mean cycles=4.7) plus aromatase inhibitor/estrogen

blockers were retrospectively evaluated. All patients underwent two ^{18}F -FDG PET/CT: baseline and post-therapy (150±37days after starting treatment). ^{18}F -FDG PET/CT response according to EORTC criteria (metabolic evaluation) was compared with standard evaluation based on clinical, laboratory and morphological imaging data. **Results:** Standard evaluation classified 7/12 patients as with stable disease, 1/12 with partial response, 3/12 (25%) with progression disease (no clinical benefit), 1/12 as undetermined (stable at clinical-laboratory tests but morphologically not evaluable because of osteoblastic bone metastases). Metabolic evaluation classified 2/12 patients as with complete response, 3/12 with partial response, 1/12 with stable disease, 6/12 (50%) with progression disease. Adding the metabolic evaluation to the standard one, 5/12 patients were classified as with stable disease, 1/12 with partial response, 5/12 (42%) with progression disease, 1/12 as undetermined (stable at standard evaluation but with metabolic progression because of the appearance of an active abdominal lymph node; progression disease was confirmed at follow-up). Overall evaluation (standard plus ^{18}F -FDG PET) changed the response classification in 3 patients when compared to standard evaluation alone (reclassifying 2 patients in progression and 1 undetermined) and increased the number of patients with no clinical benefit by over 40%. **Conclusion:** These preliminary data, although if in a small sample of BC patients treated with Palbociclib, suggest that: 1) adding ^{18}F -FDG PET/CT at standard response evaluation allows to intercept a greater amount of patients with no clinical benefit because of progression disease. This finding is supported by the well-known concept that metabolic changes occur early during anticancer therapies, often preceding clinical-morphologic changes; 2) ^{18}F -FDG PET/CT could be clinically useful in patient's management both to discontinue Palbociclib in progression cases and to select patients for whom a shorter follow-up is recommended. Further data in larger populations are needed to assess the proper role of ^{18}F -FDG PET/CT for evaluating response to Palbociclib.

EP-0381

The impact of PET/CT in detection and management of patients with synchronous and metachronous tumors

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Aim: Recent data suggest that the incidence of 2nd primary synchronous or metachronous tumor is increasing and reported as high as 10%. Meta analyses show the frequency of second tumor (SPT) as 3–5%, a third tumor (TT) as 0.5%, and a fourth tumor (QT) as 0.3%. Synchronous (within 2–6 months of diagnosis of 1st primary tumor) and metachronous (more than 6 months after 1st primary) malignant tumors are an increasingly frequent phenomenon in clinical oncology practice and can change the management and the prognosis of the oncologic patients. The aim of the study is to evaluate the role of PET/CT in detecting second primary and subsequent tumors and also to demon-

strate the influence on the treatment management in patients with histologically proven synchronous or metachronous tumors. **Methods:** Thirty patients with clinically proven at least one malignancy were evaluated and followed up for two-year period. All patients were scanned on GE Discovery PET/CT 16 slices scanner from the top of the head to mid-thigh. Study was performed one hour after injection, using the weight adjusted activity, hydration of patients with diuretic stimulation and oral/i.v contrast intake. **Results:** Seventeen out of 30 patients were female. The youngest patient was 38 years while the highest age seen was 77 years. Three of the patients have third primary tumors. Metachronous tumors were 2,75-fold higher than synchronous ones. Unsuspected synchronous and metachronous tumors were detected in 15 patients (Group 1). As second malignancies we detect five gastrointestinal (5p,33%), four urogenital cancers (4p, 27%), four pulmonary carcinomas (4p, 27%), one breast cancer (1p) and one head and neck squamous cell carcinoma (1p). In those 15 patients the management was changed and they received surgery, radiotherapy, chemotherapy, and hormonal therapy alone or as multi-modality treatment at least for the second tumors. The second group include patients with proof of malignancy by other methods. Nine patients from Group 2 had complete response after therapy for both tumors and don't need further treatment (8p, 53%). Two patients with metachronous urogenital cancers had stable disease (2p,13%). Four of patient with urogenital and gastrointestinal had progression at the time of examination (4p,27%) and in two advanced diseases were detected. One patient needs further examination (1p). **Conclusions:** FDG PET/CT is a valuable tool for detection of synchronous and metachronous tumors and for monitoring response to therapy. Integrated PET/CT can significantly modify the assessment about the tumor's dissemination and often change patient management substantially.

EP-0382

The role of ^{18}F -FDG PET/CT in the management of left atrial angiosarcoma: a case report

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Introduction: Cardiac angiosarcoma is the most common cardiac malignant tumor with an uncertain prognosis -median survival is reported to be 6 months from the time of diagnosis is made. The diagnosis is relatively late due to a nonspecific symptomatic palette, the clinical manifestations being determined by the increase in size of the tumor formation and by its localization. **Case report:** We herein report a 21-year-old patient case with no pathological history, who came in a medical service for hemoptysis and sudden chest pain. Following the investigations, a tumor mass with left atrial localization detected (80% of cardiac angiosarcomas arise in the right atrium), complicated with bilateral pulmonary embolism that resulted in pulmonary infarction. The patient initiated anticoagulant therapy with Enoxaparin and a cava vein filter was placed. Histopathological analysis confirms the diagnosis of angiosarcoma with high degree of expression of the MDM-2 gene. Surgical treatment is

excluded due to tumor localization, immediate complications and patient status. It was decided to perform ^{18}F -FDG PET/CT for staging and basal metabolic assessment and chemotherapy was initiated with fosfamide and farmorubicin; after the first 4 cycles, a follow-up PET/CT examination was performed that showed increased uptake at the tumor site and no metastases. Considering an unfavorable response, the chemotherapy was changed with line II - docetaxel and gemcitabine 2 cycles with no response. It was the modified to line III of chemotherapy with trabectedin. Following these cycles, the follow-up PET/CT scan showed progressive disease with left suprarenal metastasis, cecal and right colon lesions with high FDG uptake. It was decided to change once again the treatment with pazopanib 11 cycles because of progressive disease, the patient being currently under this therapy. The last PET/CT scan revealed clear remission of the metastases and of the left atrial tumor uptake. **Conclusion:** The role of ^{18}F -FDG PET/CT in the follow-up of a very aggressive disease like the cardiac angiosarcoma was crucial in adapting and tailoring the most suitable treatment strategy.

EP-0383

Diagnostic value of 18F FDG PET/CT in patients with history of differentiated thyroid carcinoma and Thyroglobulin Elevation but Negative Iodine Scintigraphy Syndrome, with thyroglobulin values bellow 10ng/ml

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Objectives: Determine the diagnostic value of 18F FDG PET / CT in patient with stimulated thyroglobulin (Tg) below 10 ng/dl and a history of Differentiated Thyroid Carcinoma (DTC) and Thyroglobulin Elevation but Negative Iodine Scintigraphy Syndrome (TENIS syndrome) Determine the cutoff value of stimulated Tg at which 18F FDG PET / CT has acceptable diagnostic performance for surveillance in patients with stimulated thyroglobulin below 10 ng/dl. **Materials and Methods:** This is a retrospective study from February 2012 to December 2016. A total of 118 18F FDG PET / CT scans from patients with DTC / TENIS syndrome (detectable Tg below 10ng / ml) were reviewed to determine the existence of disease recurrence and its correlation with surgical pathology results after PET. Exclusion criteria: a) patients with antiTgAc, b) patients without pathology specimens for verification, c) Absence of Tg values. A total of 42 patients were analyzed: 35 in the stimulated protocol with rhTSH and 6 on the unstimulated cohort (one of which was excluded due to unavailable TSH values). The Tg cutoff point was calculated based on a descriptive analysis and ROC curves, considering the values below 10ng/ml with higher Youden Index. **Results:** The total number of patients with rhTSH and TSH above 30µUI / mL was 35. Men: 17 (48.6%), Women: 18 (51.4%). Specimens histology: Papillary: 32 (91.4%), Follicular: 3 (8.6%), Undifferentiated: 0. Positive pathology for carcinoma = 22, Negative = 13. The cutoff Tg point below 10ng/ml with the best diagnostic yield was 7.46ng/ml, with a sensitivity of 63.64% and a specificity of 53.85%. PPV: 70%, NPV: 46.67%. Validity index: 60%. In those patients without rhTSH stimulation, the results were inconclusive given the small sample (6 patients) and the wide dispersion of the Tg values ranging between 1.20

and 482 ng / mL. **Conclusions:** 18F FDG PET/CT has a lower diagnostic yield (approximately 20%) in patients with suspected TENIS syndrome with Tg below 10ng/ml, however, if Tg values are equal or higher than 7.46ng/ml after TSHrh stimulation, 18F FDG PET/CT preserves acceptable diagnostic performance for the detection recurrent of disease.

EP-0384

Can we replace F-18 FDG PET/CT with whole-body diffusion-weighted MRI as a high quality cancer screening tool?

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Purpose/Introduction: F18-FDG PET/CT(PET/CT) cancer screening is noninvasive sophisticated method and we believe that it is superior to conventional cancer screenings because of its high detection rate, low physical burden and efficacy. But there are points of controversy about radiation exposure and poor cost-effectiveness. In our PET center, to increase accuracy rate in cancer screening, we use both PET/CT and whole-body diffusion-weighted MRI(WB-DWI). The aim of this study is to evaluate if we can replace PET/CT with WB-DWI as a high quality cancer screening tool. **Subjects & Methods:** Between February 2012 and July 2017, PET/CT and WB-DWI were performed for cancer screening in 1785 examiners. Twenty-four examiners were diagnosed by endoscopy or surgery. They were undergone ultrasonography, blood test on the same day and two fecal occult blood tests on another days. We made abnormal accumulation of PET/CT and abnormal intensity of WB-DWI as a positive. PET/CT image was taken after injection of F18-FDG(3-4 MBq/kg). On WB-DWI using 1.5T MRI, sequences are used TR 5000 ms, TE 71 ms. and b-value is used 0 and 800 or 1000 s/mm². **Results:** Of 1783 examiners(Male/Female:138/645). 15 examiners were cancers (breast 2, lung 1, thyroid 1, esophagus 2, renal 1, colon 4, prostate 1 and bladder 3) and 11 were benign or no abnormality. The sensitivity of PET/CT was 67%, specificity was 19% and diagnostic accuracy was 46%. These of WB-DWI were 60%, 100% and 77% respectively. All bladder cancers demonstrated only by WB-DWI. When we judged as positive by PET/CT and by WB-DWI together, the sensitivity, specificity and diagnostic accuracy were 46%, 100% and 88%, respectively. **Discussion/Conclusion:** At this present, WB-DWI alone was not enough to use for cancer screening. Our results suggested using both PET/CT and WB-DWI together were more useful for increase diagnostic accuracy rate in cancer screening. Particularly, WB-DWI was useful for increasing specificity. However, 6 out of 15 malignant cases were false negatives on WB-DWI. In those cases, they were positive for tumor marker, ultrasonography, and upper gastrointestinal series. Comprehensive judgment including ultrasonography, upper gastrointestinal series, blood test, and fecal occult blood test was important for cancer screening.

EP-0385

$^{99\text{m}}\text{Tc}$ -MIBI SPECT in estimation of the of neoadjuvant chemotherapy and radiotherapy effect in the larynx and laryngopharynx cancer patients

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Purpose: To explore the possibilities of ^{99m}Tc -MIBI SPECT for dynamic observation of a larynx and laryngopharynx tumor during neoadjuvant chemotherapy. **Materials and Methods:** The study included 30 patients with larynx and laryngopharynx cancer. SPECT studies were carried out 20 minutes after the injection of 740 MBq of ^{99m}Tc -MIBI using ECAM-180 gamma-camera (Siemens). Studies was conducted before and after treatment (two courses of neoadjuvant chemotherapy and 4-6 weeks radiation therapy). The images were quantitatively assessed using tumor/background indices. Indices were compared with clinical effect which was assessed by RECIST scale and pathomorphosis according to the postoperative study. **Results:** A partial response was shown in 7 (23%) patients, complete regression in 16 (53%), a stable disease was observed in 5 (17%) patients on the RESIST scale, two patients (7%) had progression of the disease in the form of primary tumor growth. Reduction of indices more than 30% was observed in 4 patients with partial response and in 7 patients with complete regression. In 9 patients with complete regression of pathological accumulation of a radiopharmaceutical after treatment was not noted. In 3 patients with partial response, the patients with progression and in all patients with stabilization the index change was not observed. **Conclusion:** Obviously, the results of SPECT with ^{99m}Tc -MIBI are an important addition to the observation and to evaluate the effectiveness of preoperative chemoradiotherapy in patients with cancer of the larynx and laryngopharynx. It should take into account the change in the intensity of accumulation of radiopharmaceutical in 6 weeks after the end of radiation therapy.

EP-33

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology ->
Bone and soft tissues cancer

EP-0386

Asymptomatic cardiac metastases detected on oncological FDG PET/CT studies: A retrospective observational study
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Introduction: Metastatic involvement of the heart is a rare occurrence and remains undiagnosed until autopsy. In some instances, patients may have cardiac symptoms, leading to ante-mortem diagnosis. Being a high volume PET/CT department, we decide to retrospectively analyse our database. **Materials and Methods:** 6000 patients who underwent 18F-FDG PET/CT imaging for various oncological indications in our department between 2013-2017 were selected for the assessment. A systematic database search was conducted for detecting those with cardiac metastases on reports of PET/CT studies. All these

studies were retrieved and reviewed by two independent observers, who confirmed the presence of cardiac metastases. **Results:** 42 patients were detected to have cardiac metastases. 32 of the 42 patients were asked to undergo 2-D Echocardiographic correlation which confirmed the presence of metastases. Rest of the patients were followed by either by imaging or by clinical evaluation. 6 patients received chemotherapy and showed response to treatment at all metastatic sites including the cardiac region. 4 patients subsequently became symptomatic for cardiac symptoms on clinical follow-up. Considering the spread pattern, 22 patients showed a contiguous extension to the pericardium, whereas 20 patients showed intra-cardiac lesions. Of those with intra-cardiac origin, the distribution of primary malignancy was: lymphoma - 7, head and neck-5, esophagus-2, NUT carcinoma-1, dermatofibrosarcoma-1, lung-1, renal cell carcinoma-1, colon-1, unknown primary-1. **Conclusion:** Whole body imaging with PET/CT uncovers such rare metastatic sites especially in asymptomatic patients, which otherwise would have been undiagnosed. It is a valuable addition to the existing literature on cardiac metastases, and also highlights the role of FDG PET/CT in detection of such rare sites which can very often have a significant impact on patient management.

EP-0387

Sarcomas and Nodal Staging - Improving Scan Interpretation of the Isolated FDG-avid Lymph Node
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Isolated 18-FDG avid lymph nodes may dramatically affect the staging of tumours and their management. Yet many such lymph nodes are reactive in nature rather than reflective of metastatic disease. Additional investigations are frequently necessary, which are often invasive, such as EBUS procedures, and rort by significant morbidity. The clinical significance of isolated 18FDG avid lymph nodes is frequently difficult to ascertain on the 18FDG-PET scans alone. Combining scintigraphic and radiological characteristics may improve the interpretation of such findings. **Aim:** To retrospectively identify scintigraphic and radiological features that may assist in improving the differentiation of malignant nodal involvement from benign disease in patients with documented sarcomas. **Methods:** 22 patients with documented sarcomas and oligo-metastases (n = 1-3) in any lymph node basin on 18FDG-PET scintigraphy were included. A total of 28 nodes were assessed. Radiological features, including size and shape of the lymph nodes, as well as scintigraphic parameters, such as location and tracer avidity, were evaluated. Follow-up 18FDG-PET scans were used to determine the likelihood of malignant involvement. **Results:** Malignant involvement was established in 13 patients (15 nodes). Such nodes demonstrated higher SUVmax values, were more likely to be located in the draining lymph node basin of the primary lesion, and were larger and more round-shaped than benign lymph nodes. Lymph nodes in distant lymph node basins were more likely to be benign. Using an algorithm based on these observations, the benign nature of these lymph nodes was determined in a greater proportion of patients when combining the find-

ings of the 18FDG-PET scan with the low dose concurrent CT scan, than when relying on either modality alone. **Conclusion:** Combining the scan features on 18FDG-PET scintigraphy with those on the low dose concurrent CT scan improved the specificity of findings of isolated tracer-avid lymph nodes in patients with sarcoma. These findings will be tested in a larger cohort of patients and then assessed prospectively.

EP-0388

Clinical findings and ¹⁸F-FDG PET/CT in diagnosing malignant peripheral nerve sheath tumours in neurofibromatosis type I

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Introduction: Neurofibromatosis type I (NF1) is a rare multisystemic disease in which patients can develop multiple benign and malignant tumours, especially of the peripheral nerve system. Patients with NF1 have a lifetime risk of developing a malignant peripheral nerve sheath tumour (MPNST) of 8–13%. Several clinical and imaging findings on MRI are highly suggestive of MPNSTs, but there is no absolute proof. The gold standard is histological tissue examination. F-18-FDG PET/CT has been used in other tumour types to differentiate between benign and malignant lesions. **Aim:** The aim of our study was to identify potential clinical findings and imaging characteristics with F-18-FDG PET/CT that can predict MPNSTs. **Methods:** This retrospective study included 31 patients with NF1 that were referred for F-18-FDG PET/CT because of clinical suspicion of MPNST (pain, growth or neurological deficit). 36 scans were assessed. The PET/CTs were performed according to our local protocol. Standardized uptake values (SUVmax/mean/peak) were determined (EARL reconstructions) for the culprit lesion, possible additional suspect lesions, benign control lesions and the liver. Several ratios were calculated. The gold standard was either tissue biopsy or a follow up of at least 2 years. **Results:** Of all the 31 culprit lesions that were identified on the scan, only 7 were malignant. SUVmax did not differentiate sufficiently between benign and malignant lesions. Several ratios were calculated: Culprit lesion SUVmax/Liver SUVmax, Culprit SUVmax/Control SUVmax, Culprit lesion SUVmax/Liver SUVmean, Culprit lesion SUVpeak/Liver SUVmax. Except for the Culprit SUVmax/Control SUVmax ratio the ratios showed no overlap between malignant and benign lesions. The ratio Culprit SUVpeak/Liver SUVmax ratio showed the least variation between the highest and lowest calculated ratio (3.28 ± 0.49 for MPNST and 0.80 ± 0.49 for neurofibromas). Sensitivity, specificity and correlation with clinical findings were not calculated due to the low incidence of MPNSTs in our study group. All patients with MPNSTs had symptoms of neuropathic pain. None of the additional visually suspected lesions that were found on the PET/CT showed malignant degeneration on the biopsy or during the 2 year follow up. **Conclusion:** The most robust imaging characteristic was the ratio Culprit lesion SUVpeak/Liver SUVmax. Due to the small sample size and low incidence of MPNSTs in our patient group, no significant results were found. Further research is needed, preferably in multicenter studies, to get a larger sample size for statistical analysis.

EP-0389

Bone-Dominant Disease by 18F-Choline PET/CT in Recurrent Prostate Cancer Patients

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Purpose: The aim of the study was to assess the prediction of bone-dominant disease by 18F-Choline PET/CT in recurrent prostate cancer patients. **Materials and Methods:** From two Italian institutional databases (Veneto Institute of Oncology IOV - IRCCS, Padua and Hospital of Udine, Udine), data for 160 patients with prostate cancer undergoing 18F-Choline PET/CT were collected. The inclusion criteria were: 1) the presence of a biochemical recurrence of disease (PSA value > 0.2 ng/mL) after a curative treatment (i.e. radical prostatectomy or radiotherapy); and 2) a positive 18F-Choline PET/CT for bone disease. The exclusion criteria were: 1) a negative PET/CT scan and 2) the presence of non-bone disease at PET/CT scan. Categorical data were expressed as frequency (%) and continuous variable as median (range). Chi-square was used for the comparison between categorical variables. A P value < 0.05 was considered statistically significant. **Results:** Median age was 74 years (range: 52–89). The median PSA value at the time of 18F-Choline PET/CT was 3.5 ng/mL (range: 0.2–373). In particular, 90 (56.2%) had a PSA < 5 ng/mL, while 70 (43.8%) had a PSA ≥ 5 ng/mL. Gleason Score was ranged between 8–10 in the majority of patients (n=71; 44.4%). Fifty-eight (36.3%) patients had a single bone lesion at PET/CT, while 102 showed multiple localizations. In this latter subset, 38 (37.3%) and 64 (62.7%) had < 5 and ≥ 5 lesions, respectively. Forty-seven patients (52.2%) with a PSA level < 5 ng/mL had a single bone lesion at PET/CT, conversely 59 (84.3%) subjects with a PSA ≥ 5 ng/mL had multiple lesions at PET/CT (p<0.001), more often more than 5 lesions (n=41; 70%). Furthermore, among patients with single bone lesion (n= 58), the Choline uptake was localized in the pelvis (n=19; 40%) in case of PSA < 5 ng/mL and in the column (n=7; 63.6%) in case of PSA ≥ 5 ng/mL. **Conclusions:** In recurrent prostate cancer patients, low PSA levels are frequently associated with a single bone lesion at Choline PET/CT that would be treated with a local therapy. On the other hand, the high level of PSA are more often associated with a widespread bone disease at PET/CT that would be treated by a systemic or a targeted therapy (i.e. 223Ra-dichloride).

EP-0390

Quantification of sternal uptake with Tc-99m MDP SPECT/CT

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Introduction: Establishing normal database for ^{99m}Tc MDP uptake is important for assessing bony metastases. Normal sternal uptake may have significant variation on SPECT, which is important especially for breast cancer patients but has not been well characterized. Three dimensional images with Single Photon Emission Computed Tomography (SPECT) fused with CT has been increasingly used, with the advantage of quantifying

the bone uptake. In this study, we have quantitatively assessed the normal sternal uptake on bone SPECT/CT. **Materials and Methods:** We retrospectively reviewed SPECT/CT bone scans with ^{99m}Tc -MDP from 52 patients (age: 61.1 ± 14.7 , range: 21–84, F:M=27:25) with cancer who had no sternal lesions, chest wall pathology or radiation to the chest within one year. Images were acquired on a Symbia-T SPECT-CT scanner (Siemens Medical Solutions, USA) and were reconstructed using attenuation, scatter, and resolution recovery correction and quantified in Standard Uptake Value (SUV) units (HERMES HybridRecon). Maximum SUV (SUV_{max}) and peak SUV (SUV_{peak}) were measured for each area of the sternum by an experienced reader blinded to clinical data. A reference within the vertebral body of L1 (or other level if there was degenerative change in L1) was measured. Sternal-to-lumbar spine ratios for each patient were reported using Non-parametric statistics. Values were reported as Mean $\pm$ SD (range). **Results:** The activity of ^{99m}Tc -MDP of the manubrium of the sternum, body of the sternum and lumbar spine was 3.13 ± 0.90 (range: 1.60–5.07), 3.35 ± 0.99 (range: 1.67–5.77), and 5.41 ± 1.37 (range: 3.05–10.16) with SUV_{max} respectively, and 2.67 ± 0.79 (range: 1.40–4.55), 2.77 ± 0.91 (range: 0.35–4.82) and 4.84 ± 1.27 (range: 2.84–9.57) with SUV_{peak} respectively. The SUV_{max} sternal to lumbar spine ratio was 0.61 ± 0.62 (range: 0.34–1.65) for manubrium of the sternum and 0.66 ± 0.23 (range: 0.34–1.64) for the body of the sternum. There were no correlations of uptake values with age ($p > 0.2$) or sex ($p > 0.25$), except for weak correlation of SUV_{peak} of the sternum body and age ($r = 0.43$, $p = 0.001$). **Conclusion:** Information on normal variation in the sternal and lumbar spine uptake on bone SPECT is important for assessing skeletal metastases. This study is the first to quantify the ^{99m}Tc -MDP sternal and lumbar spine uptake, which could serve as reference values for normal bone uptake.

EP-0391

Incidental extraosseous Tc99m-DPD uptake in bone scan: a 10 years single centre experience

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Purpose: To characterize extraosseous uptake incidentally detected by Tc-99m-DPD bone scan, focusing on neoplastic lesions. **Subjects & Methods:** Tc-99m-DPD bone scintigraphies reported from January 2009 to March 2018 in our Nuclear Medicine Unit ($n = 18461$ scans) were retrospectively reviewed, specifically searching for patients ($n = 137$) with extraosseous uptake in heart, lungs, liver and soft tissues. Bone scan images were acquired and interpreted according to EANM guidelines. To validate the etiology of bone scan findings, further clinical data and diagnostic imaging (CT, MR, PET-CT) was considered as standard of reference, when available. No clinical/imaging follow-up was available in 7 patients who were excluded. **Results:** Overall 130 patients were included in the final analysis. In 91/130 (70%) patients the extraosseous Tc-99m-DPD uptake (heart, lungs, splenic organs and soft tissues) was diffuse and referable to amyloidosis. Extraosseous uptake related to benign findings was found in 13/130 (10%) patients. In 18/130 (13.8%)

patients, the uptake was focal and referable to neoplastic lesions (6 showed calcified lesions whereas 12 no calcification that could explain the uptake): liver (8/18), lungs (2/18), abdomen (2/18), lung and liver (2/18), liver and abdomen (1/18), liver and pancreas (1/18), lung and spleen (1/18), pelvis (1/18). One patient with known hematological disease showed a diffuse uptake in the spleen with no corresponding calcification at the CT scan. Focal liver uptake at bone scan remained indeterminate in 4 patients (no agreement with CT). In one patient, diffuse liver uptake remained unclear because only one focal neoplastic lesion was confirmed by the CT scan. SPECT-CT was performed in only 2/130 patients (equipment available in our centre from November 2016) without recent imaging for comparison and resulted significantly helpful to anatomically localize the extraosseous uptake: one in liver and pancreas, soft tissue invasion by a sacral lesion in the other one. **Conclusion:** Incidental extraosseous Tc-99m-DPD uptake is mainly related to amyloidosis, but other causes such as metastatic calcifications, benign lesions, primary/secondary visceral localizations should be taken into account. Considering the possibility of unknown malignant lesions, it's relevant to evaluate and describe any extraosseous uptake to Tc-99m-DPD bone scintigraphy diagnostic impact. Furthermore the increased diffusion of SPECT-CT hybrid imaging would allow a direct anatomical and morphological correlation and better comprehension of the phosphonate tracer uptake mechanism in non-calcified lesions.

EP-0392

The evaluation of histologically proven bone lesions with focal uptake on FDG-PET/CT

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Purpose: FDG-PET/CT is highly sensitive for the detection of bone metastases, however, benign bone lesions such as focal bone marrow hyperplasia or hemangioma mimics bone metastases on FDG-PET/CT and would be clinically problematic for patient management. The purpose of this retrospective study was to evaluate the focal bone uptake on FDG-PET/CT for the differentiation between benign and malignant lesions in the patients with malignancies. **Subjects & Methods:** We retrospectively analyzed consecutive 33 patients (13 female and 18 male, mean age 66.8 ± 14.6 years, age range, 33 - 95 years) with suspected bone metastases because of focal uptake on FDG-PET/CT for staging or restaging of malignant tumor, which was later confirmed histological diagnosis by CT-guided bone biopsy. All patients had known malignancies (lung cancer, esophageal cancer, breast cancer, malignant melanoma, and others). The comparison of maximum standardized uptake value (SUV_{max}) of bone lesion and ROC analysis were performed. **Results:** Histologically proven bone lesions included benign lesions ($n = 12$, bone marrow hyperplasia, vertebral hemangioma, xanthogranulomatous lesion, and others), bone metastases ($n = 16$), and malignant lymphoma ($n = 5$). The mean $\pm$ standard deviation of SUV_{max} were 3.1 ± 2.0 for benign lesions, 5.7 ± 2.7 for bone metastases, 5.6 ± 2.6 for malignant lymphoma. The SUV_{max} of bone metastases was significantly higher than those in benign lesions ($P < 0.01$). On ROC analysis for distinguishing bone me-

tastasis from benign bone lesions, the sensitivity, specificity, accuracy and AUC were 81%, 83%, 82% and 0.878 (cut-off value; 3.25). On the other hand, there was no significant difference in SUVmax between benign lesions and malignant lymphoma. **Conclusion:** FDG-PET/CT would be useful to distinguish bone metastasis from benign bone lesions including bone marrow hyperplasia.

EP-0393

Diagnostic accuracy of Bone Scintigraphy in suspected cases of Osteoid Osteoma

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Purpose: To assess the diagnostic accuracy of Tc99m-MDP Bone Scintigraphy with SPECT-CT in the doubtful cases of osteoid osteoma. **Subjects and Methods:** 12 patients (mean age 21.58 ± 10.51 years, 5 female) with equivocal clinical and radiological suspicion for osteoid osteoma were analyzed prospectively from period of July 2017 to February 2018. All patients underwent three-phase planar (Tc99m-MDP) bone scan and SPECT-CT imaging was done for region of suspicious focal tracer uptake. On planar BS, focal increase in flow, pool phase activity, and focal radiotracer uptake surrounded by less marked, but still high, uptake on delayed phase was taken as positive. For SPECT-CT, the presence focal delayed tracer uptake on SPECT along with a well defined round or oval lytic lesion with soft tissue or hyperdense nidus surrounded by variable amounts of osteosclerosis on CT was taken as positive. Diagnosis on Bone scan was compared with histopathological diagnosis or clinical response to treatment on follow up. **Results:** Out of 12 patients 10 patients were presented with regional pain. Rest two were post-operative cases of osteoid osteoma, one with suspected recurrence after two years of surgery, and the other with suspected residual disease. Out of 12 patients bone scan was positive in 11 patients. Out of these 11 patients, 6 patients underwent surgical resection and histopathology confirmed the diagnosis of Osteoid osteoma. Radio-Frequency Ablation (RFA) was performed on 3 of the 11 patients, who improved symptomatically thereafter, and remained asymptomatic till last follow-up. One patient was started on NSAID, but remained symptomatic and has been planned for surgery. One patient was false-positive on bone scan and another was negative on bone scan; both patients have improved without any intervention. So sensitivity, specificity, positive predictive value and negative predictive value of planar bone scan was 100%, 50%, 90.91% and 100% respectively. Out of 12 patients SPECT-CT was positive in 8 patients. All of them were diagnosed as osteoid osteoma finally. So sensitivity, specificity, positive predictive value and negative predictive value of SPECT CT was 80%, 100%, 100% and 50% respectively. **Conclusion:** 99mTc-MDP planar bone scintigraphy shows excellent diagnostic accuracy for doubtful cases of osteoid osteoma. Addition of SPECT CT further improves the specificity of the modality by ruling out false positive cases. Further confirmation in larger sample size should establish 99m Tc-MDP planar bone scintigraphy with SPECT CT as one stop imaging modality in doubtful cases of Osteoid osteoma.

EP-0394

Cold vertebrae on 18F-FDG PETCT, pattern recognition and characterization

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Introduction: A photon deficient ("Cold") vertebra on 18F-FDG PET is a known entity and can arise as a result of varying etiologies. A proper interpretation of this observation is required to make an accurate diagnosis for appropriate management.

Methods: 12 cases with "cold" vertebrae on 18F-FDG PET/CT were selected and analyzed from a population of 400 patients with known malignancy who underwent whole-body 18F-FDG PET/CT for staging, disease viability assessment, response to treatment or suspected recurrence purposes. The patterns were studied and correlated with clinical history and the low dose CT done with the PET scan for attenuation correction and anatomical localization. **Results:** The most common cause for cold vertebrae was found to be post external radiotherapy, causing photopenia involving multiple vertebrae corresponding to the radiotherapy portals. Two other causes found in the study were the destruction of the vertebral marrow cavity by metastatic tumor cells and vertebral hemangioma. Characteristic features of "cold" vertebrae are described in the study with illustrations.

Conclusion: Pattern recognition coupled with clinical history and CT correlation of "cold" vertebrae on 18F-FDG PET/CT can help in diagnosing correct underlying etiology which can help in better management of the patients.

EP-0395

Role of (F-18) Fluorodeoxyglucose Positron Emission Tomography (F18-FDG PET-CT) SUVmax as a Predictor of histological grade according the Federation Nationale des Centers de Lutte Contre le Cancer (FNCLCC) grading system, in Soft Tissue Sarcoma (STS)

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Aim: The aim of this study was to assess the accuracy of F18-FDG PET-CT uptake to discriminate between high and low histological grade STS according the FNCLCC system. **Methods:** Our patient population included 20 patients with STS, assessed by the Committee of Sarcomas of our hospital, confirmed by AP with histological grade according the FNCLCC. We use a ROC curve analysis, to quantify the accuracy of F18-FDG PET-CT SUVmax to discriminate between high and low histological grade STS (according the FNCLCC system). The usefulness of PET in patient management was further assessed. **Results:** The mean age was 55.15 years, 45% women and 55% men. Histological types most frequent were myxofibrosarcoma (30%) and liposarcoma (25%). 60% had a high grade lesion, with SUV max between 2.9 - 24 and 40% had a low grade lesion, with SUVmax between 0 - 9.

By ROC curve analysis, a SUVmax threshold of 2.8 discriminated between high and low grade tumors ($p=0.03$) with a 100 % sensitivity, specificity of 71%, area under the curve (AUC) 0.86. In 7 patients, post treatment CT PET was performed, 5 presented a decrease in the SUVmax value, one presented elevation of the same (2nd to metastasis), and another did not modify the SUVmax value, which motivated a different therapeutic attitude.

Conclusions: -The F18-FDG PET-CT SUVmax was correlated significantly with histologic grade as determined by the FNCLCC grading scheme, discriminating high and low grade STS. -The 18F-FDG PET CT is a useful tool in staging and management in patients with STS.

EP-0396

Breast and Lung Cancer Bone Metastases Detection: Does the FDG PET/CT suffice or there is still a need for bone scintigraphy?

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Purpose: Since one of the most common sites of both breast and lung cancer metastasis are bones, and the bone scintigraphy is widely used to detect bones metastatic involvement, but the usefulness of 18FDG-PET/CT solely has not been clearly stated, in this study we tried to compare diagnostic accuracy of 18FDG-PET/CT and bone scintigraphy in detection of breast and lung cancer bone metastasis. **Subjects & Methods:** Retrospective analysis included sixty-eight patients (33 males/35 females, average age 60,01±7,68), divided in breast cancer group ($n=30$), and lung cancer group ($n=38$), who underwent both bone scintigraphy and FDG PET/CT exams within maximally 60 days interval. Studies were considered as positive or negative, and presence of metastases has been confirmed/excluded on the basis of clinical follow-up and/or other imaging techniques (MRI). Statistical analysis was done by use of two-tailed Pearson's correlation (r), and Spearman's rank correlation (ρ) (confidence level $p<0.01$), and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DA) were calculated. **Results:** We've found good correlation in whole group of patients ($r=0.684$ and $\rho=0.684$), with good but slightly lower correlation in breast cancer group ($r=0.683$ and $\rho=0.683$), and slightly higher correlation in lung cancer group ($r=0.685$ and $\rho=0.685$). Sensitivity, specificity, PPV, NPV, and DA in whole group of patients for bone scintigraphy were 86%, 76.9%, 88%, 81%, and for FDG PET/CT 89.6%, 92%, 89.6%, 92% and 91%, respectively. Sensitivity, specificity, PPV, NPV, and DA in breast cancer group for bone scintigraphy were 86%, 76.9%, 73.5%, 88%, 81%, and for FDG PET/CT 89.2%, 92%, 89.6%, 92% and 91%, respectively, while in lung cancer group for bone scintigraphy values were 86.6%, 78%, 72%, 90%, 81.5%, and for FDG PET/CT 93%, 91.3%, 87.5%, 95.4% and 92%, respectively. Better overall diagnostic accuracy of FDG PET/CT has been found, with slightly better accuracy and better NPV in the lung cancer group, comparing to both the whole and breast cancer group. **Conclusion:**

Our results are suggesting that FDG PET/CT tends to be superior to bone scintigraphy in detection of bone metastasis, even in the breast cancer patients, in whom higher number of osteoblastic metastases are expected. Though FDG PET/CT is still considered as a complementary method to bone scintigraphy in bone cancer detection, on the basis of good FDG PET/CT NPV, we are of opinion that negative FDG PET/CT finding may exclude further need for bone scintigraphy in lung cancer patients.

EP-0397

Tumor-induced osteomalacia - could we diagnose it by ⁶⁸Ga-DOTATATE PET/CT?

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Tumor-induced osteomalacia (Oncogenic osteomalacia) is a rare paraneoplastic syndrome clinically characterized by bone pain, fractures, and muscle weakness. In laboratory tests persistent acquired hypophosphatemia, isolated PTH-independent renal phosphate wasting, and low or inappropriately normal 1,25(OH)₂D are observed. The disease is predominantly caused by a small, somatostatin receptor positive mesenchymal tumor, which is frequently hidden in an unusual anatomical site and often goes undetected by conventional imaging. Conventional scintigraphic imaging using radiolabeled somatostatin analogs ¹¹¹In- and ^{99m}Tc-labeled octreotide was reported as a one of diagnostic tool. However, the scintigraphy is insufficient to provide high-resolution images and precise anatomical information. ⁶⁸Ga-DOTATATE PET/CT is a novel tool with better sensitivity and resolution specifically for somatostatin receptor positive tumors. By the literature ⁶⁸Ga-DOTATATE PET/CT demonstrates the greatest sensitivity and specificity, suggesting that it may be the best single study for localization of osteogenic osteomalacia. The aim of our study was to evaluate usefulness of ⁶⁸Ga-DOTATATE PET/CT as a imaging tool in patients with oncogenic osteomalacia in diagnosis of primary tumor. **Material and Methods:** Five patients with clinical and biochemical evidence of oncogenic osteomalacia underwent PET/CT with ⁶⁸Ga DOTATATE. The PET/CT was performed 60-70 minutes' post injection of 120-200 MBq ⁶⁸Ga-DOTATATE on Biograph 64 PET-CT TruePoint scanner (Siemens Medical Solutions). **Results:** In all patients' serum biochemistry revealed severe hypophosphatemia, increased alkaline phosphatase levels, and diminished 1,25-dihydroxyvitamin-D and calcium levels. Serum levels PTH were normal. ⁶⁸Ga DOTATATE PET/CT localized focal uptake in: head of femur with SUVmax 7.2, femur with SUVmax 14.2, pubic area with SUVmax 40.8 and hip bone with SUVmax 4.3. These patients underwent surgical excision of tumors, with histopathologically confirmation of oncogenic osteomalacia. In one of patients' examination revealed suspicion of tumors in II right rib with SUVmax 3.6, but biopsy was negative. ¹⁸F-FDG PET/CT as a next step for diagnosis, didn't revealed primary tumor location. As well in follow up ⁶⁸Ga DOTATATE PET/CT in 6 months was no abnormality. In one patient diagnosed for recurrence of disease after surgery ⁶⁸Ga DOTATATE revealed focal recurrence with SUVmax 2.6 in the same place that primary tumor location. **Conclusion:**

⁶⁸Ga DOTATATE PET imaging is a very useful imaging tool for detection of occult tumors in patients of oncogenic osteomalacia. In our small series revealed 80 % of primary tumors.

EP-0398

Role of F18-FDG PET-CT in the staging and follow-up of soft tissue sarcoma (STS)

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Aim: The aim of this study was to assess the discrimination ability of (F-18) Fluorodeoxyglucose Positron Emission Tomography (F18-FDG PET-CT) in the staging of the histological grade of malignity and the follow-up of the response events in patients with STS. **Material & Methods:** We conducted a retrospective study including 45 patients diagnosed with STS who underwent a F18-FDG PET-CT scan between January 2017 and January 2018. A total of 137 studies (19 staging and 118 control scans) have been chronologically classified. The variables SUVmax, histological grade, as defined by the French Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC), and clinical response to treatment were analyzed. A complete response to treatment was considered a desirable event, whereas a partial response, persistence, progression or tumor relapse were considered non-desirable events. We used a ROC curve analysis, to quantify the accuracy of staging F18-FDG PET-CT SUVmax to discriminate between high and low histological grade STS. The usefulness of control PET-CT in the evaluation of response events was also assessed. **Results:** In staging PET-CT scan, ROC curve analysis established a SUVmax threshold of 3.05 (Sensitivity: 100%, Specificity: 20%, IC 95%: 0–1, $p = 0.01$, area under the curve (AUC) 0.90) to discriminate between high and low grade STS. ROC curve analysis of the first 3 control PET-CT scans found the following SUVmax thresholds to discriminate between desirable and non-desirable events in the clinic response: SUVmax 1.6 (AUC 0.93) in the first control, SUVmax 1.7 (AUC 0.89) in the second control and SUVmax 0.9 (AUC 0.90) in the third one. **Conclusions:** The F18-FDG PET CT is a useful tool to discriminate between high and low grade STS and in the patients clinic response follow-up.

Aim: To verify that the implementation of the sentinel lymph node biopsy (SLNB) remains in order to avoid unnecessary axillary lymph node dissection (ALND) in patients with breast cancer. To check that lymph node staging is similar in the 3 hospitals in the coverage area of our Nuclear Medicine Department.

Material & Methods: We reviewed 513 SLNB performed in patients with Tis-T1-T2 tumors and negative axilla, from 2016 to 2017. Hospital A (HA): 77 tumors (4 Tis, 60 T1, 13 T2); Hospital B (HB): 174 tumors (16 Tis, 126 T1, 32 T2). Hospital C (HC): 248 tumors (15 Tis, 165 T1, 68 T2). Lymphatic mapping was performed by a peri-tumoral or peri-areolar intradermal injection of 74–111 MBq of Technetium-labeled (Tc-99m) nano-colloid. Planar images in anterior and lateral projections were acquired 30 and 120 minutes after the injection, and a skin mark was made to point out the SLN location. Number of SLN observed in the scintigraphy was specified in the report. Correlation between number of removed SLN and final lymph node staging was made. **Results:** Axillary drainage was visualized in 506/513 (98.6%), of them 1 SLN was observed in 322 patients (62.7%), 2 SLN in 109 (21.2%) and > 2 SLN in 65 (12.6%). There were no statistical differences between hospitals in the number of SLN visualized (mean HA: 1.24, HB: 1.23, HC: 1.15, $p > 0.05$) but there were in the number of removed SLN (HA: 1.42; HB: 1.37, HC: 1.10, $x^2 = 2.340$ $p < 0.05$). One patient with Tis presented lymph node disease (pN1a). Lymph node staging of the 351 T1 patients was: 260pN0 (74.0%), 38pNmic (10.8%), 44pN1-2 (12.5%). In this group (T1) there were differences in the number of avoided ALND (HA: 96.5%, HB: 92.5%, HC: 86.3%, $p < 0.05$), when it should be expected around the 85%. In T2 tumors the percent of avoided ALND was 100% in HA (only 17 cases), 46% in HB and 40% in HC, without differences between HB and HC ($p > 0.05$), within the expected for this size tumor (40%). **Conclusions:** It is advisable to verify that the quality standards remain in the procedure of SLNB performed in patients with breast cancer at initial stages.

EP-0402

Appropriate Use Criteria for Bone Scintigraphy in Breast Cancer: compliance in a case series

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Aim: To evaluate the compliance of our practice towards the appropriate use criteria (AUC) recently published for bone scintigraphy in breast cancer. **Subjects and methods:** A retrospective analysis of patients with breast cancer referred for bone scintigraphy between 28/07/2009 and 13/04/2010 was performed. Subsequent bone scintigraphies conducted on those patients, until 16/01/2018, were also included. According to published literature¹, for each bone scintigraphy, the clinical scenario was identified, an AUC score attributed and the imaging studies classified as “rarely appropriate” (score < 4), “may be appropriate” (score 4 to 6) and “appropriate” (score > 6). When the imaging study could not fit any of the clinical scenarios considered for AUC criteria, the score was defined as “lack of AUC clinical scenario” (LCS). Impact was evaluated on “rarely appropriate” and LCS cases, being defined as leading to clinical upstaging or downstaging, affecting patient management. Lack of clin-

EP-34

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Breast, malignant

EP-0401

Relevance of maintaining quality standards in lymph node staging of initial stages of breast cancer: A 3 hospital comparison

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ical record information for scenario evaluation was a criterion for exclusion from this study. **Results:** From a total of 394 bone scintigraphies reviewed, 13 were excluded from the analysis, due to lack of information. Within the 381 bone scintigraphies included, 324 (85%) had AUC applicable, 264 (69.3%) being classified as “appropriate”, 1 (0.3%) as “may be appropriate” and 59 (15.4%) as “rarely appropriate”. The main clinical scenarios found for the “appropriate” referrals were: restaging for patient with new bone pain in 108/264 (40.9%); restaging for asymptomatic patient with change in treatment plan in 91/264 (34.5%); and restaging for suspicion of nonosseous recurrence in 31/264 (11.7%). The main clinical scenario within the “rarely appropriate” referrals was routine surveillance, found in 36/59 cases (61%). Clinical impact was found in 8 (13.6%) of the “rarely appropriate” referrals, with 5 (8.5%) referred for routine surveillance. Within the LCS cases, 18 (31.6%) had clinical impact, and in these, the indications for referral were: in 10 (17.5%) follow-up of inconclusive bone scintigraphy; and in 8 (14%) restaging in patient with previous bone metastasis, without new symptoms or change in treatment plan. **Conclusion:** The large majority of our bone scintigraphies referrals for breast cancer were in accordance to recently published appropriate use criteria. However, we found clinical impact in scenarios not considered in this paper, as well as in almost 15% of those considered as rarely appropriate. To our understanding, this indicates the need of further improvement of appropriate use criteria for bone scintigraphy in breast cancer. ¹JNuclMed.2017;58:14N-17N

EP-0403

Risk factors and clinical significance of sentinel lymph node non-visualisation on preoperative lymphoscintigraphy in patients with primary breast cancer

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Aim: Sentinel lymph node (SLN) biopsy is indicated for almost all cN0 breast cancer. Alongside the expanding SLN indications, we experienced a drop in visualisation rate on lymphoscintigraphy. Therefore, the aim of this study was to evaluate which factors are associated with SLN non-visualisation on lymphoscintigraphy, and the impact of non-visualisation on the intraoperative SLN identification rate and regional recurrences. **Materials and Methods:** We retrospectively reviewed lymphoscintigraphies and patient data of 2054 SLN procedures performed from 2011 to June 2016 at the Netherlands Cancer Institute. Anterior and oblique lymphoscintigraphy was performed at 15 minutes and 3–4 hours after intratumoural injection of 99mTc-albumin-nanocolloid (100–140 MBq). Lymphoscintigraphy was scored as SLN visualisation or non-visualisation. The following factors were evaluated: age, body mass index (BMI), tumour characteristics (palpation, type, grade, stage, location, multifocality and receptor status), neoadjuvant chemo-/immuno-/hormone treatment, previous ipsilateral radiation therapy or surgery, presence of iodine-seeds, and axillary lymph node status. Factors with a p-value < 0.1 in univariate analysis were stepwise included in a multivariate logistic regression model. In the final model, fac-

tors with a p-value < 0.05 were considered significant risk factors for non-visualisation. **Results:** A SLN was visualised in 86.7% (1780/2054) of the procedures. In multivariate logistic regression, age ≥ 70 years [OR: 3.28 (95%-CI 2.16–4.99)], BMI ≥ 30 [OR: 1.95 (95%-CI 1.40–2.72)], T3-tumours [OR: 2.82 (95%-CI 1.39–5.69)], tumours in the medial upper quadrant [OR: 1.69 (95%-CI 1.02–2.82)], previous mantle field radiation therapy [OR: 3.98 (95%-CI 1.72–9.25)], non-palpable tumours [OR: 1.93 (95%-CI 1.39–2.66)] and simultaneous use of iodine-seeds [OR: 1.35 (95%-CI 1.02–1.79)] were significantly associated with SLN non-visualisation on lymphoscintigraphy. Neoadjuvant systemic treatment and axillary lymph node metastases were not risk factors for non-visualisation. Ipsilateral radiation therapy [OR: 6.07 (95%-CI 1.49–24.68)], surgery [OR: 3.12 (95%-CI 1.22–7.99)], and non-visualisation on lymphoscintigraphy [OR: 14.60 (95%-CI 7.53–28.31)] were independent predictors of unsuccessful intraoperative SLN identification. Overall, the SLN identification rate was 97.6% (2004/2054) due to the addition of blue dye. With a median follow-up of 49 (range: 1–114) months, univariate analysis showed that the regional recurrence rate was not significantly (p=0.421) different between the SLN visualisation (1.6%, 29/1780) and non-visualisation group (0.7%, 2/274). **Conclusion:** In routine clinical practice, SLN identification rate remains high (>97%). This study confirms risk factors for SLN non-visualisation by using an intratumoural injection in primary breast cancer. Non-visualisation on lymphoscintigraphy is not a predictor for increased risk in axillary lymph node metastases or regional recurrence.

EP-0404

MAMMI PET in the diagnosis of breast cancer

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Aim: To explore the applicable scope of the latest breast cancer detection method using MAMMI PET in the diagnosis of breast cancer **Materials and Methods:** Randomly selected clinically suspected patients with breast cancer (by any method of clinical examination, B-ultrasound(B), MRI(MR), Mammography(MG)) were admitted to hospital to carry out all examinations of B, MR, MG and MAMMI PET (MP). All patients were undergone surgical biopsy, if pathology confirmed as breast malignant tumor, the corresponding surgery for breast cancer was performed. All patients' corresponding examination and pathological data were recorded for statistics. **Results:** A total of 97 patients were enrolled in the study from 2016.11 to 2017.08, with a median age of 49 years. Seventy-one patients had pathologically confirmed breast malignancy. The Sensitivity for breast cancer of the four inspection methods were B 90%, MG 83%, MR 93%, MP 80%. The Specificity were B 65%, MG 88%, MR 77%, MP 58%. The Positive Predictive Value were B 88%, MG 95%, MR 92%, MP 84%. The Negative Predictive Value were B 90%, MG 83%, MR 93%, MP 80%. The Sensitivity for both MP and MR or MP and B were 96%, 94%. The Specificity were 46%, 62%. The Positive Predictive Value were 83%, 87%. The Negative Predictive Value were 80%, 80%. The tumor sizes in patients with false negative rate of MP were generally small(<1cm). In patients with breast-conserving surgery, MP-measured magnitude were closer to pathological size

than MR-measured (p -value < 0.05) **Conclusion:** The detection of MP was comparable to other breast cancer screening methods. However, the level of detection of MP was still insufficient for breast cancer with smaller tumor size. For patients undergoing breast-conserving surgery, MP-measured magnitude was closer to the pathological size.

EP-0405

SPECT with Radiopharmaceutical Based on Derivative of Glucose Labeled with Technetium-99m in Breast Cancer Imaging

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Purpose: to study possibility of using ^{99m}Tc -1-thio-D-glucose SPECT for visualization of breast cancer and regional lymph node metastasis. **Materials and Method:** the study included 20 patients with stage $T_{1-4}N_{0-1}M_0$ breast cancer who underwent SPECT with ^{99m}Tc -1-thio-D-glucose. Of the 20 patients, 11 had luminal B cancer, 5 had luminal A, 3 had triple-negative and in two cases had cancer in situ. SPECT was performed 240 minutes after intravenous injection of 500 MBq of ^{99m}Tc -1-thio-D-glucose using ECAM-180 gamma-camera (Siemens). **Results:** Increased radiotracer accumulation in the breast was visualized in 18 of 20 (90%) breast patients, two of these patients had inflammatory breast cancer. The size of nonvisualizable tumors was 5 and 7 mm. Pathological radiotracer uptake in axillary lymph nodes was detected in 7 of 13 (69.2%) patients with nodular lesions. **Conclusion:** Sensitivity of SPECT with ^{99m}Tc -1-thio-D-glucose in patients with breast cancer were 90%. We believe that ^{99m}Tc -1-thio-D-glucose is a prospective radiopharmaceutical for diagnosis of the breast cancer and regional metastases.

EP-0406

Local and whole-body staging in patients with primary breast cancer: A comparison of one-step to two-step staging utilizing ^{18}F -FDG-PET/MRI

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Objectives: To compare the diagnostic value of a one-step to a two-step staging algorithm utilizing ^{18}F -FDG PET/MRI in breast cancer patients. **Methods:** A total of 38 patients (37 females and one male, mean age 57 ± 10 years) with newly diagnosed, histopathologically proven breast cancer were prospectively enrolled in this trial. All PET/MRI examinations were assessed for local tumor burden and metastatic spread in two separate reading sessions: (1) One-step algorithm comprising supine whole-body ^{18}F -FDG PET/MRI, (2) Two-step algorithm comprising a dedicated prone ^{18}F -FDG breast PET/MRI and supine whole-body ^{18}F -FDG PET/MRI. **Results:** On a patient based analysis the two-step algorithm correctly identified 37 out of 38 patients with breast carcinoma (97%), while 5 patients were missed by the one-step

^{18}F -FDG PET/MRI algorithm (33/38; 87% correct identification). On a lesion-based analysis 56 breast cancer lesions were detected in the two-step algorithm and 44 breast cancer lesions could be correctly identified in the one-step ^{18}F -FDG PET/MRI (79%), resulting in statistically significant differences between the two algorithms ($p=0.0015$). For axillary lymph node evaluation sensitivity, specificity and accuracy was 93%, 95% and 94%, respectively. **Conclusion:** The results demonstrate the necessity and superiority of a two-step ^{18}F -FDG PET/MRI algorithm, comprising dedicated prone breast imaging and supine whole-body imaging, when compared to the one-step algorithm for local and whole-body staging in breast cancer patients.

EP-0407

Role of FDG PET/CT in the diagnosis, response to treatment and prognosis of patients with locally advanced breast cancer

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Purpose: To evaluate the performance of FDG PET/CT in the diagnosis of locally advanced breast cancer (BC) patients, in predicting the response to neoadjuvant chemotherapy (NAC) and outcome. **Methods:** we prospectively analysed 76 patients (mean age 54.6) with stage II-III BC who performed FDG PET/CT imaging before and after NAC in 2013. The maximum standardized uptake values (SUVmax), the Δ SUV of the two PETs, the histologic and biologic characteristics of the tumours were compared to the pathologic response (pR) after breast surgery and axillary lymph node dissection and to the presence of recurrence at four-year follow-up. **Results:** the prevalent histotype was infiltrating ductal carcinoma (IDC) in 70 women. In the diagnostic setting, PET/CT depicted all breast cancers (SUVmax range 2.4-35), showed positive axillary lymph nodes in 60 patients and revealed metastatic foci in 8 patients (95% bone and 5% liver). It localized synchronous malignant tumours in 4 patients (lung, thyroid and 2 renal cancers). After NAC a complete pR was obtained in 16 women and PET/CT imaging was true negative (TN) in 13 women and false positive (FP) in 3 cases regarding the breast lesions, whereas in the lymph node evaluation metabolic imaging was TN in 15 patients and FP in one. In this group at FU only one patient experienced brain metastases. Partial pR was achieved in 47 women where PET/CT was TP in 36 patients, FP in 1 and FN in 10 patients (SUVmax range 0.9-1.5). Axillary PET imaging was TP in 7, TN in 23 and FN in 17 patients. Among them, 17/47 women were metastatic at follow-up but in all, except one patient, PET/CT was positive. No pR to treatment and/or progression was seen in 13 women. PET/CT was TP in all the BC, in the axillary node evaluation there were 9 TP, 1 FP and 3 TN results with metabolic imaging. In this group, 7 patients became metastatic in the brain, lung (71%) and liver (43%). Results were statistically significant regarding pR, Δ SUV and SUVmax in

PET/CT before surgery ($P < 0.001$). **Conclusion:** PET/CT is a sensitive imaging tool in the diagnosis of locally advanced BC regarding T, N and M parameters. After NAC, the accuracy of metabolic imaging in predicting the pR to treatment in the tumour and in the axillary nodal basin was respectively 82% and 75%. Both scans correlated well with clinical outcome in locally advanced BC at a four-year follow-up.

EP-0408

Kinetic Analysis of the HER2-binding ABY-025 Affibody Using Dynamic PET in Patients with Metastatic Breast Cancer

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Purpose: Breast cancer patients with increased HER2-receptor expression documented by immunohistochemistry usually respond well to therapy with the HER2-targeting antibody trastuzumab. The potential of positron emitting tomography (PET) with the radiolabeled Affibody molecule (⁶⁸Ga-ABY-025) to measure HER2-expression non-invasively has previously been demonstrated. Static standardized uptake values (SUV) differentiated metastases with good correlation with immunohistochemistry of biopsies. However, using SUV, smaller liver metastases can be difficult to assess in patients with elevated liver uptake. The aim of this study was to improve quantification accuracy in liver metastases by creating ⁶⁸Ga ABY-025/PET parametric images of the tracer uptake kinetics and to investigate to what extent simple static SUVs reflect the true kinetics of the tracer. **Subjects & Methods:** ⁶⁸Ga-ABY-025 PET studies were performed on sixteen patients with known metastatic breast cancer. Each study consisted of a 45 min dynamic PET, followed by static whole-body scans at 1h, 2h and 4h post-injection (p.i.). Five patients were scanned twice one week apart to evaluate repeatability. Parametric images of influx rate (K_i) and delivery rate (K_1) were obtained using a basis function implementation of the irreversible two-tissue compartment model (BFM). Patlak graphical analysis was used to create simplified K_i images. An aortic time activity curve (TAC) was used as an input function after correction for plasma-whole blood ratio based on arterialized venous blood sampling. Additionally, a region-of-interest (ROI) based analysis was performed to validate parametric images. SUVs were collected from static whole-body PET images at 2h and 4h p.i. **Results:** Visualization of HER2-positive liver metastases was improved using parametric K_i images. Tumor-to-normal tissue ratio was 7.1 for Patlak, compared to 4.2 for SUV 2h p.i. ($p = 0.01$). Patlak and BFM K_i values in tumors derived from parametric images were nearly identical to ROI-

based analysis ($R^2 \geq 0.99$, $n = 24$). SUV for tumors correlated well with parametric values at 2h p.i. (BFM: $R^2 = 0.87$; Patlak: $R^2 = 0.92$, $n = 24$) and 4h p.i. (BFM: $R^2 = 0.81$; Patlak: $R^2 = 0.88$, $n = 24$). Comparing K_i values in the test-retest group demonstrated high reproducibility of ⁶⁸Ga-ABY-025 PET (BFM K_i $R^2 = 0.85$; Patlak K_i $R^2 = 0.94$, $n = 16$). $P < 0.001$ for all correlations. **Conclusion:** Parametric K_i Images reflect the true kinetics of ⁶⁸Ga-ABY-025 with better contrast than static whole-body images. The good correlation found between the rate of irreversible binding and static SUVs supports the use of SUV in whole-body imaging for quantifying HER2 expression.

EP-0409

Correlation And Prognosis Of Mitochondrial Metabolism And FDG Uptake In Invasive Ductal Breast Cancer

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Background: Mitochondrial metabolism was determined by studying cytochrome C oxidase (COX) activity and expression of TOMM20. We studied the immunohistochemical expression of antibodies of mitochondrial metabolism in patients with invasive ductal breast cancer (IDC) and the correlation with SUVmax of the primary tumor (pSUVmax) as well as other biological parameters. Prognostic significance of pSUVmax, expression of TOMM20 and COX4 for the prediction of progression-free survival (PFS) was also assessed. **Materials and Methods:** One-hundred sixty four female patients with IDC who underwent pretreatment F-18 FDG PET/CT were enrolled. The pSUVmax was compared with clinicopathological parameters including ER, PR, HER2, axillary lymph node metastasis (LNM), stage, TOMM20 and COX4. The prognostic value of pSUVmax, COX-4 and TOMM20 for PFS was assessed using the Kaplan-Meier method. **Results:** pSUVmax was significantly higher in patients with COX-4 ≥ 4 and TOMM20 ≥ 4 compared to patients with COX-4 < 4 and TOMM20 < 4 (4.8 ± 3.8 vs. 2.6 ± 3.5 , $P = 0.0104$; 5.2 ± 3.8 vs. 2.7 ± 3.1 , $P = 0.002$). pSUVmax was also significantly higher in higher stage ($P < 0.001$), ER-negative tumors ($P < 0.0001$), PR-negative tumors ($P = 0.0045$) and positive LNM ($P = 0.028$). pSUVmax was significantly higher in patients with progression compared to patients who were disease-free (6.6 ± 7.5 vs. 3.5 ± 3.7 , $P = 0.0049$). A receiver-operating characteristic curve demonstrated pSUVmax of 6.84, TOMM20 of 4 and COX4 of 4 to be the optimal cutoff for predicting PFS (sensitivity; 52.2%, specificity; 85.4%, $P < 0.0001$; 60.9%, 72.2%, $P = 0.006$; 56.5%, 80.8%, $P = 0.0054$). Kaplan-Meier analysis identified pSUVmax ≥ 6.8 ($P = 0.0004$), TOMM20 ≥ 4 ($P = 0.0005$) and COX4 ≥ 4 ($P < 0.0001$) as predictors of recurrence. Cox proportional-hazards analysis showed that pSUVmax ≥ 6.8 ($P = 0.0338$, relative risk 2.636), COX-4 ≥ 2 ($P = 0.0194$, relative risk 0.331) and TOMM20 ≥ 5 ($P = 0.0379$, relative risk 3.139) significantly predicted recurrence. **Conclusions:** pSUVmax on pretreatment F-18 FDG PET/CT reflect expression of COX-4 and TOMM20 and can be used as a good surrogate marker for the prediction of progression in patients with IDC. The amount of FDG uptake is determined by the expression of mitochondrial metabolism in breast cancer cell.

EP-0410**The Role Of Scintimammography In The Diagnosis Of Multicentric Breast Cancer. Incremental Value Versus Digital Mammography And Ultrasound**

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Purpose: to compare diagnostic accuracy of scintimammography (SMG), digital mammography (MG) and ultrasound (US) in the diagnosis of multicentric breast cancer (BC); to determine possible diagnostic gain from combination of MG and SMG as well as the role of this combination for treatment planning. **Material and Methods:** 367 women with histologically confirmed BC were included in this analysis. SMG was performed in prone position 5-10 min after i/v injection of 740 MBq of ^{99m}Tc -methoxyisobutylisonitrile (^{99m}Tc -MIBI) with acquisition time of 10min for every lateral and anterior projection. Digital MG was done in all women according to standard clinical protocol. In 244 of 367 evaluated women we were able to determine results of preoperative US with high-frequency (7-18 MHz), high resolution linear array transducer. Final diagnosis was established by histological examination of removed breasts. Multicentric BC was defined as 2 or more distinct invasive tumors occupying more than one quadrant or additional lesions noted more than 4 cm from primary tumor. **Results:** According to histopathological examinations multicentric BC was diagnosed in 46 of 367 (12.5%) patients. SMG was more effective than MG in detecting multicentric breast cancer: sensitivity - 83% vs 40% ($p<0.001$), specificity - 95% vs 98% ($p=0.02$), accuracy - 96% vs 88% ($p<0.001$), positive and negative predictive values - 85% vs 56% ($p=0.004$) and 97% vs 91% ($p<0.001$), respectively. Histologically multicentric BC was revealed in 35 of 244 women that had US of the breasts. Sensitivity, specificity, accuracy, positive and negative predictive values for US were 37%, 96%, 87%, 59% and 90%, respectively. SMG significantly ($p<0.001$) outperformed US for all diagnostic characteristics except specificity. Combination of MG and SMG characterized by increased sensitivity (94%), 93% specificity, 93% accuracy and positive predictive value of only 68%. Obtained results help us to propose diagnostic algorithm for selection patients with early breast cancer for breast-conserving surgery and accelerated partial breast irradiation. **Conclusion:** SMG is significantly more sensitive (83%) than MG (40%) and US (37%) in detection of multicentric BC. Taking into account very promising positive predictive value (85%) of SMG this procedure can be considered as a useful tool to guide oncologists to a more appropriate surgical and radiotherapy treatment.

EP-0411**Iodine-125 radioactive seed: A good option for locating non-palpable breast lesions**

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Purpose: Radioguided surgery using iodine-125 radioactive seeds (RSL) is shown as a feasible technique in the localization of non-palpable breast lesions, with comparable results to the use of the guidewire (WGL), which is the reference technique at our institution. We present the results obtained in our center with the use of iodine-125 seeds in the localization of non-palpable breast lesions. **Subjects & Methods:** Prospective observational study of patients undergoing surgery of breast cancer, in some cases with neoadjuvant chemotherapy, from 2015 to 2017. The placement of iodine-125 seed in the lesion was performed by ultrasound or mammography up to one week before in most patients. The distance of the seed to the skin and to the anterior and posterior borders of the lesion were measured for an adequate planning of the volume to be resected. During surgery, we used a gamma probe with a gamma radiation emission peak centered at 27KeV. The surgical incision was made at the point of maximum activity. Sentinel lymph node biopsy (SLNB) was performed in selected cases. Histological analysis of the specimens was performed considering free margins the absence of tumor in the ink. **Results:** Eighty-five women (mean age: 59.82 ± 11.8 years), 11 with neoadjuvant chemotherapy, mean size of the lesion at diagnosis (mm): 16.125 ± 7.52 ; days elapsed since seed placement to surgery: 3.81 ± 3.09 . Histology: invasive ductal carcinoma (83.5%), invasive lobular carcinoma (9.4%), others (7.1%); molecular subtypes: luminal A (43.5%), luminal B (35.3%), HER2-positive (8.3%), basal-like (2.4%). The median size of the surgical specimens was 103.82cm^3 . There was involvement of surgical borders in 21.2% of the cases, with a re-operation rate of 6.3%. The location of the lesion using gamma probe during the surgery allowed a more accessible approach and less cosmetic damage. Likewise, the possibility of placing the iodine-125 seed on days before surgery reduces scheduling conflicts between the radiology department and surgical department. **Conclusion:** Our results show how the use of iodine-125 radioactive seeds is feasible in the localization of non-palpable breast lesions, with a re-operation rate and surgical specimens volume similar to those described in the literature in both RSL and WGL, with the advantage, versus WGL, of being able to place the seed several days before surgery.

EP-0412**Pretreatment Heterogeneity Predicts Treatment Outcome Of First-line Chemotherapy In Patients With Metastatic Triple Negative Breast Cancer**

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Purpose: Intra-tumoral heterogeneity of 18F-FDG uptake in primary tumor has proven to be a surrogate marker for predicting treatment outcome in various tumors. However, the value of intra-individual heterogeneity in metastatic diseases remains unknown. The aim of this study was to evaluate pretreatment PET/CT 18F-FDG based heterogeneity for the prediction of first-line

treatment outcome in metastatic triple negative breast cancer (mTNBC). **Methods:** mTNBC patients from three clinical trials (NCT00601159, NCT01287624 and NCT02341911) with whole-body 18F-FDG PET/CT scan before first-line gemcitabine/platinum were included. The maximum of standard uptake value (SUV) across all metastatic lesions (MAX) and heterogeneity index (HI) on the baseline PET/CT were assessed. Optimal cut-offs were determined by time-dependent receiver operator characteristics (ROC) analysis. Progression-free survival (PFS) and overall survival (OS) were estimated by Kaplan-Meier method and compared by log-rank test. **Results:** A total of 42 mTNBC patients were included in this study. The median PFS of patients with high HI-T (>1.9) and high MAX-T (>10.5) was significantly shorter than patients with low HI-T (<1.9; $p=0.049$) and low MAX-T (<10.5; $p=0.001$). In terms of OS, only high MAX-T was significant for poorer outcome ($p=0.013$). The ROC curve analysis confirmed the predictive value of MAX and HI in mTNBC patients. The AUC for MAX-T and HI-T was 0.75 and 0.65, indicating a higher predictive accuracy than conventional clinical risk factors. **Conclusions:** HI and MAX measured among metastatic lesions on pretreatment 18F-FDG PET/CT scans could be potential predictors of first-line treatment outcome in patients with mTNBC.

EP-0413

Metabolic activity in relation to Bioscore in breast cancer

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Introduction: Biologic factors besides anatomic stage play important role in treatment decision in breast cancer patients, thus some of them were incorporated in the 8th edition of AJCC staging system. However the MD-Anderson Bioscore is not incorporated in the present edition, it provides good prognostic value in non-metastatic BC patients. The aim of this study is to find correlation between biologic/anatomic prognostic factors, and FDG PET/CT parameters. **Methods:** We retrospectively assessed baseline [F18]-FDG PET/CT scans of 89 breast cancer patients seen in our institute between October of 2008 and October of 2015. Inclusion criteria were largest tumor diameter more than 2 cm, lack of oncological treatment at the time of the examination, available postoperative histological results including tumor grade (G), estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor (HER2) status. If patients received neoadjuvant therapy, we evaluated the histological results of the core biopsy samples obtained before treatment. We searched correlation between SUVmax value of the primary tumor and the components of Bioscore system (G, ER, HER2 status, and pathologic stage) and with the Bioscore itself. The correlation between SUVmax and PR status, triple negative phenotype, the presence of local/distant metastases was also examined. In addition, we evaluated the connection between the aforementioned clinicopathological parameters and the following selected heterogeneity parameters: Contrast, Correlation, Covariance, Entropy, Homogeneity. **Results:** The SUVmax value of the primary tumor was significantly higher in high grade (G3) tumors than in low

grade (G1, G2) lesions (9.25 vs. 5.58; $p<0.001$). Significantly elevated SUVmax was measured in ER negative (11.29 vs. 5.9; $p<0.001$), PR negative (10.05 vs. 5.42; $p<0.001$) and HER2 positive (12.04 vs. 6.64; $p=0.01$) subtypes. SUVmax value of the primary lesion showed significant correlation with Bioscore ($p<0.001$), however there was remarkable overlap between the individual groups. SUVmax was also higher when triple negative phenotype (10.22 vs. 6.58; $p=0.006$) or metastatic axillary lymph nodes (10.46 vs. 5.07; $p<0.001$) were detected. SUVmax well correlated with pathologic stage ($p<0.001$). The presence of distant metastases was not associated with significantly elevated SUVmax of the primary tumor (8.52 vs. 7.72; $p=0.121$). None of the examined heterogeneity parameters showed significant association with any of the studied prognostic markers. **Conclusion:** SUVmax showed significant association with most of the examined prognostic factors, thus may provide prognostic value. However, further investigations are needed. We found no connection between prognostic markers and studied heterogeneity parameters.

EP-0414

The prognostic value of F-18 FDG uptake in the supraclavicular lymph node (N3c) on PET/CT in locally advanced breast cancer patients with clinical N3c

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Purpose: We investigated the prognostic value of F-18 FDG uptake in the supraclavicular lymph node (SCLN) metastasis on positron emission tomography/computed tomography (PET/CT) in locally advanced breast cancer (LABC) patients with clinical synchronous ipsilateral SCLN metastasis (cN3c). **Subjects & Methods:** Fifty-five female patients with pretreatment F-18 FDG PET/CT were included. All were treated with curative intent by neoadjuvant chemotherapy, surgery, and adjuvant radiotherapy. For semi-quantitative analysis, the maximum standardized uptake value (SUVmax) of the primary tumor, axillary lymph node (ALN), and SCLN were normalized by the mean SUV of the liver (defined as SUVR-Tumor, SUVR-ALN, and SUVR-SCLN, respectively). Cox proportional hazards models were used for prediction of disease-free survival (DFS) and overall survival (OS) using clinicopathologic and PET/CT parameters. Differences in DFS and OS were assessed by the Kaplan-Meier analysis. **Results:** Twenty-three patients (41.8%) experienced recurrence, and 13 patients (23.6%) died during follow-up (median, 70.0 months; range, 6-128 months). In multivariate analysis, SUVR-Tumor >3.26 (hazard ratio, 7.26; 95% confidence interval, 1.58-33.31; $p=0.01$) and SUVR-SCLN >1.05 (hazard ratio, 8.47; 95% confidence interval, 1.09-65.87; $p=0.04$) were significant for predicting OS. No clinicopathologic or PET/CT parameters were prognostic for DFS. The Kaplan-Meier analysis revealed poorer 5-year OS rates in patients with SUVR-Tumor >3.26 (64.7% vs. 89.7%; $p=0.01$) and SUVR-SCLN >1.05 (67.8% vs. 95.0%; $p=0.02$). **Conclusions:** Both high SUVR-Tumor and SUVR-SCLN on F-18 FDG PET/CT predict poor OS in LABC patients with cN3c. Of the metastatic lymph nodes, metabolic activity of the farthest nodal station (SCLN) is important in predicting OS.

EP-0415

Our experience in SNOLL technique in non palpable breast cancer

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Purpose: To assess the effectiveness of the SNOLL technique through our 9 years of experience in non-palpable breast cancer patients. **Subjects and Methods:** 423 patients (98.5% women; mean: 59yo) with non-palpable breast cancer whom fulfilled the SLNB guidelines were included. Standard procedure: 4mCi of nanocoloids were injected intratumorally under ultrasound control 24 hours before the surgery, followed by planar scan acquisition and dermal-marking of both tumour and sentinel lymph node (SLN) projections. Mixed technique (radiotracer and blue-dye) was performed during the surgery, by using a gamma-probe (Navigator®) and a portable gammacamera (Sentinella®) for guiding the lumpectomy. In-vivo and ex-vivo images were taken, delineating its margins with a 99mTc pointer. A true SLN was considered when activity-index regarding background was >3:1 for in-vivo, >10:1 for ex-vivo images and/or dyed with blue-dye. Images of the surgical field were obtained with Sentinella® in order to verify that there was no remaining focus of activity. **Results:** Tumour detection rate was >98%. The mean size of the lumpectomy specimen was <6cm. The surgical margin widening was performed in almost 50% of cases due to affected or insufficient margin (23.6% and 37.4%) and macroscopic aspect or persistence of remaining activity (38.8%). The surgical margin widening was positive only in 18.5%. SLN identification rate was 98.5% (average of 2.2 nodes removed per patient), mostly in the ipsilateral armpit. Drainage to internal mammary chain was observed in only 19.6% of patients. SLN was negative in 69.5%, positive in 13.4% and mic+ in 15.3%. Lymphadenectomy was performed in 16.7% of cases, being negative in 80.3%. **Conclusion:** SNOLL is a consolidated technique in our department that allows us to perform harpoon-free lumpectomies, with satisfactory rates of tumour and SLN detection in the same surgical procedure.

EP-0416

Do metabolic and volumetric parameters of lymph node in patients with locally advanced breast cancer have a prognostic value for survival and recurrence?

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Aim: Axillary lymph node status is considered as the most important prognostic factor for progression and survival in breast cancer. We aimed to investigate the prognostic value of metabolic parameters of primary tumor and lymph nodes obtained with 18 FDG PET/CT in patients with locally advanced breast cancer (LABC) who underwent neoadjuvant chemotherapy. **Material & Methods:** Fortyone patients (46.7yrs+/-10) with LABC were included. Metabolic and volumetric parameters of tumor (T) and lymph nodes (LN) for baseline and interim 18-

FDG PET/CT were measured. SUVmax, SUVmean, SULpeak, MTV (metabolic tumor volume) and TLG (total lesion glycolysis) values were calculated. Surgical results (complete pathological response:cPR and residual disease:R) were evaluated for the primary tumor (pCR-T) and lymph nodes (pCR-LN), separately. Overall survival (OS) and progression free survival (PFS) durations were obtained. Patients were divided into two groups based on the presence of progression during the follow-up period (Group I: no progression, Group II: Progression). **Results:** Lymph node metastasis was present in 35 pts (85.4%). Twelve patients (29.3%) had cPR-T and 29 (70.7%) had residual T, whereas 19 had residual LN (46%3). Median follow-up duration was 54.5 months (up to 66 mo.). Thirteen patients (31.7%) had metastasis and/or recurrence during the follow-up. Eight patient had died because of the disease. Non of the patients with pCR-T had progression or death due to disease. Only one patient with pCR-LN had progression and death. Metabolic and volumetric measures of T were not significantly different between group I and II. Metabolic parameters of LN were slightly higher in progressive group without statistical significance, whereas SUVmax-LN, SUVmean-LN, SULpeak-LN values were significantly higher in patients who did not survived. Volumetric parameters did not differ between groups. Patients with pCR-T had significantly longer PFS (Log-rank: p: 0.01) compared to those with residual T. Patients with pCR-LN had significantly longer PFS (Log rank p: 0.0001, 64.2 mo.+/-1.7 vs 39.3 mo. +/-5.2) and OS (Log-rank p: 0.009, 64.3 mo. +/-1.6 vs 51.6 mo.+7-4.3) compared to those with residual disease in LN. **Conclusion:** Presence of metastasis and level of metabolic activity of lymph nodes in locally advanced breast cancer as well as pathological response to neoadjuvant chemotherapy appear as important prognostic factors for disease free survival and overall survival.

EP-0417

Preliminary Microdose Clinical Trial: Comparison of Biodistribution of ⁶⁴Cu-NOTA-Trastuzumab with ⁶⁴Cu-DOTA-Trastuzumab in Breast Cancer Patients

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Purpose/Introduction: It was reported that PET/CT using ⁶⁴Cu-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-trastuzumab reflects human epidermal growth factor receptor 2 (HER2) expression in breast cancer patients. In this study, we evaluated the bio-distribution of ⁶⁴Cu-1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA)-trastuzumab, a novel PET tracer for the HER2, by comparing it with the ⁶⁴Cu-DOTA-trastuzumab. **Subjects & Methods:** This study was approved by the Ministry of Food and Drug Safety of Korea. Prior to injecting the radiotracer, 45 mg of cold trastuzumab was administered intravenously for 15 mins. PET was performed on 2 patients with breast cancer at 24 and 48 hours after injection of 296 MBq of ⁶⁴Cu-NOTA-trastuzumab. PET for ⁶⁴Cu-DOTA-trastuzumab was performed on 5 patients with breast cancer at 24 and 48 hours of 370 MBq of the tracer. The mean of maximum standardized uptake value (SUVmean) was evaluated from the blood, liver,

kidney, muscle, spleen, bladder, lung, and bone. **Results:** On both PET images, the overall values of SUVmean in each tissue decreased with time except for the bladder and kidney that showed an increasing pattern of SUVmean over time. In the liver, NOTA PET showed SUVmean of 4.82 ± 1.05 at 24 hours and 4.75 ± 1.13 at 48 hours, values of which are less than that of DOTA PET (6.67 ± 1.09 at 24 hours and 6.84 ± 1.04 at 48 hours). In the blood pool of PET image, the SUVmean of NOTA PET (10.89 ± 0.74 at 24 hours and 9.46 ± 1.29 at 48 hours) was greater than that of DOTA PET (7.71 ± 2.28 at 24 hours and 6.60 ± 1.44 at 48 hours). The SUVmean of bone showed slightly higher values for DOTA PET (2.11 ± 0.43 at 24 hours and 2.00 ± 0.21 at 48 hours) compared with those on NOTA PET (0.55 ± 0.20 at 24 hours and 0.46 ± 0.11 at 48 hours). Other tissues including kidney, muscle, spleen, bladder, and lung showed similar values of SUVmean on both NOTA and DOTA PET. Any adverse events related to ^{64}Cu -NOTA-trastuzumab and ^{64}Cu -DOTA-trastuzumab were not reported. **Discussion/Conclusion:** ^{64}Cu -NOTA-trastuzumab may be superior in detecting metastatic lesions in the liver due to lower uptake of normal liver tissue than ^{64}Cu -DOTA-trastuzumab. The biodistribution and safety results of ^{64}Cu -NOTA-trastuzumab were comparable with that of ^{64}Cu -DOTA-trastuzumab.

EP-0418

Impact of 18-F FDG PET/CT on staging of locally advanced breast cancer.

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Introduction: Breast cancer is the most frequently diagnosis cancer in women. 18-F PET/CT has become an essential tool in diagnosis and management of oncology patients, however, controversy still exist in relation of the application of PET/CT in staging of locally advanced breast cancer, and for some authors it is a second option. **Methods:** Between 2011–2017, patients with biopsy-proven of locally advanced breast cancer ($\geq T3\text{--}N2$) and/or potentially operable ($>3\text{cm}$) were retrospectively evaluated. In most cases, the initial staging imaging studies were realized using chest radiography, abdominal ultrasound and bone scintigraphy. Additionally, 18F-FDG PET/CT was realized to establish its diagnostic performance. All patients were asked to come for PET/CT with at least 6 h fasting. The images were obtained on a dedicated PET/CT scanner (Siemens, Biograph 16) 60 min after intravenous injection of 370 MBq of 18F-FDG. PET images were reconstructed by iterative method. **Results:** The results were confirmed by further imaging and at least one year follow-up. A total of 57 patients were evaluated. Mean age: 54 yo. The mean size of primary tumor was 55mm. In 42/57 there was a significance FDG uptake in the primary lesion. Axillary disease was found at diagnosis in 48 patients which was confirmed with PET/CT, axillary ultrasound and MRI in 87%. PET/CT detected 9 cases with N3 lymph node disease (internal mammary/supraclavicular lymph nodes), that were not diagnosed with the initial staging imaging techniques. Metastases were found in the initial staging in 20 patients. PET/CT diagnosed M1 bone metastases in 15 patients (7 of them had a negative bone

scintigraphy), M1 liver metastases in 3 patients (2 of them had negative abdominal ultrasound) and M1 pulmonary metastases in 7 patients (All of them with a negative chest radiography). PET/TC also diagnosed distant lymph nodes (M1) in 4 patients. According to the results, PET/TC indicated a higher clinical stage in 8 patients (14%). **Conclusions:** 18F-FDG PET/CT in staging of locally advanced breast cancer allows to recognize a more accurate clinical stage and to identify the most appropriate therapy.

EP-0419

Total Lesion Glycolysis Of Primary Tumor Using 18F-FDG PET/CT For Predicting Axillary Lymph Node Metastasis In Clinically N0 Breast Cancer

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Purpose: This study aimed to demonstrate the clinical significance of total lesion glycolysis (TLG) of primary breast cancer using 18F-FDG PET/CT to predict axillary lymph node (ALN) metastasis in invasive ductal breast cancer (IDC) with a clinically negative-axillary lymph node (cN-ALN). **Methods:** One hundred thirty-five patients, newly diagnosed with IDC with CN-ALN between July 2016 and October 2017, were retrospectively enrolled. We estimated volume-based PET/CT parameters including the maximum standard uptake value (SUVmax), metabolic tumor volume (MTV), and TLG, as well as clinicopathologic findings. All patients received breast surgery followed by pathologic axillary lymph node examination. **Results:** Within the 135 patients, 31 patients (23.0%) were diagnosed with pathologically proven metastatic ALN. In univariate analysis, SUVmax, MTV, and TLG of the primary breast tumor were correlated with metastatic ALN along with tumor size, lymphovascular invasion, CD34, and D2-40. On multivariate analysis, TLG (> 5.74 , $p = 0.009$) had independent significance for predicting ALN metastasis in IDC with cN-ALN. **Conclusion:** We demonstrated that TLG of primary tumors can be useful in predicting pathologic ALN metastasis in IDC patients with cN-ALN. This research was supported by grants from the National Research Foundation (NRF-2015R1C1A2A01054113 and 2015R1C1A1A02037051) of South Korea.

EP-0420

Molecular subtypes of invasive breast cancer Correlation between PET/CT and MRI findings

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Purpose: In our study, we investigated the diagnostic value of F18-FDG PET/CT and MRI findings in determining molecular subtypes of invasive breast cancer. In addition, the relationships between the volume measurements in PET/CT and MRI and the

pathological volume of the mass were evaluated. **Methods and Materials:** A total of 55 primary invasive breast cancer masses in 51 female patients who had histopathological diagnosis and underwent FDG PET/CT and MRI before therapy were retrospectively analysed. The correlations between molecular subtypes and SUVmax, SUVmean, MImean, MTV and HU values from FDG PET/CT findings; shape, margin, intratumoral enhancement, kinetic curve type and ADC values (based on 2013 BI-RADS MRI classification) from MRI findings were evaluated. In addition, the relationships between the pathologic tumor volume and the tumor volume measured by MRI and PET/CT were evaluated. **Results:** The SUVmax and SUVmean values of the luminal B subtype of invasive breast cancer were higher than the luminal subtype A ($p = 0.002$, $p = 0.017$, respectively); the triple negative subtype had a higher SUVmax value than the luminal subtype A ($p = 0.028$). There were statistically significant strong positive correlations between MTV and FTV ($p = 0.000$; $r = 0.857$); MTV and the pathologic tumor volume ($p = 0.006$, $r = 0.796$); FTV and the pathologic tumor volume ($p = 0.006$, $r = 0.921$). **Conclusion:** Our findings suggested that SUVmax value was superior to MRI findings in predicting molecular subtypes. In addition, we determined that MRI was superior to PET/CT in predicting the pathologic tumor volume.

EP-0421

Female-specific risk factors and genetic make-up: do they have a role in the aftermath of Radiotherapy for early breast cancer?

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Purpose: Radiotherapy (RT) reduces local recurrences and deaths from early-stage breast cancer (EBC). Excess long-term cardiovascular mortality in women treated with RT until mid-1980's and a higher incidence of ischemic heart disease (IHD) in left-sided EBC patients (LEBC) compared to right-sided ones have also been described. Late cardiotoxicity is still an issue with modern therapeutic regimens and a challenge is to detect early signs of RT-induced cardiovascular damage. Myocardial perfusion imaging (MPI) and coronary flow reserve (CFR) estimation may detect early endothelial dysfunction and predict IHD. Therefore, the aim of our study was to test MPI and CFR as early markers of RT-associated endothelial damage. **Materials and methods:** MPI was performed in 70 patients with EBC (median age at diagnosis, 52.22 years) before RT using dipyridamole/rest Tc-99m Tetrofosmin gated SPECT and in 25 of these CFR was estimated. MPI was considered abnormal when reversible and/or fixed defects were detected. **Results:** At baseline 12 patients showed myocardial perfusion defects (MPD) and 11 had IHD risk factors. After RT 7 among 17 patients with a normal pre-RT MPI showed MPD; 3 of 12 patients with MPD at baseline increased MPI abnormalities. Nine patients with MPD showed angiographically normal coronary arteries. Patients with baseline or post-RT MPD did not have clinical cardiac events in the follow up period. **Conclusions:** Our observations highlight that a stress test at baseline in patients with a high likelihood of a

"vulnerable endothelium" can identify patient at highest risk of RT-induced vasculotoxicity, that the presence of "female specific risk factors" should be investigated at baseline and, lastly, that CFR estimation may be a "gender-specific" diagnostic tool to detect microvascular damage of IHD. Therefore, a "sex & gender" approach to female oncologic patients is also needed to reduce the burden of IHD.

EP-0422

Impact of (18) F-FDG PET/CT in detection of breast cancer recurrence

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Aim: impact of (18) F-FDG PET/CT in assessment and management of patients with breast cancer recurrence. **Materials and Methods:** We analyzed 32 patients (age 34-80, mean 55.4 ± 11.5) with breast cancer diagnosis who were referred to (18) F-FDG PET/CT imaging by their oncologist because of suspected breast cancer recurrence. They have elevated CA 15-3 marker (11), suspicious CT/MR findings (19) and bone scintigraphy (11), suspicious mammography (1), positive abdomen ultrasound (1), positive breast (1) and neck ultrasound (1). Patients were examined with whole-body (18) F-FDG PET/CT approximately 60-90 minutes following iv. injection of (18) F-FDG. Images were interpreted independently by 2 nuclear medicine physicians and 1 radiologist. Impact of the images result on management of patients was evaluated on the basis of clinical decision obtained from patient files. **Results:** Histological type of cancer included invasive ductal carcinoma (22), invasive lobular carcinoma (3), and one case each of tubular, papillary, apocrine, cribriform, medullar, mixed tubular/ductal/lobular and ductal/lobular carcinoma. PET/CT was positive in 19 patients (59%), 15 of them had distant metastases, most of them in bones, lungs and liver. 9/19 (47,36%) were treated with chemotherapy; 3/19 (15,8%) had combined chemo/radiotherapy; 5/19 (26,31%) were operated and confirmed patohistological metastatic disease in the neck, axilla, ovarium and lung. In 4/5 (80%) after surgery there has been a change of therapy, they were treated with chemotherapy, 1/5 (20%) had combined chemo/radiotherapy. In 2 cases (10, 52%) only follow-up was recommended. 2 patients had false positive result (inflammatory/degenerative change in IX rib) with withdrawal of scintigraphy finding in 3 months period and in mastoid bone confirmed with MRI that it is bone hemangioma. 8/11 (73%) with elevated CA 15-3 had positive PET/CT. PET/CT was negative in 13 patients (41%). False negative result had 2/13 (15, 4%) patients, one case with bone metastases confirmed with bone scintigraphy and metastases in the lung and liver seen on CT. They were further treated because of metastatic disease with lesions in liver, lungs and bones. Diagnostic significance: sensitivity 89, 48%, specificity 84, 61%, positive predictive value 89, 48%, negative predictive value 84, 61% and accuracy 87, 5%. **Conclusion:** High sensitivity, specificity, positive and negative predictive value determine (18) F-FDG PET/CT as a useful imaging modality in detection of breast cancer recurrence and in our study (18) F-FDG PET/CT had impact on future management on patients in 89.47 % cases.

EP-0423

Improved Lesion Visibility In Breast Cancer Patients Using Prone FDG-PET

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Aim: Breast FDG-PET/CT is typically performed with the patient in supine position. This may hamper optimal visualization of the primary tumor and axillary lymph nodes, because of breathing artifacts and gravity-related tissue compression. FDG-PET/CT in prone position might improve the qualitative and quantitative assessment of FDG-avid lesions. We evaluated the impact of prone imaging on lesion visibility with FDG-PET compared to supine imaging in breast cancer patients. **Materials and Methods:** We included 20 breast cancer patients who underwent a FDG-PET/CT scan with a state-of-the-art PET/CT scanner (Ingenuity TF, Philips Healthcare). Imaging was first performed in supine position, immediately followed by an acquisition in prone position using a breast support device (VANDERWILT techniques bv). PET images were reconstructed using a 3D ordered-subset iterative time-of-flight reconstruction with 2x2x2 mm³ voxels. On both supine and prone images, we determined the number of FDG-avid lesions, maximum standardized uptake value (SUV_{max}), mean standardized uptake value (SUV_{mean}), Total Lesion Glycolysis (TLG) and Tumor-to-Background-Ratio (TBR). Lesion visibility was associated with increased FDG-uptake of lesions as compared to the surrounding background, and corresponding CT abnormalities. The Wilcoxon signed-rank test was used to evaluate differences between prone and supine imaging. To study a possible bias due to time differences between both acquisitions, we calculated the Spearman's correlation coefficient (ρ) of the relative change of SUV_{max} (Δ SUV_{max}), SUV_{mean} (Δ SUV_{mean}), TLG (Δ TLG), TBR (Δ TBR) and the time difference between the two acquisitions (Δ t). **Results:** In 3 out of 20 patients, we found more lesions on prone PET images. In two of these patients, three additional breast lesions were found. In the other patient, an additional axillary lesion was found. Furthermore, 59 FDG-avid lesions were found on both types of images. Average SUV_{max}, SUV_{mean}, TLG and TBR were significantly higher on the prone images with increases of 11% ($p=0.031$), 10% ($p=0.006$), 24% ($p<0.001$) and 16% ($p=0.001$), respectively. SUV_{max} and SUV_{mean} increased in 66% and 73% of the lesions respectively; TLG and TBR both increased in 71% of all lesions. The correlation coefficients between Δ t and Δ SUV_{max}, Δ SUV_{mean}, Δ TLG and Δ TBR were -0.017, 0.027, -0.19 and -0.025 respectively. None of these correlation coefficients deviated significantly from zero ($p\geq 0.15$). **Conclusion:** This pilot study shows that prone FDG-PET imaging can improve lesion visibility in breast cancer patients compared to supine imaging. Moreover, more breast lesions and axillary metastases might be detected with prone imaging. This may improve diagnostic performance and influence decision-making regarding treatment plans.

EP-0424

The value of SPECT/CT for evaluating solitary spine lesion discovered by the planar bone scintigraphy in patients with breast cancer

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Purpose: The purpose of this study was to investigate the role of SPECT-CT in evaluating solitary spine lesion discovered by the whole-body planar bone scintigraphy (BS). **Materials and Methods:** We prospectively studied 452 patients (mean age 65 years) with breast cancer. All of them consecutively underwent ^{99m}Tc-methylene diphosphonate (MDP) whole-body planar scintigraphy and 2-bed SPECT-CT. Patients with solitary focal uptake radiotracer in the spine on BS were selected. All lesions were analyzed with the SPECT/CT. **Results:** Our study found that 26 patients (6%) had solitary bone lesions on BS data. SPECT-CT correctly excluded bone metastases in 15 (58%) and confirmed in 8 (31%) of these patients. Three patients (12%) retained unclear bone changes on SPECT-CT and require the follow-up. **Conclusion:** SPECT-CT can help verify most (89%) of solitary lesions revealed with a routine whole-body planar bone scintigraphy.

EP-0425

Is Dual-Energy Computed Tomography-Based iodine Content Correlate with Metabolic Parameters of 18F FDG PET/CT in Breast Cancer Patients?

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Purpose: The aim of this study is to investigate the correlation between metabolic parameters of FDG PET/CT and Dual-Energy Computed Tomography (DECT)-based iodine content (IC) in breast cancer patients. **Material and Method:** Forty-five newly diagnosed breast cancer patients (37 IDC, 6 IDC, 1 mixed, 1 mucinous carcinoma, mean age, 48.42 $\pm$ 10.63) were evaluated retrospectively. FDG PET/CT parameters (SUV_{max}, SUV_{mean}, SUL_{peak}) and DECT-based mean iodine content (IC_{mean}) [mg/dL] were measured. We also evaluated the correlation between normalized IC, (NIC), [Lesion IC_{mean}/Aorta IC_{mean}] and normalized SUV (NSUV) [LesionSUV /Aorta SUV_{mean}] values. The mean study interval between FDG PET/CT and DECT was < 22 days. Statistical analyses were performed using SPSS 19. Pearson correlation was used to analyze between DECT and FDG PET/CT values. **Results:** There is no correlation between IC_{mean} and SUV_{max} ($r=0.092$, $p=0.547$), SUV_{mean} ($r=0.0790$, $p=0.607$), SUL_{peak} ($r=0.087$, $p=0.569$). Also we did not find any correlation when we compared normalized values [Between NIC_{mean} and NSUV_{max} ($r=-0.214$, $p=0.158$), NSUL_{peak} ($r=-0.123$, $p=0.427$), NSUV_{mean} ($r=-0.204$, $p=0.178$)]. **Discussion:** We could not find correlation between DECT and FDG PET/CT parameters. DECT is associated with tumor perfusion, while FDG PET/CT shows glucose metabolism. Tumor perfusion and glucose metabolism are

different physiologic processes. Metabolism of the tumor is not always associated with perfusion. The clinical contributions of these two imaging modalities are different.

EP-0426

The role of a dedicated breast PET (MAMMI PET) in patients treated with neoadjuvant chemotherapy for locally advanced breast cancers: better than other parameters or not

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Purpose: The histological response to neoadjuvant chemotherapy (NACT) is an important prognostic factor for patients with locally advanced breast cancers (LABC). The aim of this study is to compare the role of a dedicated breast PET (MAMMI PET), MRI, and serum values of CA153 to assess response to preoperative NACT in patients with LABC. **Subjects & Methods:** Fourteen patients with LABC were retrospectively evaluated. Most of them received up to 6 cycles of preoperative NACT followed by curative surgical resection of the primary tumor. Response to treatment was assessed using MAMMI PET (EORTC guidelines), MRI (RECIST criteria) and CA 153, performed at least baseline, after 2-4 cycles and pre-operatively. Final histopathology following surgery after six cycles of NACT served as reference. **Results:** The size of the primary tumor ranged from 0.57cm to 4.9cm, the maximum value of the standardized uptake value of FDG (SU-Vmax) ranged from 9.35 to 98.4 (mean, 25.68) and the T/B ratio (tumor/background) ranged from 3.2 to 12.64 (mean, 8.46). Post-NACT MAMMI PET examinations showed complete metabolic response in 2 (14.3%) patients, partial metabolic response in 10 patients (71.4%), stable metabolic disease in 1 (7.1%) patient. In contrast, only 4 patients achieved a RECIST response on post-NACT MRI, while 9 patients had stable disease. In addition, the serum values of CA153 of these patients were also detected. 10/14 patients had elevated serum CA153. After NACT, 2 patients' CA153 decreased sharply (>50%) and 8 patients' CA153 decreased slightly (<50%). Of note, one patient went early resection due to clinical progression after an initial response to 2 cycles of NACT, which was confirmed by MAMMI PET but not on MRI or CA153. **Conclusion:** In this small series, MAMMI PET is more reliable than other parameters in evaluating response to NACT in LABC patients, changed management in one patient. These results warrant prospective validation in larger cohort of patients.

EP-0427

Online access to diagnostic reports seen in the perspective from breast cancer patients

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Introduction: The Danish eHealth portal *Sundhed.dk* has provided quick and easy access to health care data for patients over the past years. Hence, patients can access results of own diag-

nostic tests online prior to a scheduled clinical visit. The diagnostic report may be difficult for the patient to understand and give rise to misinterpretations, which may again cause unnecessary frustration and anxiety. **Aim:** This study sought to investigate the use of online access to diagnostic reports on *Sundhed.dk* and aimed to identify main attitudes towards it including potential barriers and facilitators. **Design and method:** A prospective mixed-methods study was conducted at our institution during 2018. The study comprised 46 women with metastatic breast cancer who were regularly imaged with FDG-PET/CT or CT. All patients received an online questionnaire regarding use and attitudes towards online access of diagnostic reports. Furthermore, semi-structured interviews were made with four women regarding their more profound personal experience. Descriptive statistics were performed for survey data, and qualitative data were transcribed and analyzed using thematic coding. **Results:** A total of 38 (83%) women completed the survey; 23 (61%) were aware of the opportunity of accessing reports online, while 15 of those (40%) actually used the online access. We found no difference in age between women who used online access (n=23, mean 68 years, range 42-84) and women who did not (n=15, mean 69 years, range 48-80) (p=0.09). Reasons for not using online access were: a) anxiety of reading the diagnostic report without help of a health care professional and b) fear of misinterpretation of results due to the medical terminology used in reports. The main reason for using online access was a wish of increased insight in diagnosis and treatment in order to increase self-efficacy and empowerment. The interviews revealed that women using online access took an active and critical patient role and used it to maintain overview of the stage of their disease. Nevertheless, some patients experienced difficulties in understanding the consequences of diagnostic reports for their future treatment. **Conclusion:** Most breast cancer patients had a positive attitude regarding electronic access to diagnostic reports, and women using this opportunity experienced a greater participatory role in their disease and its management. Some patients also experienced dilemma and increased distress given this opportunity. This study suggests that direct access to electronic diagnostic reports should be considered along with a health care support function to ensure optimal patient care.

EP-35

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology ->
Colorectal, malignant

EP-0428

Diagnostic performance of PET/MR in identifying high-risk primary rectal cancer patients

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Purpose/Introduction: To assess the diagnostic performance of PET and MR parameters to identify high-risk rectal cancer

patients. **Subject & Methods:** Fifty-three patients with biopsy proven rectal adenocarcinoma were submitted to whole-body PET/MR for primary staging. One reader analyzed the MR (blinded to PET findings) regarding T stage, mesorectal fascia involvement, extramural vascular invasion, and presence of locoregional nodal disease. Another reader (also blinded to the high-resolution part of pelvic MR) measured the semiquantitative PET parameters using a dedicated software (PETVCAR, GE Healthcare) and assessed the M stage. Standard of reference was biopsy when feasible or imaging follow-up. Mann-Whitney test was performed to compare PET parameters between high and low-risk patients. ROC analysis was also used to define the diagnostic performance of PET parameters in identifying the tumor risk. **Results:** PET-volumetric parameters, namely TLG and MTV, performed better than SUVmax and mean to distinguish low and high-risk patients. MTV (48.9 vs. 18.4, $p = 0.006$) and TLG (629.4 vs. 190.4, $p = 0.008$), but not SUVmax (23.4 vs. 19.2, $p = 0.306$) or SUVmean (11.7 vs. 9.9, $p = 0.285$) were significantly higher in high-risk patients. Patients with advanced T stage, positive regional node and metastatic disease also presented significantly higher MTV and TLG values. No difference was found in any PET parameters in patients according to the involvement of mesorectal fascia and presence of EMVI. The AUC to distinguish low and high-risk patients was 77.9% ($p = 0.006$) for MTV and 77.0% ($p = 0.008$) for TLG and the best cut-off value (sensitivity of 83.7% and specificity of 70%) of MTV and TLG to detect high-risk patients was 16.1 and 172.8, respectively. **Discussion/Conclusion:** In addition to MR adverse risk factors, the volumetric-based PET parameters (MTV and TLG) allow the identification of high-risk patients, which could tailor therapy management. Thus, PET/MR provides morphologic and metabolic parameters to identify high-risk rectal cancer patients that need more detailed staging in a whole-body setting. The volumetric-based PET parameters (MTV and/or TLG) might be included in clinical reports instead of SUVmax.

EP-0429

Usefulness of pre-treatment 18-F FDG PET/CT for tumor relapse in rectal cancer achieving pathological complete remission after neoadjuvant chemoradiation therapy and curative resection

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Purpose: This study aimed to investigate metabolic parameters in pretreatment 18-F FDG PET/CT scans for the prediction of tumor relapse after pathologic complete remission achieved in locally advanced rectal cancer (LARC) patients, who have undergone neoadjuvant concurrent chemoradiation therapy (NCRT) and complete resection. **Material and Methods:** We retrospectively analyzed 44 patients, between December, 2008 and August 2017 who underwent pretreatment 18-F FDG PET/CT, NCRT, curative resection and achieved pathologically complete remission. Patients were observed for post-operative tumor recurrence. The standardized uptake value (SUV, mean, and maximum), total lesion glycolysis (TLG) of rectal cancer lesions were calculated. TLG of primary rectal region (T-TLG) and

lymph nodes (N-TLG) were separately evaluated and combined TLG (total-TLG). Statistical analysis was performed on these PET parameters and clinical parameters for prediction of recurrence. **Results:** LARC recurrence was seen in 6 patients (3.1 to 114.5 months). Of the clinical, pathologic, and PET parameters, CEA, T-TLG, total TLG was significantly correlated with LARC recurrence in univariate analysis and N-TLG was borderline significant ($p = 0.049, 0.048, 0.043$ respectively). However, multivariate analysis revealed that CEA, N-TLG and total TLG significantly predicted tumor recurrence ($p = 0.072, 0.014, 0.047$, respectively). Univariate Cox regression analysis showed that N-TLG and T-stage can predict LARC recurrence, but multivariate Cox analysis showed that only N-TLG was significantly associated with LARC recurrence (OR = 1.060, $p = 0.029$). **Conclusion:** Large lymph node metabolic burden (N-TLG) was associated shorter RFS in LARC recurrence after complete remission

EP-0430

Roll Of PET/MRI In Assessing The Response To Neoadjuvant Chemoradiation Therapy In Patients with Locally Advanced Rectal Cancer

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Aim: To assess the value of simultaneous PET-MRI with 18F-FDG in predicting the pathologic response in patients with locally advanced rectal cancer (LARC) treated with preoperative chemoradiation therapy (CRT). **Materials & Methods:** We performed a retrospective analysis from July 2015 to August 2017 of all the patients with LARC who underwent a PET/MRI study. Of 35 patients, we analyzed the metabolic and morphologic changes of the tumor in 25 patients with LARC (mean age 62.8 years, range 33–78y) treated with CRT. They all had a 18F-FDG PET/MRI study before and after the neoadjuvant therapy, consisting of a whole body (WB) and pelvis acquisition PET/MRI and a dedicated high-resolution rectal MRI with diffusion-weighted image (DWI). We calculated the SUVmax value and the apparent diffusion coefficient (ADC) value on DWI in both studies. The pathologic response by imaging was compared with histopathological examinations after surgery and then classified as complete response (CR) when there was no evidence of tumor or partial response (PR) otherwise. Patients without histopathological confirmation were excluded. **Results:** PET/MRI was interpreted as CR in 7/25 (28%) and as PR in 18/25 (72%). Patients with PET/MRI CR had a mean SUVmax pelvis value of 2.6 (0–4.3) a mean SUVmax WB of 2.7 (0–6.9) and a mean ADC value on DWI of 0.62 (0.52–0.76). Patients with PET/MRI PR had a mean SUVmax pelvis value of 7.0 (3.3–12.4), a mean SUVmax WB of 7.6 (2.6–13.9) and a mean ADC value of 0.51 (0.43–0.63). 5/7 patients with CR by PET/MRI had histopathological complete response. 10/18 patients with PR were confirmed by histological results, 6/18 had a histopathological CR and 2/18 were not undergoing surgery (wait and see approach). Our study reflects that in 60% of cases (15/25) both PET/MRI findings and histopathological results were consistent, with higher values of SUVmax and lower ADC

values in those patients with PR. **Conclusion:** Simultaneous PET/MRI can provide metabolic, morphologic and functional information of tumors after neoadjuvant chemoradiation therapy in patients with locally advanced rectal cancer. In combining this information, more accurate assessment of residual tumors after CRT may be possible, although for accurate evaluation of the clinical role of PET/MRI in rectal cancer restaging after CRT, further studies with a larger population are warranted.

EP-0431

PET Pronostic Biomarkers Exploratory Analyses About Initial FDG-PET In Patients With Anal Carcinoma

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Introduction: In anal squamous cell carcinoma (SCC), pre-treatment prognostic factors able to identify more accurately patients with high risk of recurrence who may benefit from optimized treatment are lacking. There are increasing evidences that FDG PET examinations are useful in anal SCC management. Our objective was to explore, by two different analyses, the value of pre-treatment quantitative imaging to predict progression-free survival (PFS) in anal SCC patients. **Subjects & Methods:** We conducted a retrospective study on FDG PET examinations for 81 consecutive anal SCC patients at initial staging. Along with clinical variables (age, sex, T-stage, N-stage, HIV and human papilloma virus infections) collection, tumor and lymph nodes (LN) FDG metrics (SUV_{max}, TLG, MTV) were measured using 7 3D-thresholding methods on PET images: 3 with fixed SUVmax threshold (T35%, T41% and T50%) and 4 adaptative methods [M1¹, M2², M3³, M4⁴]. Each semi-quantitative PET variable is associated with 26 events free survival as a residual disease, local recurrence, distant metastasis or deaths at 0.10 threshold in univariate analysis. A multivariate analysis was conducted with an AIC criterion based Cox model. Evidence ratio (ER) was calculated for each model when PET variable remained significant after adjustment. Due to a small sized cohort with few events compared to the information to be processed, 2 analyses were conducted according to 4 quartiles and median FDG quantitative parameters respectively. **Results:** Six (7.5%), 18 (22.2%), 39 (48.1%) and 18 (22.2%) patients had respectively disease of stage I to IV. Median follow up was 3.3y (2.5-5y). As clinical data, male sex was the uniquely prognostic biomarker (HR: 3.32; CI: 1.38-8.02; p=0.007) of progression free survival (PFS) on univariate analysis. Out of the 57 tumor image intensity features, only 27 were predictive of PFS (0.0032<p<0.0395). The four-quartile multivariate analysis ordered total MTV_{tumor+LN}, TLG_{LN}, MTV_{tumor} with higher ER (1.0 to 4.8) for T35%, T41%, M2 and M4 methods whereas median multivariate analysis exhibited higher ER (1.0 to 5.2) for T35%, T41% and M1 MTV_{tumor} respectively. **Conclusion:** Whatever how quantitative FDG PET data analysis was conducted (quartile or median) "TLG_{LN}, total MTV or MTV_{tumor}" seemed to

be the best pronostic variables to assess PFS in this anal SCC population. An external cohort is warranted to ascertain these results in terms of defined variables and divisions. 1. Vauclin et al. doi:10.1088/0031-9155/54/22/010. 2. Black et al. Int J Radiat Oncol Biol Phys, 2004. 3. Nestlé et al. EJNMMI, 2007. 4. Tylski et al. doi:10.2967/jnumed.109.066241.

EP-0432

Relationships Between Hypoxia Induced Factor-1 α and 18F-FDG PET/CT Parameters in Colorectal Cancer

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Aim: The hypoxia-inducible factor 1 (HIF-1) has an critical role in oxygen homeostasis and it is transcriptional activator of angiogenesis, erythropoiesis, iron and glucose metabolism. Glucose metabolism rate is increased in some tumors via HIF-1 α . In this preliminary study our aim is to evaluate the relationship among hypoxia in colorectal cancer, PET parameters, necrotic tissue size and pathologic prognostic factors via using HIF-1 α .

Materials and Methods: In our study there were 63 patients (22F, 41M) who were diagnosed with colorectal cancer via colonoscopic biopsy. All patients staged with preoperative PET/CT and operated subsequently. All operation specimens evaluated pathologically and diagnosis confirmed. In immunohistochemical evaluation scoring was done according to nuclear HIF-1 α expression, staining density and intensity. Metabolic tumor volume (MTV) was calculated via PET images and tumor volume was calculated via CT images. Percentage of tumor necrosis calculated by difference between tumor volume and MTV. Total lesion glycolysis (TLG) was calculated by multiplying MTV by SUVmean. **Results:** Tumors were located rectum in 24 patients (38.1%) and colon in 39 patients (61.9%). There was moderately meaningful positive correlation between tumor SUVmax and percentage of tumor necrosis when considering all patients (r=0.443). There were no statistically significant difference between HIF-1 α expression levels and tumor SUVmax, TLG, MTV and percentage of tumor necrosis (p>0.05). There were no statistically significant difference between HIF-1 α expression levels and tumor stage, lymphovascular invasion, perineural invasion and extracapsular/capsular lymph node involvement (p>0.05). Significant nuclear immunohistochemical staining was not seen in tumor cells which adjacent to necrosis area. On the other hand strong nuclear immunohistochemical staining was seen in tumor cells which adjacent to invasive border, inflammatory cells and fibroblasts. **Conclusion:** Existence of positive correlation between tumor SUVmax and percentage of tumor necrosis shows that there is hypoxic cells in cancer tissue which has high FDG uptake. But relationship between existence of HIF-1 α and enhanced glucose metabolism and pathologic prognostic factors of tumor was not showed. No significant nuclear immunohistochemical staining adjacent to necrosis area and strong nuclear immunohistochemical staining in tumor cells which adjacent to invasive border, inflammatory cells and fibroblasts make think us that HIF-1 α can play a role in invasion area at tumor microenvironment.

EP-0433

Clinical workflow of PET/MR for primary staging of rectal cancer

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Purpose/Introduction: Analyze the clinical workflow of a PET/MR for rectal cancer staging, regarding MR imaging protocol, total scan time, prevalence and distribution of metastasis. **Subjects & Methods:** Fifty-five patients with rectal adenocarcinoma were submitted to whole-body PET/MR for primary staging. MR sequences and total scan time were recorded. One reader analyzed the MR (blinded to PET findings) for locoregional staging. Another reader (blinded to the high-resolution MR of the pelvis) analyzed the PET/MR according to T, N and M staging. A third blinded reader analyzed only the liver MRI. Standard of reference was biopsy when feasible or imaging follow-up. **Results:** PET/MR workflow consisted of a dedicated pelvic MR, including high-resolution T2w and DWI, followed by whole-body PET/MR from head to mid thigh, ending with a T2w and DWI of the liver. Any dedicated MR sequence was used for the thorax. The mean total acquisition time of PET/MR was 64 minutes, ranging from 53 to 90 minutes. The PET acquisition time was on average 17 minutes, ranging from 12 to 25 minutes and the only-MR time was 52 minutes on average, including the dedicated pelvic and the liver sequences. One patient has not completed the exam due to claustrophobia and one patient was recalled due to low imaging quality (movement artifacts). For primary lesion detection, PET and DWI were positive in 54 out of 55 patients (one patient was negative even at MR). Metastatic disease was observed by PET/MR in 21 (38.2%) patients, mainly in the liver (12/21, 57.1%) non-regional lymph node (10/21, 47.6%), lungs (7/21, 33.3%) and peritoneum (1/21, 4.8%). Liver DWI detected 64 lesions in 12 patients and PET detected 62 lesions in the same 12 patients. Any brain metastasis was found. **Discussion/Conclusion:** PET/MR for rectal cancer staging is feasible, with a tolerable scan time and showing a high incidence of synchronic metastasis. DWI of the liver and of the rectum could be omitted in a staging/detection setting. PET coverage could start from skull base instead of vertex. Optimization of MR protocol would decrease scan time and allow the inclusion of other MR sequences.

EP-0434

Role Of ¹⁸F FDG PET/CT In The Evaluation Of Distant Metastases In Anal Carcinoma Patients

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Background: Anal squamous cell carcinoma is a rare cancer. However, its incidence is increasing mostly in patients with HIV and HPV infection. At initial staging, regional MRI or endo-anal ultrasound should be included, as well as TC for detection of distant metastasis. However, all these techniques fail to differentiate local recurrence from post-treatment inflammatory changes. Although with relatively small samples, there is some evidence supporting the clinical impact of ¹⁸F-FDG scanning in

these patients. **Objective:** It is well known that the diagnoses of distant metastases is clinically relevant. Thus, the aim of our study was to investigate the value of ¹⁸F-FDG PET/CT for the assessment of systemic disease in patients with anal carcinoma. **Material and Method:** We retrospectively analyzed 35 patients who underwent PET/CT scans at our center from April 2011 to March 2018. 86 % of patients were women (n = 30). Mean age was 58.9 ± 9.6 yr. Scans were performed 60 minutes after the injection of 4.07 MBq/Kg ¹⁸F-FDG. The study was performed for initial staging in 17% (n=6) and for restaging in 83% (n=29). **Results:** Overall, PET/CT shows a detection rate of 80%. When performed as initial staging, PET/CT detected local lesions in 100% and regional/distant metastasis in 50% (mostly iliac and inguinal lymph nodes). In restaging, PET/CT was able to diagnose local recurrence in 58.6% and regional/distant lesions in 55.2% (iliac and inguinal lymph nodes in 11 patients, lung lesions in 4 and liver lesions in 3), with an overall detection rate of 75.8%, allowing a better treatment management. **Conclusion:** ¹⁸F-FDG PET/CT is a useful technique for the detection of systemic disease in patients with anal carcinoma with impact in treatment management.

EP-0435

PET/MR characterization of mucinous versus nonmucinous components of rectal adenocarcinoma: a comparison of tumor metabolism and cellularity

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Purpose/Introduction: To analyze the relation of mucinous component of rectal adenocarcinoma to FDG avidity and diffusion restriction. **Subjects & Methods:** Ninety-four patients with biopsy proven rectal adenocarcinoma were submitted to whole-body PET/MR for primary staging. One reader analyzed the MR (blinded to PET findings) regarding locoregional staging, including the presence of mucinous component. Another reader (also blinded to the high-resolution part of pelvic MR) analyzed the PET/MR according to T, N and M staging. Two different readers drawn in consensus the volume of interest (VOI) larger than 0.5 cm³ of the mucinous component (MC) and the non-mucinous component (NMC) of the primary tumor on high-resolution T2w sequence and propagated the VOI to PET, DWI and ADC. SUVmax, SUVmean, TLG, MTV, ADCmax, ADCmean and ADCmin values were recorded and compared using Mann-Whitney test. **Results:** Seventeen patients (18.1%) presented MC on MRI. The SUVmax and SUVmean of the NMC were significantly higher than of the MC (16.7 vs. 7.4, p = 0.002 and 13.4 vs. 5.4, p = 0.001). Any of the ADC values was significantly different between MC and NMC groups. Among the 17 patients with MC, 16 (94.1%) were at least mrT3b, 15 (88.2%) presented positive extramural vascular invasion, 14 (82.4%) had involvement of mesorectal fascia, 13 (76.5%) were N-positive and 8 (47.1%) presented distant metastasis, reinforcing the correlation of MC and tumor risk. **Discussion/Conclusion:** The MC identified on PET/MR presents lower glycolytic metabolism than the NMC and is associated with high tumor risk. Tumor cellularity was not different

between MC and NMC. Imaging readers should be aware of this pattern, recognizing that both primary and metastatic disease of mucinous tumors present low FDG avidity.

EP-0436

Comparison of F-18 FDG PET/CT and DWI-MRI in early assessment of neoadjuvant radiochemotherapy response in locally advanced rectal cancer patients

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Aim: The aim of our study is to evaluate if different metabolic parameters obtained by FDG PET/CT and DWI-MRI can aid in predicting neoadjuvant radiochemotherapy (RCT) response in locally advanced rectal cancer patients (LARC). **Material and Methods:** Patients diagnosed for LARC were included in this single-center prospective study. Patients have received neoadjuvant radiotherapy (50,4 Gy) and chemotherapy (Capecitabine and oxaliplatin based) followed by surgical resection. Patients had F-18 FDG PET/CT and MRI including diffusion weighted imaging (DWI-MRI) at initial staging, interim (2 weeks after onset of RCT) and after completion of RCT (post-Tx). SUV parameters (SUVmax, SUVmean, SUVpeak, SULpeak), MTV and TLG were recorded for PET images. Also, ADC values (b=400 and b=800) were measured for DWI-MRI. Finally, tumor regression grade (TRG) were obtained from postoperative histopathology results and included in the analysis. Spearman correlation analysis, Mann-Whitney U test and ROC analysis were performed for statistical analysis. **Results:** Total 20 patients were included in this study. Compared to initial PET scan, decrease in SUVmax, SUVmean, SUVpeak and SULpeak in interim PET were correlated with the same parameters in post-Tx PET scan (SUVmax: p=0.017, r=0.556; SUVmean: p=0.04, r=0.494; SUVpeak: p=0.008, r=0.604; SULpeak: p=0.027, r=0.519). No correlation was found for MTV and TLG, as well as for ADC values (p>0.05). Only 3 patients had TRG of 0 or 1 and scored as responders. Total 2 patients were followed without operation and was under complete remission for 6 months after completion of RCT and also scored as responders. On interim PET, no significant difference was found among change in SUV parameters between responders and non-responders. Total 15 patients had available ADC values and change in interim ADCmin value (b=800) was significantly different in the responder group compared to non-responders (p=0.026). ROC analysis revealed that a threshold value for change in ADCmin of >41.6% can identify responders with a sensitivity of 75% and specificity of 90.9%. **Conclusions:** FDG PET failed to detect therapy response during CRT in our cohort. However, DWI-MRI was found to be more promising in interim detection of CRT response.

EP-36

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Endocrine, malignant I

EP-0437

The Value of Somatostatin Receptor Scintigraphy (SRS) in Patients with NETG1/G2 Neuroendocrine Neoplasms of the Small Intestine (SI-NENs)

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Background: The aim of this retrospective study was to review the value of Somatostatin Receptor Scintigraphy (SRS) in initial detection of neuroendocrine neoplasms of the small intestine (SI-NENs), evaluation of tumour extent and as imaging follow-up after radical surgery in patients with confirmed well (NETG1) or moderate (NETG2) differentiated SI-NEN. **Subjects and Methods:** A total of 180 patients with confirmed SI-NEN were included. The SRS was performed to evaluation of primary SI-NEN, also to assess clinical stage of disease, based on current World Health Organization (WHO) classification and during clinical follow-up. Overall 534 examinations were performed using ^{99m}Tc HYNICTOC (Tekrotyd®; Polatom, PL). Images were acquired between 1 - 3 h after i.v. injection of radiotracer. The acquisition of head, neck, chest, abdomen and pelvis were performed using a whole-body (WB) SPECT/CT approach. WB-SPECT data was acquired in 60 projections using 128x128 matrix, 360° rotation, 25 s per projection, with no zoom. Reconstruction algorithms were based on the commercially available iterative reconstruction algorithm Evolution - OSEM (with resolution recovery), including 10 subsets and 4 iterations with standard Gaussian filter on a Xeleris workstation (GE Healthcare, USA). **Results:** There were 111 subjects with NETG1 (62%) and 69 subjects with NETG2 (38%). In 26 patients (14%) SRS was used to assessed initial diagnosis, overall 48 (9%) SRS were performed. Results were as follow: true positive (TP)=42 (87.5%), true negative (TN)=6 (12.5%), no false negative (FN) or false positive (FP) results of SRS (sensitivity and specificity of SRS per patient was 100%). In 145 subjects (81%) SRS was used in evaluation of clinical stage, overall 466 (87%) examinations were carried out. There were TP=389 (83%), TN=73 (16%), FN=2 (<1%) and FP=2 (<1%) results. The sensitivity and specificity per patient was as follows: 98% and 95%. The sensitivity and specificity per study: 99% and 97%. In 9 patients (5%) SRS was used as imaging follow-up after radical surgery, there were overall 20 examinations (4%). There were 4 (20%) TN and 16 (80%) TP re-

sults. In total, which consists of initial diagnosis/staging and follow-up, the sensitivity was 99% and specificity 96% per patient and per study sensitivity was 99.5% and specificity was 98%. **Conclusion:** SRS using ^{99m}Tc HYNICTOC is an excellent imaging modality in detection of primary NETG1/G2 SI-NEN. It also has highly significant value as an examination tool to assess clinical stage of disease and as an imaging follow-up after radical treatment.

EP-0438

Is 68Ga-DOTANOC PET/CT useful in patients referred for suspected NEN?

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Purpose/Introduction: to retrospectively assess the potential role of 68Ga-DOTANOC PET/CT in patients (pts) referred for suspected neuroendocrine neoplasms (NEN). **Subjects and Methods:** Data of pts undergoing 68Ga-DOTANOC PET/CT were prospectively collected in an electronic archive. Pts referred for suspected NEN between September 2017 and March 2018 were included. Suspicion of NEN was based on: i) equivocal morphological imaging (CT, MRI, US), ii) clinical symptoms and iii) laboratory data (increased NEN markers, e.g. cromogranin A). MEN1 pts underwent PET/CT as part of the routine clinical management and were therefore separately analyzed. PET/CT was performed according to EANM guidelines. **Results:** Among 282 pts studied with PET/CT, 63/282 pts (22.3%) were referred for suspected NEN (PET/CT resulted positive in 26/63, 36%). Equivocal conventional imaging findings were observed in 42/63 (66.6%). PET was positive in 23/42 (54.7%) cases (8 lung, 7 pancreas, 3 ileum, 5 NE lesions of unknown primary), negative in 17/42 (8/17 showed faint FDG positivity: 5 lung, 1 mediastinum, 1 small bowel and 1 pancreatic tail; 3/17 small bowel findings both FDG and DOTANOC negative; under PET detectability 4/17: 2 lung, 1 parathyroid, 1 liver; suspected lesion at site of biodistribution 2/17: adrenals) and inconclusive in 2/42 (faint uptake at pancreas uncinata process and liver). Increased markers or clinical symptoms or both were observed in 19 cases and PET/CT was positive in 2/19 (10%). In particular, PET/CT was negative in the 5/63 pts (7.9%) presenting with clinical NE-like symptoms only. Among 8/63 (12.7%) pts with increased NE markers, PET/CT was negative in 6 (4/6 in PPI therapy), positive in 1 and equivocal in 1. Among the pts presenting with both increased markers and NE-like symptoms (6/63 pts, 9.5%), PET/CT was positive in 1 and negative in 5. Only two MEN1 pts were included and PET/CT scan was positive in one case and negative in the other. **Discussion/Conclusion:** In pts with suspected NEN without pathologic confirmation, 68Ga-DOTANOC PET/CT was positive in approximately one third of cases. The lowest positivity rate was observed when suspicion was based on the mere detection of increased markers and/or the presence of NE-like clinical

symptoms. Equivocal conventional imaging findings were PET positive in approximately half the cases.

EP-0439

Pancreatic Head/Uncinate Process Increased Uptake At 68Ga-DOTANOC PET/CT: Frequency, Changes Over Time And Correlation With Diabetes

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Purpose/Introduction: Although mostly physiologic, pancreatic head/uncinate process (UP) variable 68Ga-DOTA-peptides uptake can represent a pitfall in PET/CT reading, especially when focal. Factors contributing to its appearance are not clear yet. An increased frequency of UP uptake has been reported in patients (pts) affected by diabetes mellitus (DM). **Aim:** Aim of the study is to describe the frequency of 68Ga-DOTANOC UP uptake and to evaluate its variations over time and its possible correlation with DM. **Subjects and Methods:** Pts who underwent 68Ga-DOTANOC PET/CT were included in a prospective electronic archive and those studied from September 2017 to February 2018 were analyzed. Exclusion criteria were i) CT/MRI showing UP lesions; ii) previous surgery at the UP. PET/CT was performed following standard EANM procedure. 68Ga-DOTANOC uptake at the UP was classified as diffuse or focal and compared with the pattern observed in previous PET/CT scans (if available) to evaluate changes over time. Increased UP uptake was also correlated with the presence of DM. **Results:** Overall, 172 pts were included [age median: 65ys; age range 20-87ys]. UP increased uptake was detected in 77/172 (44.8%) pts: focal in 15/77 (19.4%; mean SUVmax=6.8 ± 2.9 [3.3-16.4]), diffuse in 62/77 (80.6%; mean SUVmax= 6.8 ± 2.7 [2.9-13.0]). Previous 68Ga-DOTANOC PET/CT scans were available in 75/172 pts (43.6%) and were retrospectively reviewed (268 scans; range previous PET per pt: 1-20). In most pts the uptake pattern was stable over time (54/75 pts, 72%): undetectable in 43/75 pts (57.3%), focal in 2/75 (4.7%) and diffuse in 9/75 (12%). In 21/75 (28%) pts the uptake pattern varied over time: focal/diffuse in 5/75 (6.7%), focal/absent in 4/75 (5.3%), diffuse/absent in 11/75 (14.7%), absent/focal/diffuse in 1 (1.3%). DM was documented in 29/172 (16.9%) pts and was not present in 125/138 (in 18/172 DM data were not available). Among DM pts, only 10/29 (34.4%) presented UP increased uptake (focal in 3, diffuse in 7) and it was not more frequent than in non-DM pts (p=0.2). UP 68Ga-DOTANOC uptake was evident in 61/215 non-DM pts (48.8%; diffuse: 50/61, 82%; focal: 11/61, 18%). **Discussion/Conclusions:** Non-malignant UP 68Ga-DOTANOC uptake is a frequent finding, slightly higher than previously reported, and mostly presenting with a diffuse pattern. Comparing multiple PET/CT in the same pt, the uptake was mostly stable, however in approximately one third of cases it varied over time. In our

series, UP uptake frequency was not significantly different between DM and non-DM pts.

EP-0440

A step towards a multidisciplinary interpretative algorithm for indeterminate adrenal lesions: the value of visual and semi-quantitative 18F-FDG PET/CT and ceCT parameters.

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Purpose/introduction: To assess the value of 18F-FDG PET/CT and contrast-enhanced-CT (ceCT) visual and semi-quantitative parameters for indeterminate adrenal lesions' characterization.

Subjects & Methods: Records of patients (pts) referred to our Endocrinology Unit, between 2006-2016, for indeterminate adrenal lesions were retrospectively collected (n=113). Inclusion criteria were: 18F-FDG PET/CT, ceCT, hormonal profile performed before diagnosis; histological proof/clinical-radiological diagnosis (Standard of Reference) of adrenal hyperplasia/adenoma/carcinoma. PET/CT and ceCT scans were blindly revised. Visual (+/-; site; pattern) and semi-quantitative parameters were calculated (PET: Lesion SUVmax and mean=L, SUVmaxAdrenal/Lesion-to-SUVmeanLiver-Ratio=ALR, Adrenal-to-Contralateral-Adrenal-SUVmax-Ratio=AAR; ceCT: diameter (max, min in mm), Hounsfield Unit-HU (all phases), absolute and relative wash-out at late15min-phase). Lesions were grouped by: a) specific type; b) benign/malignant; c) secreting (SAGH)/non-secreting; d) cancer/lipid-poor-atypical adenoma. All clinical (age, gender, cortisol-post-dexamethasone-suppression-test), PET and ceCT data were included in statistical analyses (SPSS; p<0.05) to search for possible significant associations/predictors. Diagnostic performances (AUC) and optimal cut-offs (ROC) were also evaluated. **Results:** Overall, 36 pts were included: 32/36 (89%) benign, in particular 23/32 adenomas [17/23 lipid-rich (4/17 SAGH); 6/23 lipid-poor/atypical (2/6 SAGH)] and 9/32 hyperplasia (5/9 secreting); 4/36 (11%) carcinomas. Considering PET-only, there was a statistically significant difference in SUVmaxL, SUVmeanL, ALR between lesion types (p=0.008; 0.011; 0.009) and between benign/malignant (p=0.007; 0.006; 0.004). A strong positive correlation with visual PET (+/-) was found too (p=0.004; 0.008). Diagnostic performance resulted statistically significant only in discriminating benign/malignant, when specifically using either visual analysis (p=0.016; sensitivity100%, specificity75%, PPV33%, NPV100%, accuracy78%), SUVmaxL (p=0.007; accuracy 83% with 5.75 cut-off), ALR (p=0.004; 86% with 2.6). There was a statistically significant difference in cortisol between lesion types (p=0.015) and between secreting/non-secreting (p=0.003). Cortisol correlated only with AAR (p=0.035); AUC was significant only in discriminating secretion (p=0.003). Regarding ceCT-only, there was a statistically significant difference in min diameter and HUpre between lesion types; additionally in

max diameter and HU15min between benign/malignant; only in diameter and HU15min between cancer/atypical adenoma. These parameters resulted significantly performant in discriminating benign/malignant (p=0.004; 0.007;0.009;0.008; cut-offs: min 26 mm, max 50 mm, HUpre 28, HU15min 62, yielding to 86, 94, 81, and 67% accuracy respectively) as well as cancer/atypical adenoma (90% accuracy with 24mm, 29mm, 62 HU15min). Neither absolute nor relative wash-out resulted statistically significant, however positive correlation was found with SUVmaxL and ALR. **Discussion/Conclusion:** 18F-FDG PET/CT and ceCT parameters are helpful in assessing the malignant potential of indeterminate adrenal lesions. However a "grey-zone" of benign avid lesions still exists, therefore accurate multidisciplinary characterization is mandatory.

EP-0441

Sub-classification of G3 Gastroenteropancreatic Neuroendocrine Neoplasms: Can PET/CT with [⁶⁸Ga]Ga-DOTA-NOC and [¹⁸F]FDG play a role?

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Introduction: According to the World Health Organization classification 2010, gastroenteropancreatic neuroendocrine carcinomas (GEP-NEC) are defined as poorly differentiated neuroendocrine neoplasms with proliferation index (Ki67) superior to 20% or more than 20 mitosis per 10 high power fields and hence of grade G3. Increasing evidence suggests that these tumors are not a homogenous entity, and can be further sub-classified into biologically relevant groups. Radiolabelled somatostatin analogue PET/CT is an essential imaging technique in the functional analysis of well differentiated tumors, while [¹⁸F]FDG PET/CT is a critical tool in the assessment of high metabolic tumors, typically poorly differentiated neoplasms. **Aim:** Assess the potential role of [⁶⁸Ga]Ga-DOTA-NOC and [¹⁸F]FDG PET/CT in the *in vivo* sub-classification of G3 GEP-NEC. **Methods:** All G3 GEP-NEC patients who performed [⁶⁸Ga]Ga-DOTA-NOC and [¹⁸F]FDG PET/CT for staging purposes were retrospectively selected. The primary end point was death. Staging Ki67 index (biopsy), chromogranin A and neuron specific enolase (NSE) measurements were recorded, as well as follow-up time. [⁶⁸Ga]Ga-DOTA-NOC lesion uptake was compared to the liver activity, and classified as low, moderate or high. Maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) was noted for all [¹⁸F]FDG PET/CT. **RESULTS:** A total of 11 G3 GEP-NEC patients (7 males and 4 females; 67.4±5.9 59-77years) were selected (7 pancreatic, 3 gastric and 1 rectum tumors). Ki67 index average was 63.3±27.4 (20-90%). Staging chromogranin A and NSE plasmatic values were 697.9±594.8 (132-1982ng/mL) and 121.6±245.2 (9-814 ng/mL), respectively. Mean overall survival was 12.6±10 (0-36) months. [⁶⁸Ga]Ga-DOTA-NOC lesion uptake was classified as high in 4 patients, moderate in 2, and low in 5. [¹⁸F]FDG avid lesions mean SUVmax was 17.1±5.9 (10-29 g/mL). Mean MTV and TLG was 823.1±844.8 (55-2570 cm³) and

4937.5±6154.4 (248–21365 g), respectively. Although no statistically significant correlation was reached, higher MTV and TLG values were loosely associated with a worse prognosis. **Conclusion:** As previously described, G3 GEP-NEC proved to be a very heterogeneous group, with an overall survival ranging from 0–36 months, underlining the necessity for more accurate risk stratification tools. Despite no statistically significant correlation was reached, probably due to a very small sample size, higher MTV and TLG values were loosely associated with a worse prognosis.

EP-0442

Pancreatic uncinate process uptake in 99mTc-Hynic-Toc SPECT/CT

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Purpose: To assess physiological ^{99m}Tc-HYNIC-TOC (Tektrotyd) uptake in the uncinate process of the pancreas head (UPP) and compare it to pathological uptake in patients with neuroendocrine tumors (NET). **Materials and Methods:** Sixty six patients who underwent somatostatin receptor scintigraphy with Tektrotyd from January 2015 to March 2018 were evaluated in retrospect. All patients (56% male, mean age: 57 years) underwent a Tektrotyd study either for diagnosis/staging of confirmed or suspected NET, or for suspicion of NET recurrence. Planar whole-body images were acquired at 10 min and 3h postinjection of 740 MBq of Tektrotyd with SPECT/CT of the thorax/abdomen at 3h. UPP uptake was assessed visually on planar images and SPECT/CT acquisitions at both 10 min and 3 h paying attention to morphology and intensity of uptake. On abdominal SPECT/CT acquisitions UPP uptake was compared with uptake in the liver. A volume of interest (VOI) encompassing the entire uptake on the head of the pancreas was manually drawn to measure the average counts per pixel. A similar VOI was drawn on the liver parenchyma. The ratio between the pancreatic and hepatic uptake (L/H ratio) was calculated. UPP uptake was considered physiological in patients with normal CT and/or RM in addition to an uneventful clinical follow up for at least 6 months. **Results:** Almost half of the patients, 49% (31/66) showed UPP uptake of which 9.6% (3/31) was pathological focal uptake due to confirmed NET (2 insulinomas and one well differentiated tumor) and 90.3% (28/31) was uptake considered to be physiological. None of the latter showed uptake on early images while late images showed focal uptake in 53.5% of patients (15/28) and diffuse in 46.5% (13/28). L/H ratio was <1 in 96.4% of patients with physiological uptake, while 3.6% (1 patient) had a L/H ratio =1.72. In the 3 NET patients the L/H ratios were 0.65, 3.81 and 6.36 respectively. **Conclusion:** Most patients with pancreatic head uptake were considered to have physiological uptake in the uncinate process. Visual assessment and quantification help to distinguish physiological from pathological uptake.

EP-0443

High Grade Neuroendocrine Tumours : Value of 111In-pentetreotide Scintigraphy

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Introduction: Nuclear Medicine Imaging of neuroendocrine tumors (NET) depends on pathological tumor categories. High-grade NET are more likely to demonstrate avid uptake on 18FDG-PET than somatostatin receptor scintigraphy (SRS). The aim of this study was to assess the diagnostic utility of 111In-pentetreotide scintigraphie in patients with histologically proved grade 3 NET. Patients and **Methods:** Eighty seven patients with NET were studied with whole-body Somatostatin receptor scintigraphy (at 4 and 24 hours) and SPET/CT (at 24 and optionally 48 hours) after injection of 185–222 MBq 111In-pentetreotide. Fourteen patients (7 female and 7 male; Mean age 58.6 ± 15 years) had high grade (Ki 67 > 20%) NET. Indications were search for unknown primitive (6 patients) and / or staging (8 patients). **Results:** Somatostatin receptor scintigraphy revealed positive uptake in 7 primitives tumors (50%) with initially unknown primitive in 3 of them. The locations were 2 NET of lung, 1 stomach, 1 ileum and 2 pancreas. 8 / 14 patients (57%) had SRS positive in metastasis :3 liver, 2bone 4lymphonodes and 1 muscle. **Conclusion:** 111In-pentetreotide scintigraphy had acceptable performance for localizing the primary tumor and evaluating disease extension in patients with high grade NET. It could be used for diagnostic and therapeutic management of this group of NET if PET imaging was not available.

EP-0444

68Ga-DOTANOC PET/CT In Neuroendocrine Tumors: Preliminary Results Of Data Collection In An Electronic Archive

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Purpose/Introduction: Neuroendocrine tumours (NEN) show heterogeneous presentation both at diagnosis and during the natural disease course. The collection of clinical and imaging data in a prospective archive may provide valuable information for patients (pts) management as well as for a better employment of PET/CT in the diagnostic flow-chart. **Subjects & Methods:** Clinical, laboratory and imaging data of pts with pathologically proven NEN or suspected NEN who underwent 68Ga-DOTANOC PET/CT at our center were prospectively enrolled in an electronic database. PET/CT was performed as part of the routine diagnostic flow-chart. Pts enrolled between September 2017 and January 2018 were included in the analysis. PET/CT was performed and interpreted (visually and semi-quantitatively) according to the EANM guidelines. **Results:** Overall 184 pts were included (122/184 were referred from other Italian

hospitals). NET were mostly well-differentiated (49.1% G1, 43.5% G2). Most primary tumors were detected in the gastro-entero-pancreatic tract (66.3%) and in the lungs (5.3%). Unusual localizations were found in 7% of pts. Indications to PET/CT included ad interim evaluation (n=50), suspicion of NEN without pathological confirmation (n=32), follow-up (n=32), post-surgical staging (n=17), suspected relapse (n=11), unknown primary tumour (UPC, n=15), restaging post-therapy (n=4), PRRT selection (n=3). PET/CT was positive for NET lesions in 109/184 cases, in 24/109 (22%) the disease was limited to the primary lesion. Metastatic disease was present in 85/109 with nodal involvement in 25/109 (23%) and diffuse metastatic disease in 60/109 pts (55%). Overall, lymph-nodes were the most frequent metastatic site (n=58, 53.2%). Among the pts presenting with diffuse metastatic spread, secondary lesions were mostly observed in the liver (46/60, 76.7%), followed by lymph-nodes (33/60, 55%), bone (20/60, 33.3%) and lungs (6/60, 10%). PET positive non-malignant findings were frequently observed (58/184, 31.5%) and unequivocally interpreted (uncinate process, accessory spleen, inflammation/infection). In the subset of pts studied for suspected NEN (32), PET was positive only in 12/32 (37.5%). **Conclusions:** Clinical and imaging data collection in an electronic archive is crucial considering NEN rarity as well as their heterogeneous clinical presentation and behavior for a more tailored employment of PET/CT in the diagnostic flow-chart.

EP-0445

The value of hybrid In-111-Octreotide SPECT/CT imaging in neuroendocrine tumors

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Purpose: Hybrid In-111-Octreotide SPECT/CT imaging is a promising procedure for the study of neuroendocrine tumors. While planar images can only vaguely discriminate the localization of invaded sites and physiologic uptake of the radiopharmaceutical is often mistaken for sites of disease, SPECT/CT provide fusion of functional and anatomic imaging in one device.

Aim: The aim of this study is to assess the incremental value of In-111-Octreotide SPECT/CT imaging in the initial staging and restaging patients with neuroendocrine tumors. **Method-Material:** From January 2011 to March 2012, 25 patients -12 male and 13 female, aged 35 to 72 y.o.- with diagnosed neuroendocrine tumor underwent 111-Octreotide scintigraphy, either for initial staging of their disease or after clinical and/or biochemical evidence of relapse. Whole body imaging was performed at 4 and 24h after the IV administration of 185MBq In-111-octreotide. Static and tomographic views of brain, thorax, abdomen and pelvis were also obtained at 4, 24 and when necessary 48h. Images were reviewed by two experienced nuclear medicine physicians (NM). Results were scored 0-3, 0 for negative study, 1 for equivocal (surgical incision, intestinal activity), 2 for CT lesions only, 3 for lesions with increased uptake of the radiopharmaceutical. **Results:** According to SPECT/CT 7 patients were scored as 3: liver, brain, peritoneal implantations, supraclavicular and abdominal lymph nodes enriched with somatostatin receptors.

In one case consolidation of the upper left pulmonary lobe did not accumulate the radiopharmaceutical (score 2); however the patient presented additionally with invaded lymph nodes (score 3). In one case a finding at the breast presented at CT only (score 2) proved to be breast cancer. 5 patients were scored as 1 and 12 as 0. According to only planar imaging 4 patients were scored as 3, 4 as 1 and 17 as negative. The effective dose estimated for the In-111-octreotide scintigraphy is 26mSv. Additionally the patient receives 5-8mSv, depending on patient's height, from CT, when SPECT/CT is acquired. **Conclusion:** Our preliminary data suggest that Hybrid In-111-octreotide SPECT/CT has a promising role in identifying lesions enriched with somatostatin receptors as well as in the management of patients suffering from neuroendocrine tumors, with adding only small amount of radiation to the patient. SPECT/CT provides more accurate tumor localization, as well as the identification of physiologic activity. Moreover accidental findings on CT should, also not overlooked.

EP-0446

Optimization of 99mTc-Tektrotyd® scans protocol. Our experience.

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Purpose: To evaluate the clinical impact after the implementation and optimization of the somatostatin receptor scintigraphy protocol with 99mTc-Tektrotyd® in our nuclear medicine department. **Subjects & Methods:** Descriptive study of 72 scans in 53 consecutive patients (29 females; mean-age: 58,8±12,7 years-old) with 99mTc-Tektrotyd® (900,21MBq mean activity) between 2015-November and 2018-April. Intestinal preparation, post-injection acquisition period, intestinal artefacts visualized and scan results were reviewed to assess the clinical efficacy and imaging quality. **Results:** 99mTc-Tektrotyd® scans were performed as extension (42/72), locating occult primary tumors (4/72), assessment of recurrence (16/72) and as a control test (10/72). Confirmed diagnosis by pathology was obtained in 32/72 studies. The scan was positive in 27 patients, being well-correlated with pathological anatomy (13/27), other imaging tests (23/27) and clinical follow-up (1/27). The first 5 cases were performed according to the protocol described in the radiopharmaceutical technical specifications and revealing significant intestinal artefacts in all of them (mild-intensity: 2/5; moderate-intensity: 3/5 patients). Measures to minimize the potential intestinal artefacts (fiber-free diet, liquid diet and oral laxative in the previous 24 hours) and image acquisition 120 minutes after-injection was performed in all patients. A significant improvement of intestinal artifacts was observed with this optimized protocol, especially those who strictly followed the dietary measures, being nonexistent in 29/66 scans and slight in the remaining. One patient did not undergo the optimized preparation, and moderate intestinal uptake was observed. **Conclusions:** In our experience, the somatostatin receptor scan with 99mTc-Tektrotyd® showed excellent correlation with clinical follow-up, other imaging tests and pathology. Optimizing of established acquisition protocol, especially regarding adherence to dietary measures, has demonstrated a significant decrease in the

artifacts by the intestinal tract which results in improved image quality. Furthermore, some advantages over ^{111}In -Octreoscan in terms of increased product availability, reduced scan time and effective dosimetry to the patient were evidenced.

EP-0447

Evaluation of ^{18}F -DOPA PET/CT capacity to detect primary neuroendocrine tumors.

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Objective: To evaluate ^{18}F -6-fluoro-L-DOPA (^{18}F -DOPA) PET/CT capacity to detect primary neuroendocrine tumors (NETs) in patients in whom other conventional diagnostics image studies were not conclusive by the time of the first diagnose or in recurrence suspicion. **Methods:** A retrospective analysis was made in 12 patients (5 male and 7 female), between June 2017 and February 2018. Four patients initial diagnose was Multiple Endocrine Neoplasia type 2A (MEN 2A) and eight patients had Paragangliomas. Main reason to perform image studies were suspicion of recurrence in 9/12 patients (75%) and as an initial diagnose in 3/12 patients (25%). All patients had already performed other image test with no conclusive or discordant results. Nine patients did an Magnetic Resonance (MR), four a Tomography (CT), three did both exams (MR and CT) and 6 patients did a Somatostatin Receptor Scintigraphy (SRS). A diagnostic detectability lesion by lesion analysis was made with ^{18}F -DOPA and results were compared with other image techniques. Gold standard consisted as total number of lesions detected by all image test that were performed. **Results:** ^{18}F -DOPA studies were positive in 11/12 patients (92%), CT and MR were positive in 4/12 patients and SRS in 1/6 patients. ^{18}F -DOPA identified unknown disease in 5/12 patients (41.6%) in contrast with CT, MR or SRS. Every lesion showed an increased metabolism with a mean SUVmax of 7.95 gr/ml. ^{18}F -DOPA detected more disease extension in 8/12 patients (66%), while CT and MR in 2/12 patients (16.6%). In lesion by lesion analysis, ^{18}F -DOPA was able to detect a much larger number of lesions 35/37 (94%) in contrast with radiological techniques, CT (4/37) and MR (8/37). **Conclusion:** ^{18}F -DOPA PET is a valuable diagnosis tool in patients with NETs given its superior capacity to detect lesions in contrast to other image techniques.

Introduction and Purpose: Somatostatin receptor expression imaging with Tc-99m HYNIC TOC gamma camera imaging is simple and economic method to evaluate the patients of NET in diagnosis and guiding the treatment. This study is to evaluate the usefulness of Tc-99m of HYNIC-TOC scintigraphy in the management of various neuroendocrine tumours. **Materials & Methods:** It was a retrospective cross-sectional study from department of Nuclear Medicine, JIPMER, Puducherry, India. Records and images of Tc-99m HYNIC-TOC scans performed between Jan'15 and April'18 were retrospectively reviewed from hospital information system. A total of 67 Tc-99m HYNIC TOC scans were included in the study. Demographic details and all relevant clinical details were collected. Whole body images were acquired under Symbia T6 dual head SPECT/CT gamma camera, 2 hours after administering the 20mCi of Tc-99m HYNIC TOC intravenously. SPECT/CT of the abnormal areas were acquired after the whole-body acquisition. The results of Tc-99m HYNIC TOC study was confirmed with biopsy, biochemical results, CECT and MRI. **Results:** A total of 67 scans were included in the analysis. The referral was for initial diagnosis, staging, recurrence and response detection in 27, 21, 9 and 10 scans respectively. A total of 46 scans were positive and 21 were negative for presence of disease. The study cohort included referral for gastroenteropancreatic NET (GEPN), medullary carcinoma of thyroid (MCT), tumour induced osteomalacia (TIO), paraganglioma and neuroblastoma (P&N) and other NET's comprising carotid body tumors, meningioma, bronchial carcinoid, NET of breast, cervix and perianal region. The overall sensitivity, specificity, diagnostic accuracy, positive likelihood ratio, negative likelihood ratio were 80.77%, 73.33%, 79.10%, 3.03, and 0.26 respectively. For GEPN group sensitivity, specificity, diagnostic accuracy, positive likelihood ratio, negative likelihood ratio were 80.95%, 83.33%, 81.48%, 4.86 and 0.23 respectively. For TIO the sensitivity, specificity, diagnostic accuracy, positive likelihood ratio, negative likelihood ratio were 100%, 66.67%, 83.33%, 3.0 and 0 respectively. For P&N group the sensitivity, specificity, diagnostic accuracy, positive likelihood ratio, negative likelihood ratio were 83.33%, 66.67%, 77.78%, 2.50 and 0.25 respectively. All scans were positive for disease in MCT. In other NET groups the diagnostic accuracy was 81.82%. **Conclusion:** Tc-99m HYNIC TOC imaging has valuable role in initial diagnosis in patients with high clinical suspicion, for initial staging, recurrence detection and treatment planning. In centres with lack of PET/CT facility it plays very important role in management of patients with various NET.

EP-37

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology ->
Endocrine, malignant II

EP-0448

Tc-99m HYNIC-TOC scintigraphy in the evaluation of Neuroendocrine tumour (NET): Single centre experience

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EP-0449

Comparison between whole-body ^{18}F -FDG PET/CT and MRI in patients with SDH gene mutation paragangliomas: a preliminary study

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Objective: Our aim was to assess a comparative analysis between the diagnostic correlation of whole-body ^{18}F -FDG PET/CT and MRI in a prospective study of consecutive patients with SDH gene mutation and known or suspected paragangliomas.

Material and Method: Fourteen patients out of thirty-one diagnosed of SDH gen mutation with known or suspected paragangliomas were enrolled prospectively over a year period. The inclusion criterion was a maximum delay of 3 months between both techniques. Whole-body PET/CT and MRI images were performed and informed by an expert nuclear medicine and radiologist with more than 4 years of experience. Lesion size, standard uptake value (SUV) and apparent diffusion coefficient (ADC) among other technical features were considered to classify each lesion as positive or negative with PET/CT or MRI. **Results:** Six patients out of fourteen accomplished the inclusion criteria. The average age was thirty-five years (range 16–61 years). The average delay between both explorations was 1.5 months. Four of the six patients had mutation in the SDHD gene and two expressed the SDHB gene. Two patients were negative in both techniques. Four patients were positive by both scans. The PET/CT identified 12 tumoral lesions (7 paragangliomas, 2 pheochromocytomas, 3 bone metastases) versus 7 lesions diagnosed by MRI (4 paragangliomas, 2 pheochromocytomas, 1 bone metastasis). **Conclusion:** In paragangliomas, both whole-body FDG-PET/CT and MRI provide information about the extent of disease. In our limited experience PET/CT seems to detect more tumoral lesions per patient than MRI. Larger series are needed to obtain more conclusive results.

EP-0450

⁶⁸Ga-dotanoc Pet/ct For Restaging Gastrointestinal Neuroendocrine Tumors After Primary Treatment

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Purpose: To evaluate the utility of ⁶⁸Ga-DOTANOC PET-CT for restaging in patients of gastrointestinal neuroendocrine tumors after treatment. **Methods:** 115 patients with histopathological diagnosis of gastrointestinal neuroendocrine tumors (foregut-27, midgut-74, hindgut-14) who underwent treatment were included. To validate the results, histopathological correlation/conventional radiologic imaging and clinical follow up were considered as the reference standard. **Results:** Based on reference standard 81 patients had disease and 34 patients were disease free. PET-CT was positive in 80 patients (TP-72, FP-8) and negative in 35 patients (TN-29, FN-6). Sensitivity, specificity, positive and negative predictive values were 92.31%, 78.38%, 90.0 %, and 82.86 % respectively. The accuracy of the study was 87.83 %. **Conclusions:** ⁶⁸Ga-DOTANOC PET-CT is highly efficacious in restaging patients with gastrointestinal neuroendocrine tumors. It appears to be promising for assessing the disease burden in this group of patients.

EP-0451

Impact Of ^{99m}Tc-HYNIC-Tyr3-Octreotide Scintigraphy On Clinical Decision Making In Patients With Neuroendocrine Tumors

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Aim: Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms that are derived from the neural crest cells. They are characterized by their low incidence and symptoms related to the excess of hormonal production, although they can also cause symptoms related to the mass effect or distant metastasis. Somatostatin receptor scintigraphy (SRS) with ^{99m}Tc-HYNIC-Tyr3-Octreotide is used for detection and localization of NETs that express somatostatin receptors. The aim of our study was to assess the impact of the SRS results in the management of patients with NET.

Material and Methods: Retrospective study of 59 consecutive patients referred to SRS with ^{99m}Tc-Octreotide (24 men), mean age 58 y/old (22–87), 7 of them with more than one study, with a total of 72 studies. Whole body imaging and SPECT were performed at 2–4 h after IV injection of 407–703 MBq of ^{99m}Tc-Octreotide, and SPECT-CT fusion when possible. Diagnosis was the referral reason in 33 patients and follow-up evaluation in 26. Clinical follow-up was obtained during months 43 (2–72). **Results:** 42/59 patients presented a negative study for somatostatin receptors and 17/59 were positive. In the 17 positive patients, the SRS findings correlated with lesions described in other imaging techniques (US, CT, MRI, PET). SPECT and especially SPECT-CT fusion helped to the right location of lesions in all cases in which it was performed. The tumor types were: mesentery carcinoid (1), pancreatic (2), typical pulmonary carcinoid (2), atypical pulmonary carcinoid (3), ileal (1), pituitary adenoma (1), pheochromocytoma (1), colon carcinoid (2), thymoma (1), probable intestinal origin (1), pending biopsy results (2). Medical record information could be obtained in 15/17 patients. In 13/15 (86.66%) there was an impact on the patients management. In 9 patients, somatostatin analogues treatment was initiated after SRS results. In 2, analog treatment was started and the possibility of ¹⁷⁷Lu-treatment was evaluated but it was not started (progression and death of patients). In 2, the primary tumor was located with subsequent surgery. One patient without changes in patient management and one pending to initiate possible treatment. **Conclusions:** There was a significant clinical impact of ^{99m}Tc-Octreotide SRS results on the management of our group of patients with NET. It is a useful test for the diagnosis and follow-up of NETs, which dosimetric advantages comparing with ¹¹¹In-Octreotide, gammacamera optimal energy and reduced acquisition times, completing study in one day. It locates lesions with overexpression of somatostatin receptors with the possibility of starting treatment with analogs, surgery and new therapies with radionuclides and treatment response evaluation. Studies with positive SRS showed concordance with the findings described in other imaging techniques.

EP-0452

Hybrid In-111-Octreotide SPECT/CT imaging in neuroendocrine tumors: contribution in image interpretation and interobserver variability

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Purpose: The aim of this study is to assess the value of In-111-Octreotide SPECT/CT imaging in staging and restag-

ing patients with neuroendocrine tumors and its impact in interobserver variability during interpretation of the images. **Method-Material:** 25 patients, with neuroendocrine tumor underwent 111-Octreotide scintigraphy, for initial staging or after clinical and/or biochemical evidence of relapse. Whole body imaging was performed at 4 and 24h after the IV administration of 185MBq In-111-octreotide. Static and tomographic views of brain, thorax, abdomen and pelvis were obtained at 4, 24 and, when necessary, 48h. Images were blinded and reviewed by two experienced nuclear medicine physicians (NM). A third reader, an experienced radiologist, provided consensus in cases of disagreement of the exact location of the findings. Consensus was therefore achieved in cases of disagreement. However interobserver variability was a major question of the study and was searched. Results were scored 0-3, 0 for negative study, 1 for equivocal (surgical incision, intestinal activity), 2 for CT lesions only, 3 for lesions with increased uptake of the radiopharmaceutical. **Results:** Final consensus SPECT/CT results: 12 patients were scored as 0 and 5 as 1. 7 patients were scored as 3: liver, brain, peritoneal implantations, supraclavicular and abdominal lymph nodes. In one case CT revealed consolidation of the upper left pulmonary lobe, however without accumulation of the radiopharmaceutical. This patient presented additionally with invaded lymph nodes (score 3). In one case, accidental finding at the breast presented at CT only (score 2) proved to be breast cancer. Final consensus planar results: 17 patients were scored as 0, 4 as 1 and 4 as 3. Agreement between NM readers was reached for liver lesions >1.5cm, liver cysts, thyroid nodules >5mm, brain lesions, surgical incisions and breast lesion. Disagreement was noticed for small liver lesions located near the gallbladder- for which the radiologist added his experience-, peritoneal implantations and abdominal lymph nodes <8mm. In total, agreement was reached for 20/25 patients (80%) when only planar images were reviewed, which increased to 23/25 (92%) with SPECT/CT. **Conclusion:** Hybrid In-111-octreotide SPECT/CT has a promising role in identifying lesions with somatostatin receptors and in the management of patients with neuroendocrine tumors, with higher diagnostic accuracy compared to only planar imaging. Interobserver variability is minimal when SPECT/CT images are interpreted compared to only planar imaging, due to more precise tumor localization and identification of physiologic activity. Accidental findings on CT can also be identified.

EP-0453

CT pattern of 68Ga-DOTANOC positive neuroendocrine skeletal lesions

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Purpose/Introduction: Different morphological abnormalities may correspond to 68Ga-DOTANOC-avid bone findings. Aim of the present study was to retrospectively evaluate the CT pattern

of 68Ga-DOTANOC positive neuroendocrine skeletal lesions. **Subjects and Methods:** PET/CT reports between January 2012 and March 2018 including the description of 68Ga-DOTANOC avid bone lesions were retrospectively analyzed. Corresponding PET/CT images were reviewed and 68Ga-DOTANOC avid bone lesions and their low-dose CT (LDCT) pattern were classified as follows: i) sclerotic, ii) lytic, iii) mixed (both sclerotic and lytic lesions), iii) focal areas without corresponding LDCT abnormality (PET+/CT-). When available, all PET/CT scans were compared with diagnostic CT images (dCT) performed within two months. Among the patients (pts) with PET+/CT- lesions, follow-up PET/CT (when available) were reviewed to assess whether bone changes occurred. **Results:** Overall, 131 pts with 68Ga-DOTANOC bone avid lesions were included. In 62/131 (47.3%) pts, PET/CT scans revealed a sclerotic pattern and 18/62 pts also showed further PET+/CT- lesions. Lytic lesions were described in 31/131 (23.7%) pts and 11/31 pts presented further PET+/CT- lesions. Mixed pattern was present in 14/131 (10.7%) pts and further PET+/CT- lesions were detected in 6/14 pts. PET+/CT- lesions only were observed in 24/131 (18.3%) pts and in 8/24 pts follow-up PET/CT scans were available for comparison (only 3/8 pts developed a LDCT corresponding abnormality-2 lytic, 1 sclerotic- while the others remained LDCT negative). Overall, almost half of the pts (59, 45%) presented PET+/CT- lesions. dCT was available for 39/131 pts (29.7%) and on a patient-based analyses was falsely negative in 2 pts while confirmed skeletal lesions in the remaining 37 pts. **Discussion/Conclusion:** 68Ga-DOTANOC bone avid lesions mostly present with either corresponding sclerotic abnormality at LDCT or with a PET+/CT- pattern.

EP-38

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Gynaecological, malignant

EP-0454

¹⁸F- FDG PET/CT in the evaluation of ovarian carcinoma

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Introduction: The aim of this study is to evaluate the role of hybrid imaging ¹⁸F-FDG PET/CT techniques in the diagnosis and follow-up of ovarian carcinoma. **Subjects and Method:** We performed a retrospective study between 2013-2017 on 98 patients with ovarian carcinoma who underwent 146 PET/CT scans. The mean patient age was 45 years old. The inclusion criteria were: patients with ovarian carcinoma with confirmed histopathological diagnosis within the records of the "Ion Chiricuta" Institute of Oncology Cluj-Napoca; CA125 marker values out of the normal range and negative conventional imaging (CT, IRM, Echography) or CA125 marker values within the normal range and inconclusive conventional imaging (CT, IRM, ultrasound); the evaluation of metastases from adenocarcinoma with unknown primary origin. **Results:** Among our database of 146 PET/CT scans, 71 scans

(72,4%) were positive for metastatic disease. 22 patients (31%) had major changes in their therapeutic strategy, which lead to multiple PET-CT scans after their surgical and/or chemotherapy treatment, in order to assess its efficiency. We evaluated which site is the most common for disease spread among these patients, during their initial and follow-up scans. We found as most frequent site the peritoneum, 9 patients (40,9%); liver, 7 patients (31,8%); bone, 2 patients (9,09%). Regarding the lymph nodes involvement, the sub diaphragmatic lymph nodes were metastatic in 17 patients (77,27%); the supra diaphragmatic lymph nodes were metastatic in 6 patients (27,27%); 4 patients (18%) presented pathologic uptake in the spleen. Discussion: Ovarian carcinoma is considered a very aggressive pathology. To this date, there is no efficient screening method, which results in more than 75% of the cases being diagnosed during the 3rd or 4th stage of the disease. The major challenges of this pathology includes the serosal spread of the metastases, which are undetectable by conventional imaging techniques until the tumor bulk is sufficient to present itself as foci larger than 0.5 mm. **Conclusion:** We consider hybrid imaging techniques of being vital in the diagnosis and screening of patients with ovarian cancer. 18F-FDG PET/CT is able to detect lesions and disease spread sooner than other imaging techniques and is also a helpful tool for appreciating the status of the patient during treatment strategy personalization.

EP-0455

F-18-FDG PET-CT in Peritoneal Carcinomatosis: A Case-Review of an Oncology Centre

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Introduction: Peritoneal carcinomatosis (PC) significantly decreases overall survival, mainly in gynaecological and gastrointestinal malignancies. Preoperative diagnosis of PC can be very challenging and imaging techniques are limited in detecting localized PC, especially small lesions. Aim: To characterize the patients with PC positive F-18-FDG PET-CT (PETscan) in an Oncology Centre and compare its performance to other diagnostic modalities. **Material and Methods:** We retrospectively reviewed all the consecutive PETscans performed from March 2016 to March 2018, positive for PC. We collected demographic and clinical data, namely the primary tumour location, main tumoral markers at the time of the PET scan, exam indication, time evolution since diagnosis, as well as concomitant CT and/or MRI results and the agreement between these exams. Our “gold-standard” for final diagnosis included surgical direct visualization and/or biopsy of peritoneal lesions and/or the subsequent follow-up. **Results:** Sixty-four PETscans were included. Patients had a mean age of 62.33±13.98 years old and 64.1% (n=41) were women. Gynaecological tumours were the most prevalent type of cancer (n=28; 43.8%), being ovary cancer the main subtype (67.9%; n=19), followed by breast cancer (17.9%; n=5). The second most common type of cancer was gastroin-

testinal: 39.1%; n=25, being gastric cancer the most common subtype (48%; n=12), followed by colorectal cancer (20%; n=5). In agreement with these findings, the main tumoral marker in gynaecological tumours was CA-125 (median=218.55 U/mL; min=18.31, max=32202.00) and in gastrointestinal tumours was CEA (median=7.04 U/mL; min=0.00, max=92.90). Seven (10.9%) patients had an unknown primary cancer. PETscan was mainly requested for staging purposes (50%; n=32) and evaluation of treatment response (34.4%; n=22). Sixty-two patients had a median time of disease evolution of 1 year (min=0; max=24 years). Fifty-two patients had a concomitant CT, which was positive for PC in 47 cases. Only 6 patients had MRI, which was positive for PC in 5 cases. Twenty-three patients had abdominal surgery, which was positive for PC in 21 (91.3%) cases, negative in 1 (4.3%) and uncertain in 1 (4.3%). Ten patients had biopsy-proven PC. The final diagnosis was positive for PC in 62 (96.9%) patients, negative in 1 patient (1.6%) and uncertain in 1 patient (1.6%).

Conclusion: PETscan is a valuable tool in the evaluation of PC in patients with several types of cancer, even in recently diagnosed patients. Besides, it has an excellent correlation with surgical and biopsy outcomes, as well as with imaging modalities.

EP-0456

F-18-FDG PET-CT in the Evaluation of Ovarian Carcinoma - a 9 year-experience of an Oncology Centre

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Introduction: Ovarian cancer is the most fatal gynaecologic malignancy. Although there is still conflicting data on the value of ¹⁸F-FDG PET-CT (PETscan) as an initial staging tool, it has proved its utility at relapse and response to treatment evaluation. Aim: To describe the utility of PETscan in the evaluation of ovarian cancer in an Oncology Centre. **Material and Methods:** We retrospectively reviewed all PETscans requested for ovarian cancer evaluation between 2009 and March of 2018. Only primary histologic proven ovarian carcinomas were included. We collected demographic and clinical data, CA-125 value at the time of the PETscan and analyzed its indication and result, as well as the maximum SUV (SUVmax) of the ovarian lesion or the relapse. We also evaluated if patients had a previous PETscan and classified the response to treatment as “stable” - if no significant differences were found -, “improving” - if there was a metabolic improvement of previous lesions - and “in progression” - if there were new lesions -. Finally, we correlated PETscan results with those from concomitant CT and/or MRI. **Results:** Twenty-three PETscans were included. The patients had a median age of 67.0 years old (min=45; max=81). Only one patient had previous hysterectomy and oophorectomy. Serous carcinoma was the most prevalent histological subtype (n=12), followed by clear cell carcinoma (n=9), endometrioid (n=1) and mucinous (n=1). The median CA-125 value was 418.0 U/mL (min=39.6; max=3798.0). PETscan was mainly requested to evaluate response to treatment (n=12), followed by initial staging (n=9) and relapse evaluation

(n=2). The majority of the patients (n=17) were FIGO stage IV. The main lesion was detected in all cases (median SUV_{max}=6.8 [min=1.4; max=19.8]). PETscan was positive for metastases in 20 cases (n=8 of initial staging; n=1 of relapse evaluation and n=11 of response to treatment evaluation). Four patients had biopsy-proven metastases detected on PETscan. Nine patients had a previous exam and the disease was considered “stable” in one case, “improving” in 4 cases and “in progression” in 4 cases. In one case it lead to a change in the initial treatment strategy. Eight patients had CT and 5 MRI, which were in agreement with the PETscan results in all cases. **Conclusion:** PETscan is a valuable tool in the evaluation of ovarian carcinoma in patients with a very large range of CA-125 value and within several stages of the disease. Despite our reduced sample, it showed an excellent correlation with other diagnostic modalities.

EP-0457

FDG PET-CT in locally advanced cervical carcinoma patients (LACC): prognostic impact and clinical management

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Purpose: To evaluate the prognostic impact of early FDG-PET/CT scan performed in patients with LACC treated with chemo-radiotherapy before intra-uterine brachytherapy. **Methods:** We included 19 patients with LACC (range 32-82 years) that referred to our institution between 2013 and 2017. Patients were treated with concomitant chemo-radiotherapy and subsequent brachytherapy. FIGO STAGE: 1/19 was IB1, 11/19 was IIB, 2/19 was IIIB, 1/19 was IIA, 2/19 was IIIA and 2/19 was IVA. 6/19 patients presented regional lymph nodes involvement and one patient had also positive lombo-aortic lymph nodes. 16/19 patients underwent radiotherapy and concomitant weekly chemotherapy with Cisplatin (40mg/mq²), while 3 patients received also a neo-adjuvant chemotherapy. 14/19 patients were treated with IMRT technique and 10 of them received IMRT-SIB (2.2 Gy x 28 fractions on GTV-cervix and GTV-LNs PET-positive, 1.8 Gy x 28 fraction on pelvis ± LN lombo-aortics). The total brachytherapy dose was 21 or 28 Gy in 3-4 fractions, 7 Gy per fraction, with the aim to obtain a total dose (EBRT plus BT) in the range of 85-90 Gy (4 pt 28 Gy, 1 pt 25 Gy, 14 pt 21 Gy). All patients performed an early FDG-PET/CT study after chemo-radiotherapy and before starting brachytherapy. PET Images that showed SUV max values greater than 3 were rated as positive. **Results:** Regarding the early-PET scans, 13/19 were negative while 6/19 resulted positive. 2/13 (15%) patients with negative early-PET showed a relapse: one patient showed pelvic nodal relapse after 15 months and one cervical, annexial and nodal relapse after 5 months from the end of brachytherapy. 3/6 patients (50%) with positive early PET-CT had progressive/relapse disease: one patient had systemic (lung) progressive disease after 4 months, one nodal, cervical and bone relapse after 18 months and one vaginal relapse 5 months from the end of brachytherapy. **Conclusions:** these preliminary results suggest that early-PET scans performed be-

fore brachytherapy could have a predictive value to assess the risk of recurrence/progression in LACC patients. Patients with positive early-PET at the end of chemo-radiotherapy may benefit from adjuvant systemic treatment after brachytherapy.

EP-0458

Clinical impact of 18F-FDG PET/CT on the staging and restaging of gynecologic cancers

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Objective: 18F-FDG PET/CT is gaining popularity as an adjunct modality in planning treatment algorithm for gynecological malignancies, however clinical studies addressing its impact in patient management are lacking. We investigated the clinical impact of 18F-FDG PET in the assessment of gynecological malignancies having pelvic or extrapelvic lymph nodes with equivocal characteristics on conventional imaging. **Methods:** We retrospectively evaluated 18F-FDG PET/CT scans of patients with gynecologic tumors who were referred to King Hussein Cancer Center from January 2010 to August 2014. PET/CT results were compared with MRI and CT findings. We also evaluated the role of 18F-FDG PET/CT in changing treatment plan and its sensitivity, specificity, PPV and NPV based on histopathological findings and results of serial follow up conventional imaging scans as a gold standard. **Results:** 97 patients (median age: 49 years old) underwent 18F-FDG PET in the study period (40 cervical, 37 endometrial and 20 ovarian cancers). PET/CT scan provided additional information in 23 patients; upstaging in 4.1% (4 patients; 3 true positive) and down staging in 19.5% (19 patients; 15 true negative). As a result, treatment strategy was changed from curative to palliative in three patients, and additional curative therapy was implemented following exclusion of distant metastasis in 11 patients. Median follow up time for the whole cohort was 35 months (range 6 - 60 months). NPV of 18F-FDG PET/CT in detecting extrapelvic lymphadenopathy was 83.3%. **Conclusions:** 18F-FDG PET/CT has high clinical impact in management of gynaecological cancers as it alters the treatment plan in a substantial number of patients who had equivocal findings on conventional imaging, as well as offers high NPV in excluding extrapelvic lymphadenopathy.

EP-0459

The experience of ^{99m}Tc-Al₂O₃ using for the detection of sentinel lymph nodes in endometrial cancer patients

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Purpose: The purpose of the study was to evaluate the feasibility of using the new radiopharmaceutical, based on technetium-99m-labeled gamma-alumina (^{99m}Tc-Al₂O₃), for the detection of sentinel lymph nodes in endometrial cancer patients. **Materials and Methods:** Nanocolloid ^{99m}Tc-Al₂O₃ with size of nanoparticles 80-100nm coated with organic covering was

studied. During passage through the lymphatic way nanoparticles lose organic coating and strongly accumulate in the sentinel lymph nodes without redistribution. The study included 36 patients with endometrial cancer T1aNxM0 - T1bNxM0 stage. The day before surgery, two submucosal injections of $^{99m}\text{Tc}-\text{Al}_2\text{O}_3$ at a dose of 20 MBq per quadrant were made in each quadrant around the cervical tumor. SPECT study was performed at 18 hours after injection, intraoperative detection was executed by gamma probe at 20 hours after injection. Patients were then underwent pelvic lymph node dissection. After lymphodissection, the removed lymph nodes were re-examined with gamma probe to detect SLNs missed during intraoperative examination. **Results:** In all patients 36 SLN were identified by SPECT and 48 SLN by gamma probe. Accumulation of $^{99m}\text{Tc}-\text{Al}_2\text{O}_3$ in SLN was average - 6% by SPECT and average - 8% by gamma probe. The most common site for SLN detection was the internal iliac vessels 35,5% (n=17), in the course of the external iliac vessels, with 18.7% (n=9), in the course of common iliac vessels of 16.6% (n=8), a single SLN was located in the same region of the obturator fossa and the aortic bifurcation and iliac arteries. The excised SLNs were evaluated by imprint cytology with subsequent routine histological examination. When conducting a rapid cytological evaluation of sentinel lymph nodes were identified in 2 cases of metastatic lymph nodes, and for the 1 patient had micrometastases. **Conclusions:** The clinical study of $^{99m}\text{Tc}-\text{Al}_2\text{O}_3$, a new radiopharmaceutical agent, have shown that the studied nanocolloid has high uptake level in SLN and can be successfully used for visualization of SLN in patients with endometrial cancer. SPECT and intraoperative gamma probe-guided identification performed after injection of $^{99m}\text{Tc}-\text{Al}_2\text{O}_3$ enable the detection of SLNs with 97,2 % sensitivity.

EP-0460

The contribution of 18F-FDG-PET/CT in restaging patients with endometrial cancer

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Purpose: Endometrial cancer is one of the most common gynecologic malignancies in European countries, with good prognosis at early stages. However prognosis becomes poorer at advanced stages as well as at recurrence. Accurate staging after treatment is of incremental value. In this retrospective study, we evaluated the role of 18F-FDG-PET/CT in restaging patients with endometrial cancer after therapy. **Method-Material:** 34 PET/CT examinations, of 28 patients with endometrial cancer, were retrospectively reviewed. All patients had received the appropriate treatment according to the disease (surgical removal, chemotherapy, radiotherapy) and were referred to PET/CT department for restaging after treatment. 60 min after the intravenous administration of 18F-FDG whole body Positron Emission Tomographer/ Computed Tomography was performed at a Siemens Biograph LSO PET/CT tomographer. All of the patients were previously restaged by conventional imaging (CT). Com-

parison between the results of the two imaging modalities occurred. **Results:** In 11/34 (32.3%) cases both CT and PET were positive; in 1/11 PET revealed more metastatic lesions concerning lymph nodes and osseous disease; PET did not show small pulmonary nodules in 2 cases and one small liver metastasis in 1 case. In 2/34 (5.8%) cases CT was positive showing pulmonary nodules but PET was negative as these nodules did not accumulate the radiopharmaceutical. In 6/34 (17.6%) cases both CT and PET were negative. In 5/34 (14.7%) cases CT was negative, while PET was positive (lymph nodes, peritoneal implantations, osseous metastasis, and local disease). In 10 (30%) cases CT was stable compared to previous examination or equivocal. PET was positive in 4/10 (lymph node invasion in 3, local disease in 1), negative for 5/10 (all true negative in 3 year surveillance) and equivocal in 1/10. **Conclusion:** PET/CT is a whole body imaging modality, helpful in restaging patients with endometrial cancer, with generally higher accuracy compared to conventional anatomic imaging. Particularly, it is helpful in characterizing lymph nodes, peritoneal implantations, local disease and osseous metastasis. Attention should be paid in the evaluation of small pulmonary nodules and small liver lesions.

EP-0461

Charicteritics Of Bone Metastasis Detected Using F-18 Fluorodeoxyglucose PET/CT In Patients With Cervix Cancer

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Objective: Cervix cancer is usually localized disease compared with other ovarian/endometrial malignant lesion with systemic disease. Usually bone metastasis is rare in the gynecologic malignancy, therefore bone scan is not indicated. The prognosis of gynecological cancer patients with bone metastasis is poor. We performed F-18 FDG PET/CT for staging and evaluation of metastasis in 3340 patients with cervix malignant lesion. Therefore we evaluated the incidence and imaging characteristics in case of bone metastasis using F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) in the patients with the cervix cancer patients. **Material and Method:** Between 2009 and 2017, we retrospectively analyzed PET/CT scans with pathological-proven cervix cancer (3682 PET/CT studies of 1580 patients). Bone metastases were proved by MRI following FDG PET/CT or clinical follow up. Maximum SUV (mSUV) of primary cervix malignant lesion was evaluated. **Results:** Incidence of metastatic bone metastasis in 1580 patients with cervix malignancy was 14 patients (0.88%). Seven patents (50%) among 14 patients showed only single bone metastasis on the PET/ CT. The most common metastatic sites were vertebrae (10 patients) and pelvic bones (9 patients). One patient showed only rib metastasis. Measured maximum SUV of primary cervix malignant lesion was 14.2 ± 8.4 . And proportion of patients with mSUV more than 7.5 of primary cervix malignant lesion was 81%. **Conclusions:** We found that the incidence of bone metastases in the cervix cancer was very low (0.88%). Measured mSUV of primary cervical malignant lesions with bone metastasis was very high in most patients. Although incidence of bone metastasis in cervix

cancer was very low, bone also could become metastatic sites in case of high mSUV of primary cervix malignant lesion and advanced metastatic lesions. Vertebra was the most common metastatic bone site.

EP-0462

18F-FDG PET/CT in patients with vulvar and/or vaginal cancers - A 5 year experience of an Oncology Center

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Aim: To assess 18F-FDG PET/CT role in patients with vulvar and vaginal cancers. **Material and Methods:** A retrospective study was conducted on a cohort of 21 patients with proven biopsy vulvar (n=18) or vaginal cancer (n=3) who performed 18F-FDG PET/CT, between January 2013 and April 2018. Fourteen patients had been previously submitted to surgery: hemivulvectomy (n=4), radical vulvectomy (n=6) and vulvectomy with pelvic lymph node dissection (n=4). We collected demographic and clinical data of the patients, as well as 18F-FDG PET-CT indication, its result and the primary tumor maximum standard uptake value (SUVmax). Also, we correlated 18F-FDG PET-CT results with other diagnostic modalities, namely CT, MRI and histologic analysis. **Results:** Patients had a mean age of 72.5 ± 12.5 years old. Squamous cell carcinoma was the main histological subtype (n=20). 18F-FDG PET/CT was mainly requested to evaluate relapse (n=11), followed by initial staging (n=6) and treatment response (n=4). The primary tumor was detected in 20 out of 21 patients (median SUVmax 9.3 [min=5.0; max=51]). Additional sites of 18F-FDG uptake were identified in inguinal (n=6) and iliac lymph nodes (n=5) and at distant metastatic lesions (n=2). The presence of metastases was confirmed in all cases by biopsy, CT, MRI and/or with patient clinical follow-up. MRI and CT were performed in 6 and 5 cases, respectively, and the results were in agreement with the 18F-FDG PET/CT in 10 out of 11 cases. In one case, metastatic iliac lymph nodes identified on 18F-FDG PET/CT were not detected by CT. **Conclusion:** In this preliminary study, 18F-FDG PET-CT showed to be an useful method in the management of vulvar/vaginal cancers, namely in defining metastatic disease extent and contributing for an accurate staging.

EP-0463

18F-FDG PET/CT in management of cervical carcinoma - A 5 year experience of an Oncology Center

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Aim: To assess 18F-FDG PET/CT role in the management of patients with cervical carcinoma. **Material and Methods:** We retrospectively reviewed 33 18F-FDG PET-CT performed in an Oncology Center to evaluate cervical carcinoma. We collected demographic and clinical data of the patients, as well as the

18F-FDG PET-CT indication, its result and the primary tumor maximum standard uptake value (SUVmax). We correlated the 18F-FDG PET-CT results with other diagnostic modalities, namely CT and histologic analysis. Finally, we analyzed the impact of 18F-FDG PET-CT in the management of the patient defined as a change to/from a non-interventional strategy (observation or additional imaging), to/from an interventional strategy (biopsy or treatment). **Results:** Patients had a mean age of 63.1 ± 23.8 years old. The main histologic subtype was squamous cell carcinoma. 18F-FDG PET/CT was requested to evaluate relapse (n=23) and treatment response (n=10). Increased 18F-FDG uptake was seen in the primary tumor in all cases (median SUVmax 7.8 [min=5.4; max=19.9]). Additional places of 18F-FDG uptake were identified in pelvic (n=9) and extrapelvic lymph nodes (n=4), and at distant metastatic lesions (n=2), namely in the lungs. The presence of metastases was confirmed by CT in 10 cases and biopsy in 3 cases. Changes in patient management was observed in 2 patients (6%). **Conclusion:** This preliminary study showed that 18F-FDG PET/CT might be useful in defining the extent of metastatic disease and in the management of patients with cervical carcinoma, with an important impact on staging and treatment strategy.

EP-0464

¹⁸F-FDG-PET/CT Staging Of Paraaortic Lymph Node Metastases In Locally Advanced Cervical Cancer, A Reliable Alternative To Surgical Staging?

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Purpose/Introduction: One of the main prognostic factors in locally advanced cervical cancer (LACC) is the presence of paraaortic lymph node metastases. In this patients, who will undergo treatment with concurrent radiochemotherapy, it is of vital importance to study the paraaortic lymph node status in order to determine the area that needs to be covered by the radiation fields. On the different guidelines there is not a well established knowledge about which diagnostic tests should the oncologist perform in this context. The aim of this work is to determine the value of ¹⁸F-FDG-PET/CT diagnostic test (S,E,PPV and NPV) in this context against gold standard (surgical staging - laparoscopic paraaortic lymphadenectomy) **Subjects and Methods:** Data regarding result of ¹⁸F-FDG-PET/CT and histopatological examinations of 37 patients with histologically proven LACC were gathered. All those patients with LACC were performed initially ¹⁸F-FDG-PET/CT examination and after were submitted for laparoscopic paraaortic lymphadenectomy, within 3 weeks after the imaging test. Regarding imaging protocol, ¹⁸F-FDG-PET/CT was performed after a minimum of 6h- fasting and glycaemia <200mg/Dl. Metabolic data were acquired 60' after the intravenous administration of a 5 MBq/kg dose (0.135 mCi/kg), Interpretation of the studies was performed by two expertise nuclear physicians, and , if there were discrepancies, a third one was requested to determine the result of the test. **Results:** ¹⁸F-FDG-PET/CT for detection of paraaortic lymph node involvement revealed the following results: S (44,4%), E (96,4%), PPV (80%) y NPV (84,4%). **Discussion/Conclusion:** In our pop-

ulation, our diagnostic test showed a low sensitivity S (44,4%), with a high false negative rate (55,56%) for detection of metastatic paraaortic lymph node involvement. With this results, in our setting, 18F-FDG-PET/CT currently its not a reliable diagnostic alternative to laparoscopic lymph node lymphadenectomy.

EP-39

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Head and neck, malignant

EP-0465

Value of FDG PET/CT in the detection of the cancer of the unknown primary and its correlation with carcinoembryonic antigen level

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Purpose: Checking the detection rate (DR) for cancer of unknown primary (CUP) by FDG PET/CT and it's correlation with carcinoembryonic antigen (CEA) level. **Methods:** 287 cases were selected out of 654 cases of CUP (287/654; 44%) that were referred for FDG PET/CT during the period 2007-2017. The included cases had: 1-biopsy-proven malignancy whose primary origin remains unidentified after a reasonable diagnostic evaluation. Most of the cases (56%) had no biopsy at the time of PET scanning or the biopsy eventually revealed no malignancy, so were excluded. 2-New case or recurrent case with biopsy findings different from the previous malignancy and the source of the second tumor unidentified. **Results:** DR of CUP by FDG PET/CT was 18% (52/287). Cervical area was the main source of the primary for 40% (21/52). About quarter of the cases (67/287) presented initially with neck lymph nodes enlargement. DR was 39% (26/67), and the location of the primary tumor was also in the neck area in 80% (21/26). Tonsils was the most frequent source of CUP in the neck; 52% (11/21), followed the base of the tongue, and larynx, each of them 14% (3/21), cervical esophagus 9.5% (2/21), thyroid and nasopharynx each 0.5% (1/21). 220 cases presented by extra cervical metastases, DR was 12% (26/220). The common primary source of CUP was the lung 26% (8/31), the stomach 16% (5/31), liver 9.6% (3/31), thoracic esophagus, cecum and pancreas each of them 6% (2/31), one case (3%) in each of the sigmoid colon, ovary, breast, testes, skin of foot, perineum, and prostate. 32 cases of the CUP cases had high carcinoembryonic antigen (CEA). Of them, the primary cancer of 34% (11/32) cases were detected, and their mean CEA was 69 ± 167 ng/ml (range 1-570). While 66% (21/32) cases their primary tumors were not detected and their mean CEA was 205 ± 570 ng/ml (range 1-2000). No significant differences between the two groups statistically, the two tailed P value = 0.45. **Conclusion:** DR was higher for CUP with cervical lymph nodes metastases than non-cervical (39% vs 12%). Tonsils should be checked carefully in cases with cervical metastases. Efficacy of FDG PET/CT in the detection of CUP was not correlated with the level of CEA.

EP-0466

Does smoking alter the FDG PET/CT uptake in head and neck cancers?

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Aim: Head and neck cancer (HNC) constitutes 5.1% (> 633 000) of all new cancers and relates to 4.8% of all cancer deaths annually worldwide with Head and Neck Squamous Cell Carcinomas (HNSCC) contributing by far the largest number. Smoking is the major risk factor in head and neck cancers. Furthermore among patients with HNC, those with a significant smoking history have a much worse prognosis. The purpose of this study was to determine whether positron emission tomography/computed tomography (PET/CT) maximum standardized uptake value (SUVmax) differ between smokers and non-smokers with HNC. **Materials & Methods:** A review of 159 patients with head and neck carcinomas in smokers and non-smokers matched for T stage and tumor subsite was performed, with the reviewing nuclear physician blinded to the smoking history, and clinical stage. Metabolic Imaging characteristics of tumour/lesions were compared using positron emission tomography/computed tomography (PET/CT) maximum standardized uptake value (SUVmax). **Results:** The smoking HNC patients were male and younger than the non-smokers. The cancer types were classified as: Nasopharynx (41%), Larynx (20%), Tongue (8%), Tonsil (8%), Floor of mouth (7%) and others (16%). SUVmax was not significantly different in smokers compared with non-smokers ($p=0.1245$), even when analyses focused on heavy smokers (>20 pack-years vs. <20 pack-years). Furthermore, we could identify no obvious difference in the visual FDG accumulation of the paired smokers and non-smokers. **Conclusions:** In HNC patients, smoking does not significantly increase the positron emission tomography/computed tomography (PET/CT) maximum standardized uptake value (SUVmax). Additional studies are warranted to further describe other functional PET parameters according to tobacco consumption.

EP-0467

Hypoxia Imaging With [^{18}F]HX4 In Patients With Squamous Cell Head And Neck Cancer

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Introduction and Aim: Tumour hypoxia causes resistance to chemo- and radiotherapy, and is an indicator of poor prognosis for patients. Identifying tumour hypoxia to select patients for intensified or hypoxia-modified treatment regimens is therefore of high clinical importance. Tumour hypoxia can be evaluated by PET/CT using fluorine-18 labelled 2-nitroimidazoles such as [^{18}F]HX4. Our aim was to evaluate [^{18}F]HX4 hypoxia imaging in the treatment pathway of patients with squamous cell carcinoma of head and neck (HNSCC). **Patients and Methods:** [^{18}F]HX4 was prepared to good manufacturing practice (GMP) quality at Not-

tingham City Hospital, using our previously reported automated protocol.¹ The study was a single-centre, phase II Investigational Medicinal Product (IMP) trial, which received approval from the UK Medicines and Healthcare Products Regulatory Agency (MHRA), Research Ethics Committee, Administration of Radioactive Substances Advisory Committee (ARSAC) and the National Health Service (NHS) prior to commencement. The main inclusion criteria for the study were newly diagnosed, biopsy-proven HNSCC without distant metastases, and a treatment plan of radical chemoradiotherapy with curative intent. All participants gave written informed consent to take part. **Results:** We present the results for three participants who were scanned with [¹⁸F]HX4, alongside [¹⁸F]FDG PET/CT scans for comparison in two cases. Two participants were male and one female, with an age range of 53–71 years. [¹⁸F]HX4 PET/CT was performed in the short time window between completion of disease staging and the start of treatment. [¹⁸F]HX4 was administered intravenously, and patients were scanned after a target uptake period of 3 hours. Tumour to mediastinal ratios ranged from 1–3.5. **Discussion and Conclusions:** [¹⁸F]HX4 PET/CT was successfully performed, and no adverse events were encountered from administration of the radiotracer. The differences in [¹⁸F]HX4 uptake in this small series of patients exemplified the range of oxygenation present within histologically similar tumours. Furthermore, the [¹⁸F]HX4 scans visualised differences in oxygenation between the primary tumour and nodal disease within the same patient. This observation illustrates the advantage of whole-disease hypoxia evaluation by PET/CT, compared with sampling methods. Since this study was exploratory in nature, changes to patient treatment plans were not permitted based on the [¹⁸F]HX4 results. Validation of [¹⁸F]HX4-guided treatment modifications should be the focus of future studies. [1] Turton DR, Betts HM, Dutton D, Perkins AC. Automated radiosynthesis of GMP quality [¹⁸F]HX4 for PET imaging of hypoxia. *Nucl Med Biol.* 2015;42:494–498.

EP-0468

Sentinel Lymph Node Biopsy in oral squamous cell carcinoma: results and follow-up

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Purpose: To provide insight into the outcomes and follow-up of the sentinel lymph node biopsy (SLNB) in patients with oral squamous cell carcinoma (SCC) with clinical stage cT1–2N0 between validation and application phases. **Subjects and Methods:** Retrospective review of thirty-four patients (16 in validation and 18 in application phase) from 2010 to 2017. The SLNB procedure consisted of lymphoscintigraphy, SPECT/CT, intraoperative detection using gamma probe and portable gamma camera. In the follow-up patients were evaluated by physical examination, ultrasound and/or TC of the neck. Different results and statistics parameters were compared between the two phases. **Results:** Mean age of the patients of phase application was higher than the validation (66.2±16,7 vs 55.2±14,1 years; $p=0.04$). There was no difference between two groups in gender, size of tumour

and differentiation grade. Mean follow-up was 45 ± 28 months (63 months in validation and 29 months in application phase). The surgical detection rate of SLNB in patients was 100%. Bilateral drainage was demonstrated in thirteen cases, with SLNB performed in 46 lymphatic territories. A total of 110 sentinel lymph node (LN) were removed (mean 3,2;1–7). LN metastases were diagnosed in 10 (29,4%) patients (4 in validation and 6 in application phase) with ITC ($n=4$), macro ($n=2$) and micrometastasis ($n=4$) results. Only one false negative was in a patient of validation phase. Sensitivity (S) and negative predictive value (NPV) in a validation phase was 80% and 91.7%, respectively. No patients in the application phase had LN recurrence during follow-up ($S=100\%$, $VPN=100\%$). Recurrence was observed in 5 patients in validation phase, only one of them was cervical LN recurrence (4 with pN0 and 1 pN2) and 1 with pN1 in application phase. Two patients died from SCC causes (both in validation phase with pN0). No differences were evident in DSS, DFS and OS between validation and application phases (DSS: 87% vs 100%, $p=0.386$; DFS: 69% vs 94%, $p=0.203$; OS: 69% vs 94%, $p=0.529$). The same results were observed when SLNB negative vs positive were applied: DSS: 79.2% vs 90%, $p=0.5$; DFS: 91.7% vs 100%, $p=0.52$; OS: 83% vs 80%, $p=0.554$. **Conclusion:** In the patients included in this study, SLNB of cN0 oral SCC provided high accuracy rates in clinical application phase and reduced the morbidity of elective neck dissection without significant difference in the survival parameters compared to validation phase. However, studies with a larger number of patients and long-term evolution are necessary.

EP-0469

FDG PET/CT for Metastatic Squamous Cell Carcinoma of Unknown Primary of the Head and Neck

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Purpose: Squamous cell carcinoma of unknown primary (SCCUP) is mostly in the head and neck. The role of FDG PET/CT in the detection of the primary is uncertain. Published data are limited by heterogeneity of pathology, varied diagnostic criteria and small sample size. **Subjects & Methods:** A retrospective study was conducted in 40 patients who had FDG PET/CT for SCCUP. Prior to PET/CT, patients had underwent standard clinical evaluation including the history, complete physical examination with emphasis on the head/neck, and flexible rhinolaryngoscopy. Majority of the patients had regional anatomic imaging as well. All eligible subjects had available histopathological investigations, and/or clinical and image follow-up data after the PET/CT. **Results:** FDG PET/CT detected the primary in 16 of 40 patients (40%), and the most common locations of the primary were in the base of the tongue, palatine tonsil and hypopharynx. There were 10 false positive and 6 false negative PET/CT scans. There was no difference in the mean SUVs of the suspected primary lesions between true and false positive groups. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy of FDG PET/CT for SCCUP in this patient cohort were 72.7% (16/22), 44.4% (8/18), 61.5% (16/26), 57.1% (8/14) and 60% (24/40), respectively. The

tonsil was the site with the most false positive and false negative findings. **Discussion & Conclusion:** FDG PET/CT might be an effective single shot of whole-body imaging for detection of the primary in SCCUP. The tonsils and the base of the tongue were the most common sites of the primary. Low specificity remains the most notable weakness of FDG-PET in work-up for SCCUP, which was prominently in the tonsils mainly due to varied physiologic uptake and inflammation. Another significant factor of low specificity of FDG PET/CT for SCCUP is the image indication bias. Considering to look for the unknown primary, radiologists or nuclear medicine physician might trend to call more abnormal findings on the images for SCCUP compared to those for other indications. On the other hand, the most common site of false-negative FDG-PET findings was the tonsils as well. High grade physiologic uptake and small size of the lesions were the major reasons of the false negative FDG PET/CT.

EP-0470

Synchronous And Metacronic Tumors Diagnosed By PET/CT With 18F-FDG In The Staging Of Head And Neck Tumors

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Purpose: Demonstrate the usefulness of PET/CT identifying synchronous and / or metachronous tumors during the diagnosis / staging of head and neck tumors **Subjects and Methods:** We reviewed 3599 PET/CT studies with 18F-FDG conducted between October 2014 and December 2017. We included those explorations whose motive was exclusively diagnosis / staging of head and neck tumors. They were analyzed by sex, age, primary otorhinolaryngologic area tumor and location of the secondary lesion. **Results:** Of all the patients reviewed, 488 met the inclusion criteria. Of the studies carried out to stage the primary disease, in 138 cases (28%) a hypermetabolic focus suspected of malignancy was observed. 134 were males and 4 females. The average age was 65.9 years. The most frequent location of the primary tumor under study was 58 in the hypopharynx / larynx (vocal cords, piriform sinus, epiglottis), 54 in the oropharynx (soft palate, floor of the mouth, tonsil, tongue, retromolar trigone) and 6 nasopharynx. Other less frequent indications included lip, nasal region, nasosinus, maxilla, auricular pinna and adenopathies of tumors of unknown origin until the 138 cases were completed. The malignant nature of the lesions was confirmed in 68 of the 138 cases (49%): in 30 of the primary ones located in the hypopharynx / larynx (44%), 27 in those located in the oropharynx (39.5%), 1 in the nasopharynx (1.5%) and 10 from other locations (15%). Foci suspected of malignancy were described in, according to frequency order: digestive tract 34/68 (50%), 16/68 in the lung (28.9%), 3/68 in the otorhinolaryngologic area other than the initial one (5.2 %), 2/68 in the thyroid (3.4%), 1/68 in the bladder (1.7%), 1/68 in the breast (1.7%), 1/68 in the pancreas (1.7%) and 1/68 pituitary adenoma (1.7%). **Conclusions:** The PET/CT with 18F-FDG helped the early diagnosis of malignant / premalignant lesion in almost half of the explora-

tions with suspicious findings of synchronous / metachronous tumor, thus allowing an early and adequate treatment aimed at these second neoplasms.

EP-0471

Sentinel node biopsy using dynamic lymphoscintigraphy with 99mTc-Tilmanocept (Lymphoseek) in the management of early (T1-T2 N0) oral squamous cell carcinoma:a pilot study

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Lymphnode metastases are the most relevant prognostic factor in oral squamous cell carcinoma (OSCC) and are present in 25-40% of patient with early (T1-T2 N0) OSCC. Identification of metastatic nodes remains a difficult task, even using advanced imaging (false-negative rate between 25-40%). Elective lymphnode dissection (END) takes into account imaging false-negatives, but leads to overtreatment in 60-73% of patients. Lymphoscintigraphy-driven sentinel node biopsy (SNB) has given promising results in OSCC, but traditional colloid tracers suffer some limitations. Long residency in the injection site(s) and proximity of sentinel node to the primary lesion may hamper pre-operative and surgical sentinel node identification. 99mTc-Tilmanocept (Lymphoseek), a new sentinel node tracer, binds to the CD206 mannose receptor of lymph node macrophages and combines a rapid clearance of the injection site with a selective retention in the sentinel node. Our protocol includes dynamic lymphoscintigraphy for 20', immediately after peritumoral injection (4 injections, same-day protocol 37 MBq , 2-day protocol 74 MBq), using a 2-heads gamma-camera (90 degree configuration, anterior and lateral projection, matrix 128x128, 15"/frame, 1.5 zoom). A static image is acquired after the dynamic phase, to mark the surface projection of the sentinel node with an external radioactive marker. SPECT-CT is performed to better define the anatomical site of the sentinel node (matrix 128x128, 25"/frame, 120 steps, zoom 2). The surgeon performs a radioguided SNB using a hand-held gamma-probe, checking activity in the excised node and in the surgical bed. The results obtained in the first 3 patients (2 anterior and 1 posterior tongue lesions) were highly encouraging; sentinel nodes were visualized in the first 2-3 minutes in all cases, with optimal identification of their anatomical relationships in the SPET-CT images. Good target/background ratio allowed an easy intraoperative identification and excision. The results of this small pilot series support the use of 99mTc-Tilmanocept (Lymphoseek) in SNB of early oral SCC.

EP-0472

Early Experience With ^{99m}Tc-Tilmanocept For Sentinel Node Detection In Head And Neck Cancer

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Introduction: ^{99m}Tc-Tilmanocept is the first receptor-targeted radioactive diagnostic agent approved by the US FDA in 2013.

It is a mannosyl DTPA dextran that targets the CD206 receptor. Tilmanocept binds to mannose receptors expressed by reticuloendothelial tissue including macrophages and dendritic cells in lymph nodes, which present it to T-cell lymphocytes in lymph nodes. We tested ^{99m}Tc -Tilmanocept in six patients with H&N' cancer to locate SLNs draining primary tumour. **Subjects & Methods:** Six consecutive patients (5 H&N' melanoma and 1 OSCC, cN0 neck) treated in our centre between November 2017- February 2018 were enrolled. A mean dose of 50 MBq, diluted in 0.4 mL of saline solution, was injected intradermally in four points around lesion. Early and Later scans were acquired starting immediately after tracer injections in Anterior/Lateral views (LEGP collimator, 128x128 matrix, factor zoom x1.5) minimizing neck-collimator distance. SLNs identified by preoperative lymphoscintigraphy and intraoperative detection by a gamma-probe, were surgically removed and histologically examined, using a same-day protocol. **Results:** In all cases a highest target-to-background ratio was obtained in less than 15 min after injections. In 5 out of 6 patients, the SLNs were visualized by first early scan acquired immediately after injection. A radioguided SLN biopsy was performed using a same-day protocol. After histological examination 2 out of 11 harvested SLNs were metastasis positive. 2 out of 6 patients were upstaged by a positive SN and a therapeutic neck dissection was performed. **Conclusion:** Although still preliminary, the results indicated that ^{99m}Tc -Tilmanocept showed a rapid clearance from the injection depot and low accumulation in second-echelon nodes. That allowed a short injection-to-imaging time and a highest quality of imaging in few minutes. A highest target-to-background ratio was observed also at surgery, facilitating radioguided biopsy. This radiopharmaceutical might be of particular utility in patients with head and neck cancer.

EP-40

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Hemato-oncology, malignant

EP-0473

Predictive value of baseline ^{18}F -FDG PET/CT peak standardized uptake value for progression free survival in Hodgkin Lymphoma

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Aim: To evaluate the prognostic significance of baseline ^{18}F -FDG PET/CT peak standardized uptake value (SUV_{peak}) in chemo-naïve Hodgkin Lymphoma (HL) patients, besides other PET/CT quantitative parameters and clinical factors. To our knowledge the prognostic value of baseline SUV_{peak} in HL has never been assessed. **Subjects and Methods:** We retrospectively reviewed HL patients diagnosed according to the WHO classification criteria in our Institution, between 2012 and 2016. We included 53 chemo-naïve patients with available staging and interim PET

scans, followed for a minimum of 12 months after treatment. Lean body mass normalized SUV_{peak} was measured at baseline, together with maximum standardized uptake value (SUV_{max}), metabolic tumor volume (MTV) and total lesion glycolysis (TLG). We accessed whether baseline quantitative PET/CT parameters, residual uptake on interim PET (PET_i) or clinical factors, such as advanced stage and International Prognostic Score (IPS), were related to progression free survival (PFS). Cox regression models, receiver operating characteristic (ROC) analysis, and Kaplan-Meier survival curves with the Log Rank test were used ($\alpha=0,05$). **Results:** During follow-up (median time of 47,3 months) 9 patients progressed, while no deaths were observed. Univariate Cox regression demonstrated that baseline SUV_{peak} (HR 1,2; $p=0,045$) was a statistically significant predictive factor for tumor progression, unlike the remaining baseline PET/CT quantitative parameters (SUV_{max} , MTV and TLG). Advanced disease (HR 5,3; $p=0,038$) and PET_i residual uptake on previously known lesions (HR 10,0; $p=0,004$) were also significant predictive factors for progression. Multivariate analysis confirmed the predictive value of SUV_{peak} (HR 1,3; $p=0,032$) and PET_i residual uptake (HR 16,1; $p=0,003$) independently of staging, IPS and MTV. Based on ROC analysis, patients with high SUV_{peak} ($\geq 6,975$) had lower PFS ($p=0,017$). **Conclusion:** The only baseline PET/CT quantitative parameter that showed prognostic significance in HL patients was SUV_{peak} . Its greater predictive value for PFS comparing to total tumor burden parameters (MTV and TLG) is very promising in clinical practice, since it probably reflects the ability to measure tumor aggressiveness easily and reproducibly, in a similar manner to SUV_{max} , being less prone to noise related fluctuations.

EP-0474

Diagnostic performances of texture analysis-derived PET parameters in predicting evolution to symptomatic myeloma in patients without focal disease involvement at FDG-PET/CT.

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Background and Aim: FDG-PET/CT is a useful one-stop-shop tool in depicting disease involvement in patients with smouldering multiple myeloma (MM) diagnosed on the basis of laboratory signs and bone marrow biopsy; however, focal involvement is not always noticeable on FDG-PET/CT in this setting. Aim of our study was to determine whether PET-derived parameters derived from texture analysis of axial bone predict progression to symptomatic MM in patients undergoing FDG-PET/CT for staging purposes without evidence of focal sites of ^{18}F -FDG uptake. **Materials and Methods:** patients with smouldering MM undergoing FDG-PET/CT for disease staging from January 1st 2016 to September 30th 2017 were retrospectively reviewed in order to retrieve patients without evidence of focal sites of ^{18}F -FDG uptake. For each patient the axial bone including the whole spine, pelvis and the proximal half of each femoral diaphysis was contoured by placing 2-dimensional ROIs on each

slice of sagittal projections; single ROIs were summed in order to produce 3-dimensional VOIs of these structures (spine-pelvis, femoral diaphyses). A dedicated software (Lifex[®], www.lifexsoft.org) allowed to obtain, for each ROI, conventional parameters (SUVmax, SUVmean, SUVpeak, MTV, TLG), first-order textural histogram and shape features (Skewness, Kurtosis, Entropy, Energy, Sphericity, Compacity), and advanced textural second-order features (Grey-Level Zone Length Matrix [GLZLM], Grey-Level Run Length Matrix [GLRLM], Neighborhood Grey-Level Different Matrix [NGLDM] and Grey Level Co-occurrence Matrix [GLCM]). Progression to symptomatic MM was assessed on the basis of clinical-laboratory symptoms and signs. **Results:** based on the aforementioned criteria, 23 patients were included (12m, 11f; mean age $61.8 \pm 10.3y$), although outcome information to determine possible progression to symptomatic MM was available only in 17 patients: 11/17 (65%) patients never met the criteria for symptomatic MM during their follow-up, while 6/17 (35%) patients progressed to symptomatic MM so they needed to start specific treatment. Conventional parameters, as well as the first-order textural histogram and shape features did not significantly differ between patients according to their progression to symptomatic MM for both VOIs (spine-pelvis and femoral diaphyses); conversely, Grey-Level Zone Length Matrix_ Short-Zone Low Gray-level Emphasis (GLZLM_SZLGE) which depicts the distribution of the short homogeneous zones with low grey-levels, derived from femoral diaphyses, was significantly lower in patients who progressed to symptomatic MM (median 0.026 [IQR 0.022–0.031] vs median 0.059 [IQR 0.030–0.077]; $P=0.041$). **Conclusion:** our preliminary data from a small population show textural PET-derived advanced features may be expression of subtle disease distribution in the axial bone marrow, with possible prognostic impact.

EP-0475

Neural Networks improves the prognostic value of end-of-treatment FDG-PET/CT in diffuse large B-cell lymphoma

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Introduction: FDG-PET/CT at the end of first line chemo-immunotherapy in patients with diffuse large B-cell lymphoma (DLBCL) showed a good prognostic power. Nevertheless, some limitations emerged as sub-optimal accuracy in the exact prediction of time to adverse events in the follow-up. Neural Networks (NN) have been proposed to improve the prediction power of multi-regression models (MR). **Aim:** Aim of this study is to evaluate the prognostic value of end-of-treatment FDG-PET/CT in diffuse large B-cell lymphoma using Neural Networks, in particular for the prediction of the time to adverse events in the follow-up. **Methods:** FDG-PET/CT at the end of first line chemo-immunotherapy for DLBCL were retrospectively evaluated by visual method (Deauville Score: DS) and semi-quantitative parameters as SUVpeak, qPET (target SUVpeak to liver SUVmean), MTV and TLG at different SUVmax thresholds (40%, 60%, 80% of SUVmax). Death and disease progression in the

follow-up were considered as adverse events. For MR and NN, FDG-PET/CT parameters and time-to-event were considered as input variables and target variables, respectively. NN analysis consisted in a Multilayer Perceptron with 10 hidden neurons, which showed the best performance respect to 8 and 12 ones. Sigmoidal activation function for all the neurons was used. NN mean absolute error (MAE) in predicting time-to-event was calculated. **Results:** Three hundred and eight patients were retrospectively included. Scans with DS 1 were 163/308 (53%), DS 2 44/308 (14%), DS 3 36/308 (12%), DS 4 43/308 (14%), DS 5 22/308 (7%). MR were not able to predict time-to-event, showing a correlation coefficient lower than 0.30. NN showed a correlation coefficient of 0.87 for time-to-progression and 0.94 for time-to-death. NN MAE was 23.6% for time-to-progression and 21.1% for time-to-death, respectively. For a time-to-event shorter than 30 months, a linear relationship between FDG-PET/CT parameters and time-to-event was evident, NN MAE was of 40% for time-to-progression and 36.4% for time-to-death. For a time-to-event longer than 30 months, NN showed a non-linear relationship, with a MAE of 15.6% for time-to-progression and 13.3% for time-to-death. **Conclusions:** Neural Networks allows end-of-treatment FDG-PET/CT in diffuse large B-cell lymphoma to predict the time to adverse events as progression and death in the follow-up, improving over multi-regression analysis. Neural Networks showed the presence of a non-linear model in the relationship between FDG-PET/CT parameters and time-to-event not previously described.

EP-0476

Fat Body Mass Measured on CT of Pretreatment 18F-FDG PET/CT is a Prognostic Factor of Diffuse Large B-Cell Lymphoma Treated by R-ACVBP

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Introduction: R-ACVBP is an intensified chemotherapy of Diffuse Large B-Cell Lymphoma (DLBCL) whose toxicity limits its use to young patients (< 60 years-old). Our aim was to explore in patients treated by R-ACVBP for DLBCL the prognostic value of anthropometric parameters measured on CT of pre-therapeutic ¹⁸F-FDG PET/CT. **Subjects & Methods:** We retrospectively included 58 patients with DLBCL treated by R-ACVBP and who underwent a pre-therapeutic ¹⁸F-FDG PET/CT. Anthropometric parameters were measured by in-house software, called Anthropometer3D, allowing an automatic multi-slice measurement of Lean Body Mass (LBM), Fat Body Mass (FBM), Muscle Body Mass (MBM), Visceral Fat Mass (VFM) and Sub-cutaneous Fat Mass (SCFM) on CT of PET/CT. All anthropometric parameters were normalized by the patient's body surface area (BSA) used to cal-

culate the dose of R-ACVBP. Body mass index (BMI), international prognostic index (IPI) and metabolic tumour volume (MTV) were also studied. Spearman's rank correlation coefficients (ρ) were computed between anthropometric parameters. A receiver operating characteristic (ROC) curve analysis was performed. Overall survival at 5 years was studied using a Kaplan-Meier method and uni/multivariate Cox analysis. **Results:** FBM had a strong correlation with SCFM and VFM ($\rho=0.99$ and 0.78 , respectively). LBM and MBM were relatively uncorrelated to other anthropometric parameters (maximal $|\rho|=0.61$ and 0.47 , respectively). In the ROC analysis, only FBM, SCFM, VBM and LBM had an area under the ROC curve (AUC) significantly higher than 0.5 . For the correlated parameters, FBM had a better AUC than SCFM and VFM (0.75 , 0.73 and 0.72 , respectively) and was therefore the only retained. Patients with high FBM ($> 12.7 \text{ kg/m}^2$) or low LBM ($< 30.1 \text{ kg/m}^2$) had significantly worse prognosis in Kaplan-Meier ($p=0.005$ and $p=0.023$, respectively). Only FBM was significant in the Cox univariate analysis (HR: 6.37 , $p=0.02$). In a stepwise multivariate Cox analysis combining FBM and LBM, the only significant parameter was FBM. **Conclusions:** FBM measured by Anthropometer3D on the pre-therapeutic ^{18}F -FDG PET/CT of patients having a DLBCL treated by R-ACVBP is an important prognosis factor, possibly linked to chemotherapeutic bio-distribution involved in the intensification. A dose calculation of R-ACVBP taking into account FBM rather than BSA could be pharmacokinetically beneficial.

EP-0477

Predictive Value of Quantization Parameters Acquired by a Novel Lesion Detection Algorithm on Baseline ^{18}F -FDG-PET/CT in Patients with Diffuse Large B-Cell Lymphoma: Interim Analysis of a Multi-centric Study

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Aim: To evaluate the prognostic value of semi-quantitative and volumetric parameters evaluated by a novel gradient-maximizing lesion detection algorithm in the baseline ^{18}F -FDG-PET/CT scan of patients diagnosed with diffuse large B-cell lymphoma (DLBCL). **Materials and Methods:** Data of 64 DLBCL patients (30 women, 34 men; mean age 55.16 ± 16) from two Hungarian centres were evaluated as part of an interim analysis of a multi-national, multi-centric study. In each case, a baseline ^{18}F -FDG-PET/CT scan was performed before the initiation of R-CHOP-immunochemotherapy. A novel lesion detection software (Mediso InterView Fusion) was applied in the evaluation, where after detecting all local maxima positions inside of the PET image, region-growing was performed independently from each of them to find that region-specific threshold where the given region has the highest gradient. The average of the maximum standardized uptake values (SUV_{max}) and the sum of the metabolic tumor volume (MTV) and the total lesion glycolysis (TLG) was calculated of each lesion showing increased FDG-uptake corresponding to DLBCL. As these data are to be included in a larger report, we do not disclose p-values. **Results:** When dividing the patient population into two equal groups deter-

mined by the median of either SUV_{max} , MTV or TLG, the progression-free survival Kaplan-Meier curves of the latter two parameters were diverging, while it was not prominent with the former one. Univariate Cox proportional hazard regression analysis showed about 1.6 times higher hazard of relapse for large MTV as compared to small MTV; about 1.4 times higher hazard comparing high TLG with low TLG; and lead to an unreliable model of SUV_{max} . Both MTV and TLG seemed to have a prognostic value independent of the Revised International Prognostic Index (R-IPI). 18-months progression-free survival analysis could be performed in 62 patients, where receiver operating characteristic (ROC) analysis resulted in an area under the curve of 0.603 , 0.689 , and 0.660 examining SUV_{max} , MTV, and TLG, respectively. MTV and TLG was higher (median $\pm$ IQR: 574 ± 943 vs. 187 ± 535 and 5064 ± 10899 vs. 1174 ± 3498 , respectively) in the 13 patients showing progression in the first 18 months compared to those in remission, while SUV_{max} tended to be lower (median $\pm$ IQR: 7.81 ± 6.76 vs. 9.01 ± 7.09). **Conclusion:** According to our interim analysis, of the gradient-maximizing lesion detection-based baseline ^{18}F -FDG-PET/CT parameters, MTV and TLG are likely to hold a prognostic value in DLBCL patients, while the role of SUV_{max} is controversial. Further examination in a larger patient cohort and comparison with conventional lesion-delineating methods are planned.

EP-0478

Prognostic value of baseline FDG PET parameters in high risk diffuse large B-cell lymphoma patients treated with dose-dense chemoimmunotherapy including early systemic central nervous system prophylaxis in a prospective Nordic multicentre study

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Introduction: In treatment of diffuse large cell lymphoma (DLBCL), baseline and interim PET/CT early during a course of chemotherapy are increasingly being used for risk stratification, and PET/CT after treatment is used to assess response. Although the prognostic value seems promising, there is uncertainty regarding the different PET parameters' relative value. Here, patients included in the Nordic multicentre CHIC study were analysed with the aim of evaluating the ability of baseline FDG-PET parameters to predict patient outcome. **Subjects and Methods:** The study included high risk diffuse large B-cell lymphoma (DLBCL) patients. The patients were treated with dose-dense chemoimmunotherapy including early systemic central nervous system prophylaxis. Chemoimmunotherapy consisted of two courses of high dose methotrexate (HD-Mtx) in combination with R-CHOP14, followed by four courses of R-CHOP14 and one course of R-HD-AraC. Liposomal cytosine arabinoside (AraC) was administered intrathecally at courses 1, 3 and 5. Recruitment ended December 2015. FDG PET/CT was scheduled both at baseline and after chemoimmunotherapy, and overall survival (OS) and progression-free survival (PFS) are available for all patients. 51 patients

that underwent FDG PET/CT at baseline have been included for the current analyses. The following baseline PET parameters were measured for each lesion: Standardized uptake value (SUV) max, metabolic tumour volume (MTV) and total lesion glycolysis (TLG). Total MTV and TLG values (tMTV and tTLG), excluding affected spleen and liver, and the number of metabolic active lesions were calculated for each patient. Survival analyses were performed using Kaplan-Meier curves and log rank tests. The covariates were dichotomized using median cut-offs. Cox regression was performed for significant findings. **Results:** Median baseline values (range) for the tMTV and tTLG were 567,0 (3,1 - 13505,9) ml and 4615,3 (15,3- 46393,3), respectively. The median number of lesions was 10 (1-90) and the maximum inpatient SUVmax had a median value of 20,5 (5,1 - 79,0). PFS and OS rates at 30 months were 69 % and 80 %, respectively. No significant associations to survival were found for maximum SUVmax, tMTV or tTLG. The number of metabolic active lesions demonstrated a significant association ($p<0,05$) with OS. The hazard ratio was 1,034 per additional lesion ($p<0,01$). **Conclusion:** A higher number of metabolic active lesions indicated a poorer prognosis, but no significant correlations to outcome were found for SUVmax, MTV and TLG. Further work may also include additional PET parameters, as heterogeneity, clinical prognostic factors, and tumour-related molecular factors.

EP-0479

Monoclonal gammopathy of undetermined significance (MGUS): 18 FDG PET/CT findings in the follow-up setting

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Aim: The aim of this study was to describe the utility of 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET)/computed tomography (CT) for evaluation of patients with Monoclonal Gammopathy of Undetermined Significance (MGUS) in the follow-up setting. MGUS is an asymptomatic plasma cell dyscrasias characterized by a monoclonal protein (M protein) < 3 g/dL (30 g/L) in the serum and $< 10\%$ monoclonal plasma cells in the bone marrow and no evidence of end-organ damage. On average, the estimated risk of MM progression is 1% per year for MGUS. New imaging methods are demonstrating that some patients in the MGUS category are exhibiting early signs of MM. **Materials and Methods:** This was a single-institution retrospective analysis of 20 patients with MGUS diagnosis referred to 18FDG PET/CT with negative radiologic surveys or non-specific morphologic bone lesions for MM in conventional X-Ray images. **Results:** Among 20 patients (mean age: 65.42 range: 41-82; Female/Male 1:1) with MGUS diagnosis referred to 18FDG PET/CT, 60% (12) had negative radiologic surveys and 40% (6) presented non-specific lesions in conventional X-Ray images before perform 18FDG PET/CT. As 18FDG PET/CT results, 12 patients had negative findings (2 of them with non-metabolic non-specific lesions in CT and 10 without evidence of bone lesions). 8 patients had positive ^{18}F -FDG uptake, 75% (6) of them presented hypermetabolic morphologic bone lesions in CT whereas 25% (2) had focal uptake on ^{18}F -FDG-PET with negative radiologic features (sensitivity 75%, specificity 83%). Patients

with more than 1 positive uptake lesions on ^{18}F -FDG-PET had a higher SUV max value in compare to those with only 1 positive uptake lesion on ^{18}F -FDG-PET (SUV max 4.7 vs 14.6, $p=0.05$). The most frequent sites of involvement were iliac bone (37.7%), sacrum (21.4%) and sternum (14.2%). No extra-osseous manifestations was observed. **Conclusion:** While a positive 18F-FDG PET reliably predicts active MM, a negative 18F-FDG PET is supportive evidence of MGUS. Improved imaging in this patients could allow more tailored clinical management and play an important role in the disease prognosis. In our experience, 18F-FDG had resulted in 40% of upstaging. Further prospective studies are needed to address which patient benefits more from 18F-FDG PET/CT in the follow-up setting of MGUS patients and when it is appropriated to indicate it.

EP-0480

FDG-PET/CT Has a High Diagnostic Yield in Suspected Occult Cancer

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Aim: Patients with suspected serious disease, i.e. patients with non-specific symptoms and signs suggestive of occult cancer, comprise a heterogeneous population that poses a clinical challenge. The diagnostic strategy remains controversial; in Denmark, a cancer fast-track program has been instituted, but FDG-PET/CT is not generally part of the routine work-up. We retrospectively evaluated the diagnostic value of FDG-PET/CT in consecutive SSD patients referred from a dedicated SSD outpatient clinic. **Material & Methods:** All SSD patients referred for FDG-PET/CT from the local SSD clinic from 1 November 2016-1 November 2017 were included. Medical records were comprehensively reviewed for conclusions on the diagnostic workup including other diagnostic procedures, histopathology, and clinical conclusions. Mean follow-up was 11 months [range 5-17]. Patients without cancer were followed for at least six months. A PET/CT scan was considered true positive for cancer, if FDG uptake suggestive of malignancy was confirmed by biopsy, and false positive if subsequent investigations could not confirm malignancy. A scan was considered true negative, if FDG uptake was normal or reported as reflecting a benign condition, and the fast track course was completed without establishing malignant disease. A scan was considered false negative, if no abnormal FDG uptake suggestive of malignancy was reported, and a cancer was subsequently diagnosed. **Results:** Fifty-nine patients were included; 49% males and a median age of 68 years (range 37-89). Nine patients were diagnosed with cancer (prevalence 15% [7-27%]); colon, prostate, myeloma, thyroid, lung ($n=2$), and metastases of unknown primary ($n=3$). All were correctly detected with FDG-PET/CT. Forty-one were true negative, nine were false positive and there were no false negative results. Thus, sensitivity, specificity, positive and negative predictive

values, and accuracy was 100% [66–100%], 82% [69–91%], 50% [26–74%], 100% [92–100%], and 85% [73–93%], respectively. Confidence intervals are in brackets. **Conclusion:** FDG-PET/CT had a high diagnostic yield in consecutive SSD patients with clinically suspected occult cancer: Cancer prevalence was 15%, sensitivity and negative predictive value was 100%, but the short follow up period in the majority of patients must be kept in mind. FDG-PET/CT should be considered first-line imaging modality in this setting.

EP-0481

Characterization of Residual Lymphoma Masses After 2 Cycles of Chemotherapy Using Whole-Body Diffusion-Weighted MRI and FDG-PET

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Purpose: To assess the value of diffusion-weighted imaging (DWI) in characterizing residual lymphoma masses early during first-line chemotherapy, compared with FDG-PET as the reference standard. **Methods:** Our prospective study included 120 patients with bulky disease at diagnosis (1 or more masses >7cm largest diameter). Whole-body DWI at 3 Tesla ($b = 50, 400, 800 \text{ s/mm}^2$) and FDG-PET were performed within 1 week from each other, or simultaneously using PET/MRI (Biograph mMR) in the later patients, before initiation and after 2 cycles of chemotherapy, except in 6 patients (3 consent withdrawals, 2 hospital changes and 1 death after baseline scans). Cellularity and metabolism of the main bulky masses for each patient were assessed quantitatively. Volumes-of-interest encompassing the entire tumors at baseline and interim were drawn semi-automatically after adequate segmentation on both modalities to obtain the ADCmean and the SUVmax metrics. The 2014 Lugano classification was used for PET interpretation and a Deauville score of 4 or 5 was considered positive. **Results:** Preliminary results of the first 85 patients -38 diffuse large B-cell (DLBCL), 29 Hodgkin (HL) and 18 follicular (FL) lymphomas- bearing 90 bulky masses >7cm are presented. Before treatment, ADCmean of these masses was $1.094 \pm 0.340 \times 10^{-3} \text{ mm}^2/\text{s}$ (range, 0.676–2.400). They were all FDG-avid with a SUVmax of 17.8 ± 8.9 (range, 4.0–43.3). When considering the different lymphoma subtypes, HL (29 masses) had significantly higher ADCmean values than either DLBCL (41 masses) or FL (20 masses), 1.378 vs. 0.969 and $0.939 \times 10^{-3} \text{ mm}^2/\text{s}$, respectively ($P < 0.0001$), while no difference was found between DLBCL and FL. Conversely, DLBCL had significantly higher SUVmax than either HL or FL, 24.1 vs. 13.0 and 11.66 , respectively ($P < 0.0001$), while no difference was found between HL and FL. At interim, ADCmean values of PET-positive ($n=29$) and PET-negative ($n=55$) residual masses were 1.425 ± 0.409 vs. $1.933 \pm 0.501 \times 10^{-3} \text{ mm}^2/\text{s}$ ($P < 0.0001$). **Conclusions:** Whole-body DWI with ADC mapping in patients with bulky masses at baseline shows different features between HL and non-Hodgkin lymphomas. In addition, characterization of residual masses by their cellularity at mid-induction seems well correlated with metabolic response (NCT02300402).

EP-0482

Performance of advanced imaging modalities at diagnosis and treatment response evaluation of patients with post-transplant lymphoproliferative disorder: A systematic review

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Introduction and Aim: Post-transplant lymphoproliferative disorder (PTLD) is a serious complication after solid organ and hematopoietic stem cell transplantation, associated with significant morbidity and mortality. In this systematic review we evaluated the clinical performance of advanced imaging modalities at diagnosis and treatment evaluation of PTLD patients after solid organ and hematopoietic stem cell transplantation. **Methods:** We have carried out a literature search until December 15, 2017 using PubMed/Medline, Embase, “Web of Science” and Cochrane Library databases concerning the performance of computed tomography (CT), magnetic resonance imaging (MRI) and 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) at diagnosis or treatment response evaluation of PTLD patients. **Results:** A total of 11 studies were included comprising 368 patients, where positron emission tomography was the core topic in all studies selected. The methodological quality according to QUADAS-2 of the reviewed studies was moderate-poor. At diagnosis, FDG-PET/CT reportedly identified additional lesions not visualized by morphological imaging (CT and/or MRI) in 11% (37/322) of patients. FDG-PET/CT reportedly detected additional extra-nodal sites in 5% (16/322) of patients and 4% (13/322) of patients were up-staged based on FDG-PET/CT findings. At treatment response evaluation FDG-PET/CT findings altered or guided treatment in 13% (10/76) of patients. Two reviewed studies reported a negative end of treatment FDG-PET/CT to be a predictor of longer progression-free survival. **Conclusion:** FDG-PET/CT is currently the most frequently investigated imaging modality in PTLD patients. Available studies report promising results in detection, staging and therapy evaluation but suffer from methodological shortcomings. Concerns remain with regard to occurrence of false positives due to inflammatory conditions and false negatives due to physiological high background activity and early lesions PTLD (non-destructive PTLD, WHO 2017). Table 5. Summary imaging results for the detection and staging & treatment evaluation in patients with PTLD

Abbreviations: BMI: bone marrow involvement; CNS: central nervous system; CT: computed tomography; LDH: serum lactate dehydrogenase MRI: magnetic resonance imaging; PET: 18F-fluorodeoxyglucose positron emission tomography/(computed tomography); PTLD: Post-transplant lymphoproliferative disorder; SUVmax: maximum standardized uptake value.

EP-0483

Hyperwarburgism. The prognostic value of cerebral ¹⁸F-FDG uptake in patients with lymphoma

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Introduction: “Hyperwarburgism” or “exaggerated Warburg effect” is a well-documented but rare phenomenon; consists of the association of hypoglycaemia and lactic acidosis in the presence of neoplasms, especially in lymphoproliferative processes such as lymphoma. This association is attributed to the Warburg effect (avid consumption of glucose via the glycolytic pathway and concomitant production of lactate, even in aerobic conditions). The persistence of hypoglycaemia, the low cerebral avidity for FDG, with a lack of neurological signs, indicate that there is an alternative source of energy, different from glucose, which is responsible for preserving brain function and preventing neurological symptoms. Lactate, therefore, is not only the last product of glycolysis, but also a metabolic substrate for the brain in the case of hypoglycemia. **Subjects and Methods:** Lymphoma staging FDG PET-CT scans performed at Instituto Nacional de Cancerología during the year 2013, 2014 and 2015 were analyzed. Patients with inclusion criteria were included (low or absent FDG brain uptake, complete laboratory studies and follow-up). **Results:** We analyzed 587 patient files, but only 9 patients fulfilled inclusion criteria. The patients presented an average age of 60 years (Range 37 - 80), with diagnosis of diffuse large cell lymphoma B without classifying 4 patients, no centrogerminal 1 patient, and centrogerminal 2 patients, peripheral LNH T 1 patient and a patient with Burkitt's Lymphoma. The average SUVmax of the lesions was 16 (range 7.6 - 37). The SUVmax of the brain was 4.4 (range 0.9 - 7.3). The average glucose of the patients was 56 mg / dl, lactate 4.4, pH 7.3. Of the 9 patients 2 are still alive (22.2%), and 7 died before 3 months (77.7%). **Discussion / Conclusion:** Our analysis is very similar to what is described in the literature. Therefore, it is very important to take the SUVmax brain as a prognostic factor of mortality, instead of the SUVmax of the lesion, since they varied from 7.6 to 37. The low brain uptake of FDG gives patients with lymphoma diagnosis a bad prognosis, since the short-term mortality is very high (77.7%), due to the complications of the tumor (example: tumor lysis), as well as the refractory hypoglycemia they present. Chemotherapy can disrupt the metabolic pathways of malignant cells and correct these abnormalities and should be initiated without delay.

EP-0484

Prognostic Relevance Of F-18 FDG PET/CT Parameters In Newly Diagnosed Multiple Myeloma

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In this study, we investigated the relationship between the parameters obtained by F-18 FDG PET/CT and the clinical and laboratory findings in the newly diagnosed MM patients.

Subject & Methods: A total of 56 patients with MM (31 females and 25 males, mean age $62.07 \pm$ years (range 35-87 years) respectively evaluated between January 2010 and February 2017. All of the patients were new diagnosed. Diffuse bone marrow uptake (DBMU), presence of appendicular skeleton involvement (ASI), the presence of extra medullary disease (EMD) and number of the focal lesions (FLn) and SUVmax values were identified as PET parameters. **Results:** The patients with ASI on PET/CT scans were on high DS stage ($p=0.005$); had low ECOG performance score ($p=0.024$) and response to treatment was poor ($p=0.003$). In patients with EMD, the response to treatment was poor and disease was more aggressive ($p=0.003$). The levels of $\beta 2M$, IgM and haematocrit were higher in patients with ASI on PET/CT than that of ASI negative patients ($p=0.033$, $p=0.011$ and $p=0.011$, respectively). There were positive correlation between the both FLn and SUVmax levels of lesions and DS stage ($p=0.002$, $r=0.399$ and $p=0.004$, $r=0.275$, respectively). Patients with ASI on PET/CT had higher DS stage ($p=0.005$), low performance score and poor response to treatment ($p=0.024$ and $p=0.003$). There were positive correlation between FLn and levels of $\beta 2M$ ($r=0.383$, $p=0.008$), CRP ($r=0.400$, $p=0.006$) and uric acid ($r=0.335$, $p=0.014$); between SUVmax and levels of Calcium ($r=0.286$, $p=0.034$) and CRP ($r=0.358$, $p=0.016$). While OS was 58.45 months in patients with normal serum ($\%95$ CI 43,35-73,55) $\beta 2M$ values, it was 49.99 months ($\%95$ CI 36,94-63,05) in patients with higher serum $\beta 2M$ values, $p=0.240$. FLn >2 was found a cut of, with 75% sensitivity and 54.5% specificity ($p=0.09$ ve AUC=0.666). Cut of value of SUVmax with ROC analysis was >5.92 (60.7% sensitivity and 72.7% specificity; $p=0.16$ ve AUC=0.646). Then, multivariate analysis was performed to identify independent factors in MM patients with positive PET/CT scanning. The results indicated that FLS >2 and SUVmax >5.92 were independent factors to predict OS in MM patients. FLn >5 was found a cut of, with 62.5% sensitivity and 60.9% specificity ($p=0.21$ and AUC=0.615). **Conclusion:** the PET parameters identified as AIT, FLS and SUVmax correlate with laboratory parameters in prognostic outcome of patients with MM. It seems that FLS >2 and SUVmax >5.92 are independent prognostic factors effecting the OS.

EP-0485

Prognostic impact of FDG-PET/CT using quantitative analysis for patients with diffuse large B-cell lymphoma or follicular lymphoma

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Introduction: Prognoses of patients with malignant lymphoma (ML) vary depending on the histological type and grade. FDG-PET/CT can evaluate ML tumor activity using various quantitative parameters, such as standardized uptake value (SUV), metabolic tumor volume (MTV), and total lesion glycolysis (TLG). However, the number of studies on the prognostic value of FDG-PET/CT using quantitative analysis for ML is still limited. The aims of this study were to assess the severity of ML using quantitative parameters and to evaluate the prognostic value of various quan-

titative parameters using FDG-PET/CT for patients with diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL). **Subjects and Methods:** Forty-seven consecutive patients who were confirmed to have DLBCL or FL via biopsy and underwent FDG-PET/CT were included. Patients with CNS invasion, concurrent malignant tumors, or other cancer history were excluded. Consequently, this study consisted of 21 DLBCL and 21 FL patients. GI-PET was used to quantify ML activities. Volumes of interest were automatically drawn on ML lesions. SUVmean in the ascending aorta of the same patient was chosen for the threshold value for lesion VOI. SUVmax, MTV, and TLG of each ML lesion were calculated, as well as overall MTV (OMTV) and overall TLG (OTLG) of all ML lesions. All patients were observed for over 3.5 years from initial PET/CT for the occurrence of major adverse events (MAE), defined as all-cause mortality, or progression or recurrence of ML. Both the patients with DLBCL and FL were divided into two groups based on the occurrence of MAE using receiver-operating-curve analyses. **Results:** In the patients with DLBCL, the proportion of patients that experienced MAE was significantly higher in the high OMTV group and high OTLG group compared with the respective low groups (9 of 11 vs. 1 of 10, $p = 0.001$; 10 of 12 vs. 0 of 9, $p < 0.001$). In the patients with FL, the proportion of patients who experienced MAE did not differ between the high and low OMTV/OTLG groups (5 of 7 vs. 4 of 14, $p = 0.084$; 5 of 8 vs. 4 of 13, $p = 0.303$). **Conclusions:** For patients with DLBCL, quantitative indicators, such as OMTV and OTLG, obtained by FDG-PET/CT likely have a high prognostic value. For patients with FL, OTLG may not be correlated with incidence of MAE due to the variation of FDG accumulation based on the histological grades whereas OMTV could be a potential prognostic factor.

EP-0486

Radiation therapy dose consideration in Hodgkin Lymphoma after chemotherapy: implication of metabolic response assessment in 18 FDG-PET/CT

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Aim: The aim of this study was to describe the implication of metabolic response assessment in 18F-FDG PET/CT after chemotherapy in order to determine the dose prescription in patients with Hodgkin lymphoma (HL) referred to radiotherapy (RT). In early-stage HL (I-II), RT is often part of the treatment program after systemic chemotherapy. In patients with advanced-stage disease (III-IV), localized RT may be used for residual lymphoma after full chemotherapy, or as an integral part of some treatments regimens. Salvage RT play an important role in refractory disease or in relapse after complete response to chemotherapy. Modern RT has been shown to be safe mainly because highly conformal treatments techniques (3DC or IMRT) allow to reduce significantly the volume of treatment (Involved Site Radiation Therapy -ISRT-). The determinants of dose prescription for HL include not only the histologic subtype, stage and clinical risk factors but also the metabolic response assessment in 18 FDG-PET/CT after chemotherapy. In general, in cases of early HL the dose is 30Gy, whereas in patients with residual

lymphoma after chemotherapy increasing the dose to 36-40Gy should be consider. **Materials and Methods:** Single-institution retrospective analysis of 88 adult patients (> 18 years) with Hodgkin lymphoma (II-IV) referred to radiotherapy after chemotherapy from January 2013 through December 2017. All included patients had undergone end-of-treatment 18FDG-PET/CT (E-PET). **Results:** All of 88 patients (mean age: 37.5 range: 18-80; Female 34.1%-Male 65.9%) with HL (II-IV) were referred to radiotherapy after chemotherapy. A total of 88 E-PET/CT reports were available for the analysis (one for each patient). The Deauville score was recorded in the 32.9% (29) of reports. According to this score, patients were considered to have a complete metabolic response (Deauville Score 1-3) or an active metabolic disease (Deauville Score 4-5) prior radiotherapy. Radiation dose prescription was analyzed in both groups. In patients with complete metabolic response, the mean prescription dose was 30.1Gy (range: 20-40Gy) in compare with a mean dose in active metabolic disease group of 36.2Gy (range: 30-40Gy) ($p=0.01$). All patients were treated with ISRT 3D technique. **Conclusion:** PET/CT is essential in the era of ISRT. Whereas the PET images of the pre-chemotherapy PET/CT are used to delineate the initially involved lymphoma volume, the post-chemotherapy PET/CT metabolic response assessment should be consider for defining the radiation dose.

EP-0487

Contribution of colour scales in Deauville score assessment of interim and end-of-treatment FDG PET in Hodgkin Lymphoma: a preliminary study

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Purpose: The 5-point Deauville scale (DS) is widely used to assess interim and end-of-treatment FDG PET metabolic response to chemotherapy in Hodgkin lymphoma (HL) patients. This is a preliminary study aiming to determine the contribution of colour scales in qualitative assessment of FDG PET in HL as compared to black/white scale, and in particular in the DS assignment. **Methods:** Two nuclear medicine physicians scored 219 interim or end-of-treatment FDG PET scans from LH patients. Images were anonymously saved in two different color-scales: black and white inverse (BW) and Rainbow GE (COL) on GE Xeleris Workstation Console. For each colour-scale, readers assigned DS and a confidence level (ranging 0-100). DS were compared to lesion uptake ratio to mediastinal blood-pool and liver uptake. **Results:** The use of COL images lead to a change in DS in 14.6% of cases, as compared to BW images, with up-scoring of 5.9% and down-scoring of 8.7% of cases. The percentage of correctly classified cases was 77.6% with BW images, improving at 84% with COL images. With the use of COL images, the percentage of correctly classified cases among DS1,2,3 vs DS4,5 improved from 94.8% to 98% and from 94.4% to 97%, respectively. Besides, it has been observed an increase in diagnostic confidence in DS

assignment, from 77% with BW images to 88% with COL images.

Discussion: In the evaluation of interim and end-of-treatment FDG PET scans in HL patients, the use of a color scale could increase both the accuracy and the diagnostic confidence in Deauville scoring. The improvement is particularly significant in the differentiation between positive and negative scans. Further studies are needed to clarify if such improvement is confirmed in different readers groups (i.e. experts vs not-experts).

EP-0488

Incidental critical findings on F18-FDG PET CT- A Pictorial

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Purpose: To review the incidental critical findings in elective F18 FDG PET CT scan in a tertiary care cancer centre. **Subjects**

& Methods: Review of all the critical alerts raised following F18 FDG PET CT scans using the hospital electronic record system.

Results: In the period extending from Oct 1, 2017 to April 12, 2018 a total of 1773 F18 FDG PET CT scans were performed and critical findings were identified and alerts generated for 13 (0.7%) scans. Age range: 6 years to 67 years. 10 patients were male while 3 were females. Lymphoma and gastrointestinal malignancy was the commonest indication for performing the F18 FDG PET CT in 6 patients each with one patient with diagnosis of renal malignancy. 7 out of 13 critical alerts were raised for central nervous system - 6 for suspected cord compression and 1 for cerebellar extension/compression. Three alerts were raised for incidental or progressive thrombus and three for suspected perforation or fistula. **Discussion:** F18 FDG PET CT is an elective procedure performed for a wide spectrum of oncological indications. Scans performed for baseline staging and / or treatment response evaluation require a thorough review of findings, and at times serial scans and correlative imaging. The need for identifying incidental critical findings is to be balanced against releasing the patients, in a timely manner, so that the next patient in line can be put on the camera and imaged within the stipulated. Our pictorial review identifies the common incidental findings which warrant an alert for the referring team. This exercise is important for the learning and training of junior doctors involved in discharging patients in a busy PET CT service. **Conclusion:** Identification of critical findings on elective F18 FDG PET CT scan is important and should be periodically reviewed as a quality indicator.

EP-0489

The Role of FDG PET/CT Detecting Bone Marrow Involvement in Non-Hodgkin's Lymphoma Patients

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Introduction: Bone marrow biopsy is still routinely recom-

mended for staging non-Hodgkin's lymphoma (NHL). The efficacy of FDG PET/CT in detecting bone marrow involvement has been shown in recent studies. **Material and Method:** Eighty-seven NHL patients who underwent FDG PET/CT for staging were included in the study. FDG PET/CT parameters, bone marrow biopsy results, Ki67 levels and 5-year survival were analyzed. Confirmation (pathology, clinical follow-up and bone marrow findings in MRI) was accepted as a reference for bone marrow involvement. Bone marrow biopsy is routinely performed from the posterior of the iliac bone, and infiltration in other localizations will be missed. In patients with negative biopsy results; FDG PET/CT imaging was considered positive if the FDG uptake in locations other than iliac bone decreased as in other lesions on PET /CT imaging after 2-3 cycles of chemotherapy or if infiltration was detected on synchronous MRI images. The evaluation was carried out by three specialists. **Results:** The median age of the patients was 54 years (19-90 years). Fifty-six (64%) patients had diffuse large B-cell lymphoma. Bone marrow involvement was detected in 17 patients with FDG PET/CT and in 24 patients with bone marrow biopsy, whereas confirmation of bone marrow involvement in 31 patients was observed. Ki67 values of all 14 patients who were negative with FDG PET/CT and positive with confirmation were found below 25%. The sensitivity and specificity of FDG PET/CT in detecting bone marrow involvement was 54% and 100%, respectively (n=87). When Ki67 value was below 25% the sensitivity and specificity was 13% and 100%, respectively. The sensitivity and specificity was 100% when Ki67 value was above 25% (n=53). The associations between quantitative PET/CT parameters [SUVmax (P=0.001), SUVmean (P=0.002), SULpeak (P=0.002), TLG (total lesion glycosynthesis, P=0.003)] and overall survival were found statistically significant. **Discussion:** Different sensitivity and specificity values for predicting bone marrow infiltration of FDG PET/CT were reported in various studies. We found high sensitivity and specificity values of FDG PET/CT in the group with Ki67 proliferation index above 25% and low (13%) sensitivity and high specificity values of FDG PET/CT in the group with Ki67 proliferation index below 25%. It is already known that the FDG uptake correlates with the grade of lymphoma and the proliferation of malignant cells. Quantitative FDG PET/CT parameters can provide survival prediction for patients with NHL.

EP-0490

Inter-observer reliability in the assessment of interim 18F-FDG PET/CT in patients diagnosed with Hodgkin lymphoma, ¿Is rPET the solution? Pilot study

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Aim: Determine the utility of ratio between target lesion and liver SUVmax (rPET) as an alternative of Deauville scale, and its inter-observer reliability of the assessment in patients with Hodgkin lymphoma (HL) undergoing interim FDG PET/CT.

Materials and Methods: Retrospective study with 53 adults patients diagnosed of HL, undergoing 18F-FDG PET/CT, three

weeks after completing the 2nd or 3rd chemotherapy cycle; 48 of them had staging PET/CT. A semi-quantitative analysis was made, using rPET, taking the maximum metabolic activity lesion as the target lesion; The response to treatment was evaluated using the Deauville score, discarding as residual disease the lesions that clinically suggested inflammatory or infectious cause. The concordance between two observers was studied for the categorization of the Deauville score, considering as positive the studies with score 4-5. Likewise, the receiver operating characteristic (ROC) approach was applied to identify the optimal cutpoint of rPET in relation to the distinct categories of the Deauville score, to calculate accuracy values and to define the area under the curve (AUC). **Results:** Forty four of the 53 patients were in complete metabolic response (CMR) and 9 in partial metabolic response (PMR). A strong inter-observer agreement was obtained with a Cohen's Kappa coefficient of 0.77, observing three discrepancies between the positive (D4-5) and negative (D1-2-3) studies, which was clarified with a joint evaluation of the studies by the two observers. The analysis of the ROC curve for rPET as a predictor of PMR, no metabolic response or progressive metabolic disease had a cut-off point of 1.33, with a sensitivity of 100% and a specificity of 51%. Likewise, rPET cut points equivalent to the Deauville score were obtained, D1=0, D2=0.33, D3=0.74, D4=1.33 and D5=2. There was a progression in one patient that caused a treatment change. **Conclusion:** The rPET methodology optimize and improve the sensitivity of interim PET/CT, discriminating the patients who are in CMR from those with Deauville 4-5; In our series, a rPET value <1.33 excludes residual disease with a high sensitivity. It is necessary to carry out prospective studies with a greater number of patients to validate this data.

EP-0491

Added Diagnostic and Prognostic Value of FDG PET CT in Assessment of Primary and Secondary Hepatic NHL.

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Aim: to evaluate the role of FDG PET/CT in detection of primary and secondary hepatic NHL and its prognostic value. **Materials and Methods:** 33 patients (21 male, 12 female, mean age: 52.1±11.9) with pathologically proven NHL in whom FDG PET/CT scan were retrospectively assessed. Hepatic lesions analysis in total 66 PET/CT studies initially and post chemotherapy were conducted. Pathological and clinical/radiological follow-up served as standards of reference. **Results:** Primary hepatic lymphoma is reported in 5 patients (15%) of all 33 NHL patients presented with hepatic involvement. (3 males and 2 females), 3 of them had HCV and DLBCL was the dominant pathology in 4 patients (1 with Burkett's lymphoma). 3 patients presented with solitary lesion, 2 with multifocal lesions and one of them associated with diffuse pattern infiltration. In assessment of therapy response, 2 achieved CMR, 2 showed partial disease regression & 1 patient progressed. For secondary hepatic involvement, DLBCL was found in 24 patient (85%), 1 patient with Burkett's, 1

Mantle cell and 1 anaplastic NHL. Ten of them are proven to have HCV while 2 had HBV infection. Most of those patients presented with supra and infra-diaphragmatic nodal infiltrates (89%), 16 out of 28 (57%) had splenic involvement, 17 with osseous, 2 renal & 5 patients presented with pulmonary lesions. A total of 67 discrete hepatic lesion (6 solitary and 61 multi-focal) were reported, diffuse pattern present in 2 patients, combined focal & diffuse was presented in 4 included patients. Mean SUVmax value and size of these patients was 14.4 ± 11.8 and 5.2 ± 4.1 cm (range, 1.8-16 cm) respectively. Finally 11 out of 28 patients with secondary hepatic lymphoma (40%) achieved CMR, 9 showed disease regression and 8 progressed. No correlation was found between the high initial SUVmax and adverse prognosis. **Conclusion:** Primary liver lymphoma represents 15% of total hepatic NHL. Combined PET/CT provided additional functional information in diagnosis of both primary and secondary hepatic NHL and in assessment of therapy response. **Key words:** FDG PET/CT, Primary, secondary, hepatic lymphoma

EP-0492

Efficiency Of 18F-FDG-PET/CT In Assessing Bone Marrow Infiltration In Hodgkin Lymphoma And Non Hodgkin Lymphoma. It Is Really Necessary The Bone Marrow Biopsy?

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Introduction: The value of positron emission tomography/computerized tomography with ¹⁸F-2-fluoro-2-deoxy-D-glucose (¹⁸F-FDG-PET/CT) in detecting bone marrow infiltration (BMI) and its concordance with bone marrow biopsy (BMB) has being well establish in Hodgkin's lymphoma (HL), however, in clinical practice there is still debate about needing to perform BMB. In non-Hodgkin's lymphoma (NHL), especially in the diffuse large B-cell lymphoma (DLBCL), there is even more controversy regarding to its ability to detect BMI. The present study aims to evaluate the efficiency of ¹⁸F-FDG-PET/CT for detection of BMI in HL and NHL. **Subjects and Methods:** A retrospective study, including 53 cases of newly diagnosed HL and NHL. Data collection was made using the electronic medical record from November 2016 to April 2018 of patients admitted to the department of Nuclear Medicine for initial staging with ¹⁸F-FDG-PET/CT. To assess the BMI, visual evaluations of the PET/CT scan findings were made. In HL cases only focal FDG-avid lesions on PET/CT were reported as bone marrow infiltration. In NHL both diffuse bone marrow FDG uptake (bone marrow uptake > liver uptake) and focal lesions were considered positive. In both diseases the result was negative when there was no uptake in bone marrow. We calculated the ¹⁸F-FDG-PET/CT sensitivity and specificity in DLBCL and HL with the BMB as the gold standard test, considering that the BMB was not always performed in the focal deposit area. **Results:** There were 12 cases of HL and 42 cases of NHL, 37 of them with diffuse large B-cell lymphoma (DLBCL) and 4 with follicular variant. Patients with NHL had a negative study in 61% of the cases and 39% were positive (true

positive 87.5%), one of them showed a doubtful result in the biopsy (infiltration by lymphoma was not completely ruled out). We found that the visual evaluation of PET/CT showed a sensitivity of 100% (IQ95%: 73.54 - 100%) and specificity 92% (IQ95%: 73.97- 99.02%) in the detection of BMI in the DLBCL. In patients with LH, the visual evaluation showed a sensitivity of 100% (IQ95%: 2.50% -100%) and specificity 92% (IQ95%: 58.72% to 99.77%). In the follicular variant: 75% of the cases were false negative. **Conclusion:** The ^{18}F -FDG-PET/CT is a useful tool to rule out BMI in patients with HL and LDGCB. The visual assessment may also allow to avoid BMB in positive cases. However prospective and analytic studies are needed to prove this hypothesis.

EP-41

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology -> Liver,
upper GI and pancreatic (non-endocrine), malignant

EP-0493

Dual-tracer (18F-fluorodeoxyglucose/18F-fluorocholine) PET/MR as a multiparametric diagnostic tool in patients with hepatocellular carcinoma: a pilot study.

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Introduction: Accurate diagnosis of hepatocellular carcinoma (HCC) remains problematic, in spite of advanced imaging technics development. HCC is very heterogeneous group of tumours with various patterns in conventional imaging. The great challenge are small lesions of well-differentiated HCC, which are resectable but not easy to detect. **Aim:** The aim of this study is to analyse the results of multimodal dual-tracer PET/MR imaging and to compare the diagnostic accuracy of morphological and metabolic images in patients with HCC. **Materials and Methods:** 16 patients with histological confirmed HCC or with high probability of HCC (stated on the basis of laboratory and CT/MR diagnosis) were included into this study. Thirty examinations were performed (in 14 patients both 18F-FDG and 18F-FCH PET/MRI, one 18F-FDG PET/MR only and one 18F-FCH PET/MR only). Two days protocol (one day - 18F-FDG and other day - 18F-fluorocholine) whole body PET/MR was applied with the MRI sequences of T1w, T2w, contrast enhances (DCE), diffusion weightes (DWI) images and apparent diffusion coefficient maps (ADC). **Results:** In 10 patients both 18F-FDG and 18F-FCH PET was positive, in twelve patients 18F-FCH PET was positive and FDG PET was negative, in 4 cases FDG PET was positive and FCH PET was negative. Mean FDG SUVmax was 4.36 ± 2.2 , mean FCH SUVmax was 9.06 ± 3.6 . In two patients both FDG and FCH PET were negative, in this cases HCC was excluded in 6 months clinical follow up and next fine needle aspiration biopsies. In DWI hyperintense lesions were found in ten patients, but restricted diffusion was noticed in only 4 cases. Mean ADC comes to 990 ± 207 .

Therefore, sensitivity was 83% for 18F-fluorocholine, 63% for 18F-FDG, 75% for DWI and 100% for dual-tracer PET/MRI. **Conclusions:** Multiparametric imaging is absolutely necessary in patients with HCC. Dual-tracer PET/MRI seems to be advanced, comprehensive and complete imaging method in such heterogeneous disorder. But this is only pilot study, it should be extend to give reliable results.

EP-0494

Inter-observer variability assessment for hepatic function measurement based on hepatobiliary-scintigraphy

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Introduction In patients addressed for liver direct therapy, the underlying liver pathology and prior treatment may decrease functional hepatic reserve to critical levels with risk of post-treatment liver failure. In this context hepatobiliary-scintigraphy (HBS) enables hepatic function (HF) measurement. Eligibility for therapy is assessed with a recently validated cut-off value of 2.7%/min/m² as HF lowest limit. This study aims at defining the inter-observer variability of HF measurement based on HBS. **Materials and Methods** 20 patients, who underwent HBS, were retrospectively evaluated by 4 experienced nuclear medicine physicians using dedicated commercial software (SyngoMI-V-A60C). Dynamic planar acquisition (10x36 seconds during 360 seconds) was performed immediately after intravenous injection of 200 MBq of ^{99m}Tc-mebrofenin (De Graaf et al., 2010). Three time-activity curves (TAC) were generated for three regions of interest on geometric mean images: liver, heart (plus large vessels) and total field of view. HF was calculated using TAC derived values acquired between 150 and 350 seconds after injection (Ekman et al., 1996). Finally HF was normalised by patient's body-surface-area for inter-patient comparison. The largest inter-observer HF difference was computed for each patient. Then, both maximum and average values were determined for all patients. To avoid inter-patient variability, HF were normalised by the respective mean value of each patient for all physicians (mean value=1). Standard deviation (SD) was computed for the normalised HF. The 95% confidence interval (95%CI) of HF measurement was computed with 1.96xSD, assuming Gaussian-distribution (N=80). **Results:** The largest difference observed between two physicians in HF measurement was 24.1%. On the average the largest inter-observer variability on the whole cohort was 12.3%. The SD of the normalised HFs was 5.6%. The 95%CI taking into account the inter-observer variability was HF $\pm$ (0.11xHF). **Conclusion:** Our study demonstrates that the method for determining patient's HF based on HBS was reproducible and that safe HF could be defined as HF - (0.11xHF). HBS is an interesting tool to evaluate functional hepatic reserve and could be used to assess patient's eligibility before hepatotoxic therapy.

EP-0495

Total lesion glycolysis in FDG PET/CT is a useful predictor of prognosis in patients with locally advanced gastric cancer treated by radical gastrectomy

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Objective: Gastric cancer (GC), including gastroesophageal junction cancer (GEJC), is the second leading cause of cancer mortality worldwide. Effective technologies for accurate staging and quantitative evaluation are highly demanded to merit reasonable treatment and better prognosis for the patients presented with advanced GC. Co-registering metabolic and morphologic data, ^{18}F -FDG PET/CT has been widely used in the management of malignant tumors. However, the value of FDG PET/CT in the prognosis of GC is still controversial. In this study, we aimed to investigate the prognosis value of the baseline FDG PET/CT, via metabolic parameters, in patients with advanced GC treated by the radical gastrectomy. **Methods:** In total, 144 patients with LAGC (62 years, 60.62 ± 11.58 years) underwent ^{18}F -FDG PET/CT prior to any treatment. The maximum standardized uptake values (SUV_{max}), mean standardized uptake values (SUV_{mean}), metabolic tumour volume (MTV) and total lesion glycolysis (TLG) of the primary lesion were measured on PET/CT and correlated with clinicopathological features and survival. A prognostic scoring system based on pre-operative PET/CT was developed. **Results:** Significant differences in SUV_{mean} , SUV_{max} , MTV and TLG were found according to Lauren's classification, histologic grade and T category ($P < 0.05$). During the 26.5-month follow-up, 51 patients (35.4%) died and 70 (48.6%) exhibited disease progression. The optimal thresholds of MTV and TLG were 15.1 cm^3 and 47.3 cm^3 , respectively. The 3-year PFS and OS for patients with high TLG values were 30% and 38% compared to 38% and 47% for low TLG values, respectively ($P < 0.05$). Univariate and multifactor analyses demonstrated that lymph node metastasis and T stage were independent prognostic factors for PFS; T stage, histologic grade and TLG were independent prognostic factors for OS ($P < 0.05$). Molecular markers had no relationship with patient's outcomes. The PET scoring system had a high predictive value for long-term outcomes. The four-year survival rate for patients with a score of 0–2 was 32%, whereas that for patients with a score >4 was 25% ($P < 0.05$). **Conclusions:** Metabolic activity of primary gastric tumours from ^{18}F -FDG PET/CT is a prognostic factor in patients with LAGC. A pre-treatment PET scoring system can assist in the selection of patients when staging ^{18}F -FDG PET is being considered.

EP-0496

Pretreatment metabolic parameter in F18- FDG PET/CT predict overall survival in squamous cell esophageal cancer

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Introduction: Esophageal cancer is a common cancer with a poor prognosis. The aim of this study was to evaluate the

prognostic value of metabolic tumor parameter MTV and TLG measured by F18-FDG PET/CT in patients with squamous cell esophageal cancer. **Methods:** 263 patients with esophageal cancer were recruited retrospectively between January 2005 and October 2016. In our study we included 106 patients with squamous cell esophageal cancer, who underwent F18-FDG PET/CT before treatment. SUV_{max} , SUV_{mean} , MTV and TLG were measured in F18 FDG PET/CT using VOIs. Age, gender and history of smoking and alcohol was raised from patients medical records. Overall survival (OS) was examined by the Kaplan-Meier method. **Results:** We reviewed 106 patients, 87 men (82.1%) and 19 women (17.9%). The univariate analysis showed for age, >65 Jahre, HR 1.83; 95% CI 1.03–3.24; $p=0.04$], gender [HR 1.25; 95% CI 0.58–2.69; $p=0.568$], smoking [yes vs. no (reference), HR 0.98; 0.55–1.77; $p=0.578$], alcohol [HR 0.65; 95% CI 0.34–1.22; $p=0.182$], MTV [HR 1.0097; 95% CI 1.0048–1.0147; $p<0.001$] and TLG [HR 1.0011; 95% CI 1.0005–1.0016; $p<0.001$]. **Conclusion:** This study shows that in univariate analysis age, MTV and TLG of primary tumor were significant predictors of overall survival in squamous cell esophageal cancer. Univariate analysis indicated that the metabolic parameter SUV_{max} and SUV_{mean} as well as a history of smoking and alcohol and gender were no significant risk factors in squamous cell esophageal cancer.

EP-0497

Preoperative estimation of residual liver function after surgery using Tc-99m-Mebrofenin: comparison of SPECT/CT and CT volumetry

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Purpose: The postoperative liver function was estimated in patients with impaired liver which are scheduled for extended or right hepatectomy. We used dynamic Tc-99m-Mebrofenin scintigraphy followed by SPECT/CT and CT volumetry for comparison. **Materials and Methods:** The present analysis relies on a group of 39 patients suffering from liver metastases, hepatocellular carcinoma, or cholangiocarcinoma. The absolute function, i.e. the percent uptake rate per body surface area ($\% \text{ID}/\text{min}/\text{m}^2$), of the whole liver was determined by scintigraphy (Siemens Intevo) with Tc-99m-Mebrofenin in a dynamic 6 min acquisition with 36 frames (10 s per frame) started immediately after injection. This was followed by a SPECT/CT acquisition with 60 projections (8 s each) and a low-dose CT (Intevo, Siemens) in order to determine the expected fraction of preserved liver function after surgery based on the summed tracer signal in corresponding contours around the remnant and total liver volume. This functional information was compared to the volumetric information derived from the CT alone. **Results:** The average preoperative uptake rate of the whole liver were $4.5 \pm 1.9 \text{ \%ID}/\text{min}/\text{m}^2$ (1.6 to $8.9 \text{ \%ID}/\text{min}/\text{m}^2$). According to resection planning, the SPECT predicted a relative preserved fraction of liver function after surgery of $45 \pm 18 \text{ \%}$ (18 to 81 %) whereas the

CT volumetry predicted 33 ± 15 % (11 to 83 %). CT volumetry correlated well with the SPECT measures (R^2 68 %) but estimated on average only 79 % (32 to 107 %) of the remnant function predicted by SPECT/CT. Five patients with a low initial liver function were treated by portal vein embolization or in-situ-split in order to induce hypertrophy before completing the liver resection. After about two weeks, we were able to observe an increase of the function in the remnant liver on SPECT by 62 ± 34 % (30 to 112 %). **Conclusion:** The fraction of remnant liver function predicted by SPECT/CT correlated well with the prediction by CT volumetry, which, however, provided significantly lower values in most cases. Analyses regarding the association between predicted remnant liver function and observed postoperative liver failure are under way.

EP-0498

Diagnostic accuracy of 18F-FDG PET/MR in HCCs: comparison of local and metastatic staging with CT CAP and liver MRI

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Purpose: To assess the diagnostic accuracy and therapeutic management impact of whole body 18F-FDG PET/MR for local and whole body staging of HCCs. **Materials and Methods:** 61 consecutive patients followed for HCC were included in this retrospective study. All patients underwent whole body 18F-FDG PET/MR (Biograph mMR) which included whole body sequences (simultaneous multi slice with blipped Controlled Aliasing in Parallel Imaging Results in Higher Acceleration sequence design (SMS DWI), unenhanced and post contrast 3DT1 Dixon VIBE), and dedicated liver sequences (SMS IVIM DWI, T2, multiphasic 3DT1 VIBE). The accuracy of 18F-FDG PET/MR for HCC detection, local - biliary, vascular involvement - regional N staging, and distant staging was compared to that observed with CT CAP and liver MRI, with pathology, follow up or consensus interpretation of all available data as the reference standard. **Results:** Overall, 104 HCC and 17 metastatic sites were documented. Sensitivity for HCC detection was 97% (93% for TDM and MRI; $p > 0.05$). Sensitivity, specificity, PPV and NPV for vascular and biliary involvement and for regional staging were 100%. There was a significant difference in sensitivity for metastatic sites between 18F-FDG PET/MR and TDM-CAP + liver MRI (100% vs 50%; $p < 0.0007$). 18F-FDG PET/MR led to changes in therapeutic management in 21% of patients (13/61), 5 by modification of loco-regional staging, 7 by detection of additional metastatic sites and 1 by modification of loco-regional staging and metastatic staging. **Conclusion:** 18F-FDG PET/MR improves local and distant HCC tumor staging compared to CT CAP and liver MRI performed separately, with significant impact on patient treatment management.

EP-0499

^{99m}Tc-macroaggregated albumin (MAA) scintigraphy, with additional SPECT/CT, able to optimize pre-SIRT evaluation and patients selection?

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Purpose/Introduction: to investigate the role of hepatic artery perfusion scintigraphy with ^{99m}Tc-macroaggregated albumin (MAA scan) and additional sequential SPECT/CT in the selection of patients (pts) for Selective internal radiotherapy (SIRT) with resin-microspheres. **Subjects & Methods:** A retrospective single center analysis was performed on pts who underwent MAA scan including SPECT/CT, as part of the standard pre-SIRT evaluation. All the scans, performed according to EANM guidelines, were reviewed by at least two expert nuclear medicine physicians (ET, ELR, LZ) and compared with ceCT/MRI routinely performed before as restaging procedure. The following functional parameters were evaluated: a) lung shunt fraction (LSF); b) MAA distribution (extension, pattern) at the level of liver segments and c) target hepatic lesions or neoplastic thrombosis (complete/partial/absent correspondence), d) presence of extrahepatic uptake. Standard eligibility criteria for SIRT were considered. **Results:** Overall 69 consecutive pts were included (20 females, 49 males; mean age 64 ± 10.1 [39-83]). Clinical indication was primary hepatocellular carcinoma (HCC) in the majority of pts (55/69, 79.7%), cholangiocarcinoma (CC) in 11 pts, HCC + CC in 2 pts and liver metastasis from colon cancer in 1 patient. According to MAA scan results, pts excluded from SIRT were 23/69 (33.3%), respectively due to: 3/23 LSF > 20%, 8/23 partial target lesion correspondence; 1/23 incomplete thrombosis correspondence and 1/23 absent; 3/23 whole liver distribution; 4/23 extrahepatic uptake (2/4 also presenting with LSF > 20%, 1/4 demonstrating also partial target correspondence); 3/23 performance status worsening. Overall 46/69 (66.7%) pts were finally addressed to SIRT. Among the pts presenting with a single hepatic lesion (14/46, 30.4%) complete target correspondence was found in 12/14 pts (9/14 also showed thrombosis, in only 1/9 partially covered), partial in the remaining 2 cases. Among the pts presenting with multiple hepatic lesions (32/46, 69.6%), 13/32 had thrombosis: target lesion correspondence resulted complete in 9/13 pts (in 1/9 thrombosis was not covered) and partial in 2/13 pts (all with complete thrombosis correspondence). No thrombosis was evident in the remaining 19/32 pts: target lesion correspondence resulted complete in 12/19 pts and partial in 7/19. Non-pathological extrahepatic activity (i.e. artifacts) was detected in 7/46 pts. Mean LSF was $10.7\% [\pm 1.9]$. **Conclusions:** In our preliminary experience, implementing standard MAA scintigraphy with SPECT/CT, as part of pre-SIRT diagnostic flow-chart, allowed: optimal anatomical localization of hepatic lesions and extra-hepatic shunts, accurate MAA distribution assessment (in particular in terms of target lesion and thrombosis correspondence). A more tailored pts selection was therefore possible.

EP-0500

Performance and prognostic value of ^{18}F -FDG-PET/CT and ceCT in the relapse of cholangiocarcinoma

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Purpose: Primary aim was to assess the ability of ^{18}F -FDG-PET/CT to detect disease relapse in a group of cholangiocarcinoma (CC) patients previously treated with surgery and chemotherapy (CHT). Secondary aim was to evaluate the prognostic value of ^{18}F -FDG-PET/CT. **Methods:** We retrospectively analyzed a cohort of 45 patients (17 F; age range 38-79 years), between January 2012 and January 2018, diagnosed with intrahepatic (24/45, 53,3%) or peri-hilar (21/45, 46,7%) CC and previously treated with surgery and adjuvant CHT as primary treatment. Contrast enhanced CT (ceCT) performed within 15 days since PET/CT was used as gold standard. A Kaplan-Meier analysis was used to evaluate differences in overall survival (OS) between PET/CT and ceCT positive and negative scans. In this analysis, 3 patients were excluded due to a lack of follow up data. Mean follow up time was 15 months (range 2-56). **Results:** PET/CT turned out positive in 32/45 (71,1%) cases, with sensitivity, specificity, PPV and NPV respectively of 94,4%, 77,8%, 94,4% and 77,8%. CT turned out positive in 34/45 (75,5%) cases. In 91,1% cases PET/CT and CT were concordant. In 8,9% cases PET/CT and CT were discordant (2 PET-/CT+, 2 PET+/CT-). Regarding the detection of hepatic disease, PET/CT and CT were concordant in 86,7% cases, while in 13,3% cases were discordant (3 PET-/CT+, 3 PET+/CT-). Regarding the detection of metastatic nodes PET/CT and CT were concordant in 75,5% cases, while in 24,5% cases were discordant (4 PET-/CT+, 7 PET+/CT-). Regarding the detection of distant metastasis PET/CT and CT were concordant in 86,7% cases, while in 13,3% cases were discordant (6 PET-/CT+). Regarding metastatic lymph node disease, Kaplan-Meier analysis showed a high significant difference ($p=0,001$) in OS between patients whom PET/CT and CT were both positive (lowest survival rate), positive and negative, negative and positive and both negative (highest survival rate) respectively. Globally, a high significant difference ($p=0,009$) in OS was found between patients whom PET/CT and CT turned out positive. **Conclusions:** In our cholangiocarcinoma patients we found that the information we can reach from PET/CT and ceCT is complementary. CeCT is more accurate in the detection of smaller lesions, particularly sub-centimetric pulmonary nodules. PET/CT has a high sensitivity and specificity in the detection of disease relapse and showed its strong role in the evaluation of lymph node relapse. Our Kaplan-Meier analysis revealed that PET/CT positivity, particularly node positivity, could have a prognostic value in terms of OS.

EP-0501

^{18}F FDG-PET/CT and Pancreatic Intraductal Papillary Mucinous Neoplasms (IPMN): an implementation of

conventional imaging methods in the evaluation of malignant degeneration.

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Purpose/Introduction: Intraductal papillary mucinous neoplasms (IPMN) represent 20-50% of all cystic neoplasms and can be classified into benign, borderline and malignant lesions (carcinoma). The main diagnostic challenge is to stratify the risk of degeneration into carcinoma in order to avoid unnecessary surgery. Aim of this study is to evaluate the diagnostic performance of ^{18}F FDG-PET/CT in the detection of malignant IPMN compared with histological/cytological exam or imaging follow-up (CT, MRI, EUS, PET/CT) and with the data reported in the literature.

Subjects & Methods: From January 2009 to November 2017 were retrospectively evaluated ^{18}F FDG-PET/CT scan of patients with an imaging-based (CT, MRI, EUS, ERCP) diagnosis of IPMN. All ^{18}F FDG-PET/CT scans were performed within 3 months after diagnostic conventional imaging for IPMN, following standard EANM procedure, and at least two experienced nuclear medicine physician reviewed pancreas site. PET results were validated by histological/cytological confirmation when available or by follow-up with CT or MRI or EUS or PET/CT (mean follow-up: 13 months). Accuracy, sensitivity, specificity, positive and negative predictive values (PPV, NPV) were calculated. **Results:** In our study were finally included 122 pts (M=40, F=82; mean age 69 years [$\pm 2,06$]) and were analysed 161 ^{18}F FDG-PET/CT. Increased uptake at the site of IPMN was documented in 20/161 (12,4%) ^{18}F FDG-PET/CT (mean SUV_{max} = 8. Among these 20 FDG+, 17/20 (85%) were true positive for malignant degeneration whereas 3/20 (15%) false positive. No increased uptake at the site of IPMN was detected in 141/161 (87,6%) scan: 138/141 (97,9%) true negative and 3/141 (2,1%) false negative. Overall ^{18}F -FDG-PET/CT performance in the evaluation of malignant IPMN resulted: 96% accuracy, 85% sensitivity, 98% specificity, 85% PPV and 98% NPV. Our preliminary results were consistent with literature (reported accuracy: 97%, sensitivity: 88%, specificity: 98%). **Discussion/Conclusions:** Similarly to what is reported in the literature, even in our case series ^{18}F FDG-PET/CT is useful for the evaluation of malignant degeneration of IPMN implementing conventional imaging methods. In particular it may represent a non-invasive, widely available and accurate tool to optimize patient risk stratification and a more tailored surgical approach.

EP-0502

Correlation of laboratory findings with Dual-Phase FDG PET / CT findings in cases with hepatocellular carcinoma

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Purpose: It is known that abnormalities in liver function tests, elevation in alpha-fetoprotein (AFP) levels, thrombocytopenia and erythrocytosis may occur in patients with hepatocellular carcinoma (HCC). In this study, we investigated the relationship between the laboratory parameters and dual phase ^{18}F -FDG PET/CT findings in patients with HCC. **Methods:** We retrospectively and prospectively investigated fifty-two hepatocellular cancer cases that underwent dual-time-point ^{18}F -FDG PET/CT examination between February 2015 and March 2017. SUVmax and SUVmean measurements of the tumor were performed on early and delayed PET/CT images. Laboratory parameters of all cases including bilirubin, albumin, INR, AFP, ALT, AST, GGT, hemoglobin values, platelet and red blood cell counts were collected.

Results: When the laboratory findings and Child classification of the cases were compared with the changes in tumor SUVmax and tumor SUVmean values between early and delayed images, no significant correlation was found between changes in tumor SUV values and Child classification and/or laboratory findings except GGT ($p > 0.05$). There was a significant correlation between GGT levels and changes in tumor SUVmean values ($p: 0.028$), but no significant relationship was demonstrated between GGT levels and changes in tumor SUVmax values ($p: 0.087$). When the cases were divided into 'normal group' and 'high group' according to serum ALT, AST, GGT, AFP levels, no significant difference was found between the 'normal group' and 'high group' in terms of changes in tumor SUV values ($p > 0.05$). When the cases were grouped according to hemoglobin levels as normal and high, the tumor SUVmax value in the three cases with high hemoglobin levels showed a significant increase in delayed images ($p: 0.029$). When the cases were grouped as normal and low according to platelet count or when they were divided as normal and high according to erythrocyte count, no significant difference between groups was found in terms of changes in tumor SUV over time.

Conclusion: Studies have shown that thrombocytopenia and elevation of AFP are associated with portal venous invasion, elevation of AST and GGT are associated with indexes that determine HCC aggressiveness and erythrocytosis is associated with large tumor volume in cases with HCC. Although significant relationship between GGT values and changes in tumor SUV values in delayed imaging and relationship between hemoglobin levels and changes in tumor SUVmax value in delayed imaging was found in this study, there is still a need for extensive studies with other laboratory findings in wider populations.

EP-0503

Dual Time Point FDG PET/CT in Verification of Post operative Local Recurrent Soft tissue Lesions in Patients with Pancreatic Cancer.

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Aim: The purpose of this study was to evaluate dual time point for the differentiation of post-operative benign and early malignant local recurrent lesions in pancreatic cancer patients.

Materials & Methods: A consecutive 34 pancreatic cancer patients (12 female, 22 male, mean age: 58.3 ± 10.3) presented with

operative bed local soft tissue lesions. Early whole body PET/CT imaging was performed at (1h) after F-18 FDG injection and delayed imaging (2 h) post injection was performed only in the abdomen. The maximum standardized uptake value (SUVmax) of the initial image (SUVmaxE) and of the delayed image (SUVmaxD) were determined. The retention index (RI) was calculated according to the equation: $RI = (SUVmaxD - SUVmaxE) \times 100 / SUVmaxE$. These indices were correlated with histopathology and follow-up as reference criteria. **Results:** 47 total lesions were detected in 34 patients (mean size 3 ± 1.2), 11 lesion in 9 patients were proven benign 5 by histopathology and 4 in follow up, while 36 malignant lesions were identified. There is no significant statistical difference in SUVmaxE between benign and malignant lesions, while SUVmaxD and RI of the malignant lesions (mean 8.6 ± 2.7 and 35.8 ± 18.4 respectively) were significantly higher than the benign lesions. (mean 3.2 ± 1.4 and -6.2 ± 14 respectively). ($P < 0.005$). With a cutoff value of 3.9 for the SUVmaxD; Sensitivity, Specificity, and Accuracy were 96%, 70%, and 91%, respectively. The calculated positive and negative predictive values were 89% and 88%, respectively. When RI of 17 was used as the cutoff point, it showed higher specificity, accuracy & PPV (90%, 92% & 96% respectively) as compared to the other parameters. Most of malignant lesions showed an increase in SUVmax on the delayed images compared with the initial ones, except for 2 lesions that maintained stationary. Regarding the group of the benign lesions 45.5 % (5/11) showed a decrease in SUVmax, 4 elicited no change, while mild increase in SUVmax is observed on 2 lesions. **Conclusion:** Dual time point F-18 FDG PET/CT seems to be an additional method to differentiate between malignant and benign post-operative local soft tissue lesions in pancreatic cancer patients. **Keywords:** FDG PET/CT, Dual time point, retention index, SUVmax, pancreatic lesion.

EP-0504

The role of FDG PET/CT at staging and at treatment response evaluation in locally advanced esophageal cancer

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Aim: To evaluate the role of FDG PET/CT at staging and at treatment response evaluation in locally advanced esophageal cancer (LAEC). **Material & Methods:** We evaluated LAEC patients surgery treated (not junction) in our institution. 16 consecutive patients were included (8ADK, 8 SCC), stages 3p T1N0, 1p T1N+, 1p T2N+, 9p T3N+, 2p T4aN+. All of them underwent gastroendoscopy with biopsy, endoscopic ultrasonography, CT and a PET/CT scan at staging (16p) and at the end of the neoadjuvant chemo-radiotherapy treatment (NA) (13p). Maximum Standardized Uptake Value (SUVmáx) and Metabolic Tumor Volume (MTV) of primary tumor and lymph nodes were measured at both times, calculating ΔMTV and ΔSUV . EORTC image response criteria (CMR, PMR, SMD, PMD) and visual analysis were evaluated and compared with the tumor regression grade according to Mandard Criteria, considering grades 1-2 as good responders

(GR) and grades 3–5 as poor responders (PR). **Results:** At staging: -All tumors were FDG avid, including T1 (mean SUV_{max}=20.5, mean T1 SUV_{max}=7.61). -In our series SUV_{max} in ADK was higher than in SCC (28.72 vs 17.34, $P=0.02$). -Higher tumor stages correlates with higher basal MTV (T1 3.1cm³, T2 8.3cm³, T3 33.2cm³, T3 90.9cm³). Histologic correlation: -Tumor SUV_{max} at staging scan predicted a poor pathologic response (GR 16,96 vs 29,39 PR, $p=0.029$), but MTV didn't (GR 21, PR 52.25). -In our series, neither Δ MTV nor Δ SUV after NA were able to distinguish GR from PR. -Correlating EORTC response criteria with Mandard grading correlation: 12 of 13 p were assessed as a PMR (6 grade 1, 2 grade 3, 3 grade 4, 1 grade 5), and one as a SMD (grade 4). -In a visual classification (CMR, PMR, SMD, PMD), considering nearly physiological FDG uptake or esophagitis uptake pattern as CMR, we found 6 CMR (6 grade 1), 6 PMR (2 grade 3, 3 grade 4, 1 grade 5) and one SMD (grade 4). -PostNA PET/CT correctly identified the lymph node status in 87% of cases (2 initially N+, 10 initially N-, 2 initially N+ with CR) with only 1FN (metabolic response with no morphologic changes) and one 1FP (local relapse 9 months post surgery). **Conclusion:** -All tumors were FDG avid, including T1. -Tumor SUV_{max} at staging scan predicted poor pathologic response, but not MTV. -In our series, visual analysis considering those with nearly physiologically FDG uptake or with a esophagitis uptake pattern as a CMR performed better than EORTC image criteria in treatment response assessment.

EP-0505

Staging And Response Evaluation To Neo-adjuvant Chemoradiation In Esophageal Cancers Using ¹⁸F-FDG PET/CT With Standardized Protocol

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Background: Precise staging of esophageal cancer (EC) is important for selection of optimal treatment option and prognostication. Aim of this study was to assess the role of ¹⁸F-FDG PET/CT in staging and response evaluation to neoadjuvant chemoradiation (nCR) in EC patients using standardized imaging protocol.

Material and Methods: This prospective study was conducted at PET/CT Section of Department of Radiology, Aga Khan University Hospital Karachi, Pakistan from July 2017 till February 2018. We included 34 biopsy proven EC patients who had ¹⁸F-FDG PET/CT and CT of neck, chest and abdomen as part of initial staging. Eleven patients had post-nCR ¹⁸F-FDG PET/CT using standardized imaging protocol as per EANM guidelines. CT and PET/CT based staging was compared. Based on PERCIST criteria, response evaluation was assessed using change in highest SUV_{max} (Δ SUV_{max}) in baseline and follow-up scans (primary lesion, node or extra-nodal metastases). **Results:** Mean age of cohort was 57 $\pm$ 14 years (23 males and 11 females) having adenocarcinoma (AC) in 23 and squamous cell cancer (SCC) in 11 patients. Mean ¹⁸F-FDG dose, uptake time and hepatic SUV_{mean} for baseline scans were 169 $\pm$ 54 MBq, 65 $\pm$ 10 minute and 1.91 $\pm$ 0.49 which were within $\pm$ 10%, $\pm$ 15% and $\pm$ 20% for follow-up scans in 11 pa-

tients respectively. Mean size (craniocaudal dimension in mm) and SUV_{max} of primary tumor was 56 $\pm$ 27 mm and 13.4 $\pm$ 4.7. Based on ¹⁸F-FDG PET/CT findings, patients were categorized into N0 (10/34), N1 (09/34), N2 (11/34) and N3 (04/34) while 11/32 had stage IV disease. These were similar in AC and SCC groups. CT found stage IV disease in 3/34 (09%) while PET/CT found in 11/34 (32%; p value: 0.019) cases. PET/CT showed concordance with CT in 41% while discordance (all with upstaging) seen in 59%. On follow-up PET/CT, complete metabolic response was seen in 5/11 (45%) and partial metabolic response was noted in 6/11 (55% - p value non-significant) patients. Median Δ SUV_{max} over primary lesions was 49.84% (-32.69 - 100%) while over nodal sites it was 41.18% (-82.60 - 100%). **Conclusion:** We conclude that ¹⁸F-FDG PET/CT was found a sensitive tool in initial staging of EC. Compared with CT, it had higher diagnostic accuracy for distant nodal and extra-nodal metastasis. Δ SUV_{max} between baseline and post-nCR studies acquired with standardized protocol had changed management in more than half of our patients. For response evaluation in EC more studies with standardized ¹⁸F-FDG PET/CT imaging protocols are warranted.

EP-0506

Change in standardized uptake values in delayed ¹⁸F-FDG positron emission tomography images in hepatocellular carcinoma

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Purpose: Delayed ¹⁸F-FDG positron emission tomography (PET) imaging has been associated with improved diagnostic yield in several malignancies; however, data on the use of delayed imaging in patients with hepatocellular carcinoma (HCC) is scarce. This study aimed to examine tumoral and background standardized uptake value (SUV) alterations in dual-phase ¹⁸F-FDG PET/CT imaging. **Method:** Fifty-two HCC cases underwent dual-time-point ¹⁸F-FDG PET/CT examination where early and delayed images were obtained. The maximum and mean standardized uptake values (SUV_{max} and SUV_{mean}) of the tumor were determined for both time points. Similarly, the mean SUV were also determined for background (liver, soft tissue and spleen). Changes in tumoral and background SUV between early and delayed images were examined. **Results:** The mean age was 62.0 $\pm$ 12.9 years (range, 20–88 years) and the majority of the patients were male (86.5%). Tumor SUVs, both tumor SUV_{mean} and tumor SUV_{max}, significantly increased at delayed images when compared to early images ($p < 0.05$). In contrast, the average SUV_{mean} for the liver, soft tissue and spleen significantly decreased at delayed images ($p < 0.05$). **Conclusion:** A significant increase in tumor SUV at delayed images in contrast to a significant decrease in background SUVs suggests that delayed images in HCC may contribute to diagnostic performance through a potential increase in the contrast between the tumor and background. However, further studies with larger sample sizes including patients with benign lesions and different grades of the disease are warranted to better elucidate the diagnostic contribution as well as the association of delayed imaging values with prognosis.

EP-0507

Detection Efficiency Of FDG PET/CT For Primary Tumors In Patients With Carcinoma Of Unknown Primary (CUP)N. Fatima¹, M. u. Zaman¹, A. Zaman², S. Zaman², U. Zaman²;¹AKUH, Karachi, PAKISTAN, ²Dow Medical College, Dow University of Health Sciences (DUHS), Karachi, PAKISTAN.

Background: Carcinoma of unknown primary (CUP) is defined as biopsy proven tumor metastases that remains unidentified after a thorough diagnostic evaluation. It has a prevalence of 2-3% with poor prognosis and median survival can be extended by the identification of the primary origin and treating with specific therapy. ¹⁸FDG PET/CT is considered an excellent problem solving tool in the diagnostic paradigm of CUPs. The purpose of this study was to find the detection efficiency of ¹⁸FDG PET/CT in patients with CUP. **Material and Methods:** This prospective study was conducted at PET/CT Section of Department of Radiology, Aga Khan University Hospital Karachi, Pakistan from August 2017 till January 2018. Patients with history of CUP referred for ¹⁸FDG PET/CT scan for detection of primary sites during study period were recruited. ¹⁸FDG PET/CT scan was acquired using standardized protocol and patients with suspected primary sites underwent biopsies. Scan findings and biopsy results were analyzed to find the detection rate, sensitivity, area under curve (AUC) and positive predictive value (PPV). As no biopsy was performed in negative scan, true negative and specificity could not be calculated. **Results:** During study period 46 consecutive patients with CUP were included. The mean age of cohort was 58 ± 17 years (63% male and 37% female) having a mean BMI of 24.70 ± 4.97 Kg/m². Thirty four patients (34/46) found to have a hypermetabolic focus suggestive of primary tumor with known metastatic sites and subjected to biopsy which turned out to be positive in 26/34 patients. Primary tumor was detected in gastrointestinal and hepatobiliary in 08 (17%), head and neck in 06 (13%), genitourinary 04 (09%), lung 03 (06%) and miscellaneous sites in 05 (11%) patients. Detection rate, sensitivity and PPV were 57%, 68% and 76% respectively. Remaining 12/46 patients with negative ¹⁸FDG PET/CT for primary focus did not have biopsy. Receiver operating character (ROC) curve revealed good diagnostic of ¹⁸FDG PET/CT for detecting unknown primary (AUC 0.667; p = 0.054; SE= 0.083; CI: 0.504-0.830). **Conclusion:** ¹⁸FDG PET/CT detected primary tumors in 57% of patients with CUP which is compatible with published data. Due to its higher detection efficiency and PPV, this imaging tool may be considered as an alternative in early phase of investigation of patients with CUP.

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Aim: to determine the prognostic value of post-treatment 18F-FDG PET/CT in patients with Small-cell Lung cancer (SCLC).

Materials & Methods: Forty-eight patients (40 males and 8 females; mean age 64.48 years, range 48-86) with histologically proven SCLC and post-treatment 18F-FDG PET/CT scan were retrospectively reviewed. 32/48 (66.7%) had the SCLC peripheral form while 16/48 (33.3%) had the central form; 14/48 (29.2%) performed combined Chemo-Radiotherapy treatment while 34/48 (70.8%) had chemotherapy only. Presence of primary tumour (T), pathological lymph-nodes (N) and metastasis (M) was evaluated for each patient. The clinical endpoints were overall survival (OS) and progression-free survival (PFS) and the last follow-up was in January 2018. The survival time was estimated using Kaplan-Meier method, and the difference between groups was assessed using log-rank tests. A multiple Cox's proportional hazard model was performed for 18F-FDG PET/CT results and clinical variables (age ≤65 years/>65 years, male/female and central/peripheral SCLC). p< 0.05 was considered statistical significant. **Results:** All 18F-FDG PET/CT resulted positive for at least one pathological lesion. 41/48 (85.4%) patients were positive for T and 7/48 (14.6%) were negative; 28/48 (58.3%) were positive for N and 20/48 (41.7%) were negative; 9/48 (18.8%) were positive for M and 39/48 (81.3%) were negative. At the end of the follow-up 39/48 (81.3%) patients were alive while 9/48 (18.8%) were dead. Median OS was 20 months (range 5-128), median PFS was 22 months (range 2-128). We compared OS and PFS for the T, N and M. OS resulted statistically different for N (log rank=7.819; p=0.005) and M parameters (log rank=9.609; p=0.002). Mean OS in N negative patients was 121 months, while in N positive patients was 67 months; mean OS in M negative was 98 months, 49 months in M positive. PFS resulted statistically different for N (log rank=5.446; p=0.02) and M parameter (log rank=1.021; p<0.001). Mean PFS in N negative patients was 87 months, while in N positive patients was 34 months; mean PFS in M negative was 68 months, 18 months in M positive. Cox's analysis showed statistical significance only for N parameter (HR=11.66). **Conclusion:** Post-treatment 18F-FDG PET/CT is a fundamental tool in the post-treatment evaluation of SCLC patients. In particular, the identification of lymph-nodes involvement is related to a poorer prognosis in term of OS and PFS.

EP-42

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology -> Lung,
malignant

EP-0508

Prognostic role of post-treatment 18F-FDG PET/CT in patients with small-cell lung cancer

EP-0509

Cost-analysis of a new diagnostic strategy in patients with solitary pulmonary nodule: the Italian Tailored Assessment of Lung Indeterminate Accidental Nodule (ITALIAN) multicenter trialL. Evangelista¹, L. Pace², L. Mansi³, E. Mazziotti⁴, S. Del Vecchio⁴, G. Pepe⁵, L. Basso⁶, S. Annunziata⁷, A. Golemi⁸, A. Chiaravallotti⁹, R. Galicchio¹⁰, L. Guerra^{11,12}, M. Zuffante¹³, N. Frega¹⁴, V. Rizzo¹⁵, A. Lambertini¹⁶, A. Cuocolo⁴, M. Spadafora^{17,15}; ¹Veneto Institute of Oncology IOV - IRCCS, Padova, ITALY; ²Università di Salerno,

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Purpose: The aim of the study was to estimate the impact of introducing a new diagnostic strategy by comparing the costs of standard FDG whole-body (wb)-PET/CT and the costs of s-PET/CT, in the context of the ITALIAN trial. **Materials and Methods:** We estimated the differential costs of wb-PET/CT and s-PET/CT, based on the Italian costs for the FDG PET/CT procedures, by including the reimbursement of the scan and the price of FDG. The ITALIAN trial population (n=502 patients) was considered for the end-point of the present study. The costs were censored for study purpose. **Results:** Based on the ITALIAN data, s-PET/CT compared to wb-PET/CT could save more than 10 min per scan or it would need a dose of 35% less than to obtain the same chest counts and the same scan-time of wb-PET/CT. Based in the first advantage, s-PET/CT can increase the earning of 358.644,00 Euro (the reduction of scan time, significantly increases the number of procedures from 502 to 803; which is equivalent to the ratio 10:16 for wb-PET/CT and s-PET/CT, respectively), but it slightly increases the FDG cost (22.554,86 Euro vs. 36.078,79 Euro respectively for wb-PET/CT and s-PET/CT) (total money saving: 60%). In accordance with the second supposition, the FDG costs can be reduced from 22.554,86 with wb-PET/CT to 7.894,20 with s-PET/CT (money saving: 65%), by considering a dose of 7 mCi per patient, that corresponds to the mean value for the ITALIAN trial. **Conclusion:** Although present study estimates cannot easily be generalized to any local setting, the model for cost calculation is easy to be exported to another scenario by applying different local parameters. The advantages to introduce s-PET/CT in SPN can be found in a reduction of expenses for the hospital and the Italian healthcare.

EP-0510

Prognostic value of metabolic parameters measured by 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) in surgically resected non small cell lung cancer (NSCLC) patients

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Purpose: 18F-FDG PET/CT in addition to anatomical information provides semiquantitative and quantitative information regarding tumour aggressiveness and metabolic tumour volume. Metabolic parameters can play a role in risk stratification in addition to the TNM staging. Aim of the study was to investigate the prognostic value of various metabolic parameters like maxi-

mum standardized uptake value (SUV max), mean standardized uptake value (SUV mean), whole body metabolic tumour volume (WBMTV) and whole body total lesion glycolysis (WBTLG) in surgically resected NSCLC patients. **Materials and Methods:** This was a retrospective observational study approved by institutional review board. 153 eligible patients with NSCLC who underwent surgical resection between January 2009 to December 2013 were reviewed to obtain the relevant clinicopathological variables. The SUVmax, SUVmean, WBMTV and WBTLG of the tumor were measured. Continuous PET parameters were stratified using optimal cutoffs derived from ROC curve analysis. The survival curves for the groups were estimated using the Kaplan-Meier method and were compared using the log-rank test. The Cox proportional hazards model was used in multivariate analysis to identify independent prognostic factors. **Results:** The median follow-up was 36.9 months (range 9.4 - 87.7). 56 out of 153 patients (36.6%) died and 78 out of 153 patients (50.9%) had recurrence. In the univariate analysis - TNM stage, male sex, no adjuvant treatment and higher SUV max, SUV mean, WBMTV and WBTLG were statistically significant and was associated with poor overall survival(OS).TNM stage, no adjuvant treatment, and higher SUV max, SUV mean, WBMTV and WBTLG were statistically significant and associated with poor disease free survival(DFS). In the multivariate analysis, only higher WBTLG (HR = 3.08, $p = 0.007$) for DFS and higher WBTLG (HR = 2.70, $p = 0.041$) and TNM staging (HR = 1.63, $p = 0.035$) for OS were statistically significant after adjustment for significant univariate variables. **Conclusion:** Whole body tumor burden assessment with TLG has significant prognostic value in patients with operated lung cancer. Incorporation of TLG into clinical practice can further stratify patients within a stage and may be benefitted from additional therapy.

EP-0511

Prognostic Impact Of Intratumoral Heterogeneity Based On Fractal Geometry Analysis In Operated NSCLC Patients

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Introduction: Intratumoral heterogeneity is a well-known prognostic feature in malignant lesions. Our aim was to determine how intra-tumor heterogeneity based on fractal geometry analysis on FDG PET can predict survival in patients with non-small cell lung carcinoma (NSCLC) candidate to surgery. **Subjects & Methods:** Overall, 113 patients (76 male, 37 female) undergone to lung resection in our Institution and investigated with FDG PET prior to surgery were retrospectively revised. The study has been approved by the IRB. In all cases, PET DICOM images were analyzed for fractal geometry using an ad-hoc computer program to determine mean intensity value (MIV), standard deviation (SD), relative dispersion (RD), the 3D histogram of the fractal dimension (3D HIST FR DIM), the fractal dimension in 3D (3D FD), and the fractal volume. Fractal geometry parameters were compared with metabolic parameters on PET and with patients outcome, expressed in terms of disease-free survival (DFS). **Results:** The median 3D-FD and fractal volume

were 1.71 and 5.39, respectively. We found a significant positive correlation between 3D-FD and SUVmax ($\rho=0.72$, $p<0.001$), SUVmean ($\rho=0.68$, $p<0.001$), MTV ($\rho=0.93$, $p<0.001$), and TLG ($\rho=0.93$, $p<0.001$). Likewise, positive correlations between fractal volume and all metabolic parameters were demonstrated: SUVmax ($\rho=0.71$, $p<0.001$), SUVmean ($\rho=0.66$, $p<0.001$), MTV ($\rho=0.97$, $p<0.001$), and TLG ($\rho=0.96$, $p<0.001$). Additionally, patients with high 3D FD (≥ 1.71) tumors showed higher values of SUVmax (16.9 vs 7.9, $p<0.001$), SUVmean (8.5 vs 4.7, $p<0.001$), MTV (53.6 vs 4.4, $p<0.001$) and TLG (491.9 vs 21.6, $p<0.001$) than those with lower 3D FD. In the same way, tumors with high fractal volumes (≥ 7.47) were associated with higher values of metabolic parameters compared to those with fractal volume below the median. On univariate analysis, performed using Cox's proportional hazard model, 3D FD resulted significantly associated with DFS ($p=0.013$), while fractal volume and metabolic parameters did not. These data were confirmed on log rank test ($p=0.011$). On multivariate analysis, among age, stage disease, histotype, 3D FD, and SUVmax, only 3D FD was identified as the independent prognostic factor for DFS ($p=0.032$; HR 0.418, 95% CI 0.189–0.926). **Conclusion:** In our study, the intra-tumoral heterogeneity of FDG PET evaluated by fractal geometry analysis resulted a prognostic biomarker for DFS in patients with NSCLC. By combining metabolic parameters and fractal dimension from PET images, we might provide different types of information that are equally useful for prognosis evaluation.

EP-0512

By Talc pleurodesis-induced pleural changes, characterization with ^{18}F -FDG PET-CT, own experience and bibliographic review.

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Aim: The purpose in this retrospective study is to identify and characterize pleural changes associated with talc deposition in patients undergoing pleurodesis due to malignant pleural effusion using ^{18}F -FDG PET-CT. **Materials & Methods:** Nine patients who presented malignant pleural effusion in which talc was used as a fibrosing agent and PET-CT as a control imaging test were retrospectively evaluated. Of these, only 6 were able to confirm the existence of an inflammatory/granulomatous process either by pleural biopsy or radiological and clinical evolution. SUV max, HU attenuation and thickness of the plaques or nodule were the variables considered for our analysis. **Results:** A total of 13 PET-CT were performed in the 6 patients in 19 months of follow-up after pleurodesis. The mean time elapsed between the procedure and the first PET-CT was 26 months. During follow-up, a mean of 2 PET-CT were performed to each patient. The granulomas produced due the talc deposition were visualized in form of plaques and/or nodules, as a single lesion in 5 patients and multiple lesions in the rest. Parietal pleura was evident affected in 5 of the 6 patients and its most frequent localization occurred in the bases of the pos-

terior costophrenic angle. The SUV max ranged between 6.03 and 15.74 (mean 12); the UH 2,17–222 (mean 71HU) and the thickness between 5 and 39 mm (mean 15mm) in the first PET-CT. In the second PET-CT the SUVmax ranged between 4.49–14 (mean 7.6), the HU attenuation ranged between 55–299 (mean 101HU) and the thickness 4.6–17 (mean 9.75mm). In one of the third PET-CT carried out the uptake disappeared and mesothelial hyperplasia was confirmed by biopsy; in the other, a SUVmax of 7 was obtained, the mean thickness was 11.4mm and the 153HU. Only in one patient a pleural biopsy was performed, resulting in mesothelial hyperplasia. In the others, a follow up analysis was performed, taking into account the changes in the images and the clinical state; to determine tumor vs inflammatory activity. **Conclusions:** As in previous studies, an important glycolytic activity was evidenced in the pleural lesions (plaques) produced by talc, which has to be taken into account and considered when an oncologic PET-CT is evaluated. Moreover, its importance to know the radiological evolution and compare all the findings with clinical evolution,

EP-0513

PET/CT as a predictive biomarker response to treatment of patients with non-small-cell lung cancer with ALK-rearrangement treated with ceritinib

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Objective: To demonstrate the usefulness of ^{18}F -FDG-PET/CT as a predictive tool for response to treatment of patients with non-small-cell lung cancer with ALK-rearrangement (NSCLC-ALKr) treated with ceritinib. **Methodology:** We studied 10 patients with NSCLC-ALKr with ^{18}F -FDG-PET/CT as a baseline study. All patients were treated with ceritinib at dose of 750mg/day. An evaluation was made by ^{18}F -FDG-PET/CT after 1 month of treatment (28 ± 7 days) and one month after 6 cycles. Obtaining SUVmax, SUVmean, VTMA (metabolically active tumor volume) and TLG (total lesion glycolysis) values, RECIST 1.1 and PERCIST 1.0 criteria was performed. The best cut discriminative values for SUVmax, VTMA and TLG were identified by ROC curves. The analysis of semiquantitative values was made with Fisher's exact test and Cox regression. A significant value of p was considered when this was ≤ 0.05 . **Results:** The mean values of the initial SUVmean was 4.2 ± 3.6 SD, after the first cycle (interim) SUVmean was 3.9 ± 3.8 SD in target lesions; and 2.7 ± 2.8 SD after the last cycle. The mean values of the initial SUVmax were 7.4 ± 7.6 SD, 6.2 ± 5.8 SD interim; and 5.2 ± 4.3 SD after the last cycle. The mean values of the initial VTMA were 24.9 ± 65.8 SD, 23.0 ± 49.8 SD interim, and 21.0 ± 39.5 SD after the last cycle. The mean values of the initial TLG were 269.4 ± 1028.1 SD, 231.8 ± 667.2 SD interim, and of 208.0 ± 395.9 SD after the last cycle. In the analysis after the first cycle, no patient presented disease progression assessed. In the analysis after the last cycle, 7 patients presented a partial metabolic response, of which 5 had a statistically significant decrease in TLG after the first cycle; while those with stable disease did not show a statistically significant decrease after the first cycle. At the end of the last cycle through the RECIST criteria, 6 pa-

tients had stable disease, while only 4 had concordance with the PERCIST criteria in partial response. The measurement of the TLG was the most significant parameter for the prediction of response to treatment in the univariate analyzes ($p=0.001$). In the multivariate analysis with the Cox regression method, a low TLG, and the clinical stage before therapy were significant prognostic factors to present good response to treatment ($p=0.001$). **Conclusion:** The TLG is an excellent response prediction parameter superior to values of SUVmax, SUVmean or VTMA. Low TLG values after first cycle associated with a clinical stage IIIc or IVa can predict a good response to treatment.

EP-0514

Tumor Necrosis in NSCLC revealed by metabolic analysis of FDG PET/CT imaging

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Purpose: Development of novel targeted agents for NSCLC, modulating pathways involved in cell proliferation, apoptosis and angiogenesis has had a significant impact on patient management and prognosis. A substantial body of evidence suggests that tumor necrosis may be a strong predictor of aggressive tumor behavior and reduced survival in patients with NSCLC. Herein, we investigated the correlation of known and novel metabolic markers on F-18-FDG PET/CT with TN in NSCLC. **Materials & Methods:** We retrospectively assessed 50 patients (mean age 65 ± 10 years) with histologically confirmed NSCLC (24 adenocarcinomas, 23 squamous cell carcinomas and 3 poorly differentiated non-small cell cancers) and sampled surgical tumor specimens analyzed for the presence or absence of TN by histopathology. Initial staging F-18-FDG PET/CT images were analyzed for SUVmax, SUVmean, SUVmin, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) within a volume of interest using the 42%-threshold method of the maximum SUV signal intensity for the biopsied or resected tumor lesion. Metabolic information on F-18-FDG PET/CT as well as the ratio of morphologic and metabolic lesion volumes or Hot-to-Global Volume Ratio (HGVR) were calculated and correlated to the presence or absence of histologic TN. **Results:** All tumors showed metabolic FDG-PET uptake with mean SUVmax 13.7 ± 7.4 g/ml (range: 2-31), SUVmean 7.4 ± 4.5 g/ml (range: 0.9-21.1), SUVmin 4.9 ± 4.3 g/ml (range: 0.6-22.8), MTV 21.2 ± 33.6 cm³ (range: 0.5-171) and TLG 174 ± 280 g·cm³/mL (range: 0.5-1113). We found a statistically significant lower SUVmin and SUVmean in the TN group 1.8 ± 0.3 and 6.2 ± 3.5 compared to no TN group 5.1 ± 1 and 8.7 ± 5.1 ($p=0.001$ and $p=0.035$) with higher MTV (41.9 ± 8.2 versus 17 ± 3.5 , $p=0.004$), morphologic tumoral volume (48.8 ± 68.6 versus 12 ± 18.3 , $p<0.001$) and HGVR (31.8 ± 11.8 versus 6.9 ± 5.7 , $p=0.027$), but no difference in SUVmax or TLG ($p=0.347$ and $p=0.084$). **Conclusion:** This study shows that FDG PET/CT uptake values, in particular SUVmin, SUVmean and HGVR, the latter evaluating FDG avid versus non FDG avid ratio in tumoral lesions, are promising metabolic imaging marker in evaluating TN in NSCLC. The prevalence of TN in NSCLC is significantly higher in larger tumors with higher MTV and morphologic tumoral vol-

ume, supporting the suggested prognostic value of TN. These metabolic factors allow to detect necrotic changes in tissue and potentially evaluate necrotic and apoptotic- pathway-targeted therapy.

EP-0515

Tumor response to simultaneous PDK1 knockdown and inhibition of EGFR signaling in oncogene-driven non-small cell lung cancer

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Aim: Inhibition of EGFR signaling in oncogene-driven non-small cell lung cancer (NSCLC) caused a reversal of Warburg effect with reactivation of oxidative phosphorylation. We previously showed that transient downregulation of several proteins involved in glucose metabolism along with targeted inhibition of EGFR signaling caused a decrease of glucose consumption and an enhancement of ATP production in NSCLC cells. The aim of the present study was to test whether co-targeting of glucose metabolism and EGFR signaling may enhance tumor response to tyrosine kinase inhibitors (TKIs) in NSCLC. **Materials and Methods:** H1975 and A549 NSCLC cells were stably transfected with scrambled or PDK1-targeted shRNA for development of animal models bearing PDK1 knockdown tumors. Cells were preliminary tested for PDK1 expression and sensitivity or resistance to a panel of TKIs. Drug toxicity was evaluated by MTS assays using increasing concentrations of erlotinib, MAP kinase inhibitor (U0126) or WZ4002 for 72 h. Levels of HKI, HKII, PKM2, LDH-A, PDH and OXPHOS along with the phosphorylation status of PKM2, PDH and STAT3 were determined by western blot analysis in untreated and treated cells transfected with scrambled or PDK1 shRNA. In parallel experiments, glucose consumption and ATP production were determined in the same experimental conditions. **Results:** Both H1975 and A549 cells transfected with PDK1-targeted shRNA (shPDK1) showed a dramatic reduction of PDK1 protein levels as compared to cells transfected with scrambled shRNA (shCTRL). Knockdown of PDK1 in A549 cells caused a decrease of p-STAT3^{Tyr705} and HKII levels along with an upregulation of several subunit of OXPHOS. In H1975 cells, downregulation of PDK1 alone did not cause any significant changes in the expression of key glycolytic enzymes whereas p-PDH levels were reduced by the addition of 1 μ M WZ4002. MTS assays in shPDK1 H1975 cells showed no significant changes in cell viability after exposure to WZ4002 or erlotinib as compared to shCTRL cells. Conversely, PDK1 knockdown in A549 cells showed a reduction of cell viability in response to erlotinib or U0126 as compared to shCTRL cells treated with the same inhibitors. **Conclusion:** Our findings suggest that co-targeting of PDK1 and EGFR may cause an enhancement of tumor response to kinase inhibitors in A549 cells.

EP-0516

Standardized visual reading of F18-FDG-PET/CT for pretherapeutic lymph node staging in non-small cell lung

cancer under the European Society of Thoracic Surgeons guidelines

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Purpose/Introduction: Accurate thoracic lymph node (LN) staging including FDG-PET/CT is crucial for treatment planning in non-small cell lung cancer (NSCLC). A standardized approach for visual LN assessment in FDG-PET was previously proposed by our group. This is to verify its accuracy with a different PET/CT scanner under the 2014 European Society of Thoracic Surgeons (ESTS) guidelines. **Subjects and Methods:** Retrospective analysis of pretherapeutic FDG-PET/CT in 165 consecutive patients with NSCLC (m:113; f:52; age, 67 [41–88] a) using a Philips Gemini TF 16. After standardized PET windowing (upper threshold: liver SUVmean), LN uptake was assessed visually with a 4-step score (1, LN uptake $\leq$ mediastinal blood pool structures (MBPS); 2, MBPS < LN < liver; 3, liver $\leq$ LN < 'black'; 4, LN appears 'black'). LN diameter (short axis) was measured with CT. Histology served as standard of reference for this per-node analysis. **Results:** One hundred and fifty (37.4%) of the 401 LN (surgery:287; TBNA:112; biopsy:2) were malignant. One of 22 patients who could undergo surgery without invasive LN staging based on ESTS (i.e. cN0, peripheral primary $\leq$ 3cm) was finally multi-level pN2. Optimal cut-off for PET-positivity was score $\geq$ 3 (sensitivity, 87%; specificity, 91%; PPV, 86%; NPV, 92%; accuracy, 90%). In PET-negative LN (i.e. score <3), LN diameter $\geq$ 10mm and PET score=2 identified 8 true positive LN (false positive, 12). Sensitivity of combined FDG-PET/CT was 93%, specificity 87%, PPV 80%, NPV 95%, and accuracy 89%. If PET-positivity was defined by LN SUVmax >2.5, FDG-PET/CT sensitivity was 95%, specificity 68%, PPV 64%, NPV 96%, and accuracy 78%. **Discussion/Conclusion:** The previously proposed standardized visual FDG-PET reading was adequately accurate for LN staging under ESTS guidelines for NSCLC and superior to LN SUVmax >2.5. However, different PET/CT scanners require methodological adaptation (windowing, cut-off for positivity). In PET-negative LN, especially adenocarcinoma, CT (short axis LN diameter $\geq$ 10mm) can improve sensitivity of combined PET/CT.

EP-0517

Prospective comparison of ^{18}F -FDG PET/MRI and ^{18}F -FDG PET/CT for thoracic staging of non-small cell lung cancer

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Objectives: To compare the diagnostic performance of ^{18}F -FDG PET/MRI and ^{18}F -FDG PET/CT for primary and locoregional lymph node staging in non-small cell lung cancer (NSCLC). **Methods:** In this prospective study a total of 84 patients (51 men, 33 women, mean age 62.5 ± 9.1 years) with histopathologically confirmed NSCLC underwent ^{18}F -FDG PET/CT followed by ^{18}F -FDG PET/MRI in a single injection protocol. Two readers

independently assessed T and N staging in separate sessions according to the seventh edition of the American Joint Committee on Cancer staging manual for ^{18}F -FDG PET/CT and ^{18}F -FDG PET/MRI, respectively. Histopathology as reference standard was available for N staging in all 84 patients and for T staging in 39 patients. Differences in staging accuracy were assessed by McNemars χ^2 test. The maximum standardized uptake value (SUV_{max}) and longitudinal diameters of primary tumors were correlated using Pearson's coefficients. **Results:** T stage was categorized concordantly in ^{18}F -FDG PET/MRI and ^{18}F -FDG PET/CT in 38 of 39 (97.4%) patients. Herein, ^{18}F -FDG PET/CT and ^{18}F -FDG PET/MRI correctly determined the T-stage in 92.3% and 89.7% of patients, respectively. N-stage was categorized concordantly in 83 of 84 patients (98.8%). ^{18}F -FDG PET/CT correctly determined the N stage in 78 of 84 patients (92.9%), while ^{18}F -FDG PET/MRI correctly determined the N stage in 77 of 84 patients (91.7%). Differences between ^{18}F -FDG PET/CT and ^{18}F -FDG PET/MRI in T and N staging accuracy were not statistically significant ($p > 0.5$, each). Tumor size and SUV_{max} measurements showed excellent correlation. **Conclusion:** ^{18}F -FDG PET/MRI and ^{18}F -FDG PET/CT show an equivalently high diagnostic performance for T and N staging in patients suffering from NSCLC.

EP-0518

Improved Small Lesion Detection in Lung Cancer Patients with Digital PET

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Aim: For conventional PET, small lesion detection can be improved when using small voxels. Recently, a time-of-flight PET system with digital photon counting technology (Philips Healthcare) was introduced, aiming at an improved image quality compared to conventional systems. We evaluated the performance of digital PET for small lesions detection in patients with lung cancer when using small voxels, as compared with conventional PET. **Subjects and Methods:** We performed a prospective side-by-side PET comparison study in 20 patients with lung cancer referred for a FDG-PET/CT. For each patient, scans were acquired using a conventional scanner (cPET, Ingenium TF PET/CT, Philips) and a digital scanner (dPET, Vereos PET/CT, Philips Healthcare). The PET scanning order was randomized per patient. We applied a quadratic FDG-dose regimen according to European guidelines ($A = 6 \cdot w^2 \cdot t$), with A the administered FDG-dose in MBq, w the patient's bodyweight in kilogram and t the scan time per bed position in seconds. For both scanners, we used an optimized high-resolution PET reconstruction with small $2 \times 2 \times 2 \text{ mm}^3$ voxels and comparable noise levels. Per patient, FDG-positive lesions were included up to a maximum of 5. For each lesion, we measured mean and maximum standardized uptake values (SUV_{mean} and SUV_{max}) on cPET and dPET images. Lesion axial diameters were measured on CT. We per-

formed a subgroup analysis for lesions ≤ 10 mm. **Results:** Across 68 included lesions, average lesion size was 14 mm (range 4–45 mm). On cPET, the average $\pm$ standard deviation of SUVmean and SUVmax were 4.7 ± 2.2 and 6.9 ± 3.6 , respectively. On dPET, these values increased with 29% to 5.8 ± 2.7 for SUVmean ($p < 0.001$) and with 29% to 8.7 ± 4.1 for SUVmax ($p < 0.001$). For lesions ≤ 10 mm ($n=23$), we found average increases of 38% for SUVmean and 35% for SUVmax on dPET images. **Conclusion:** In patients with lung cancer, digital PET provides about 30% higher SUVs as compared to conventional PET, when using optimized small voxel PET reconstructions for both systems. For smaller lesions, SUVs on digital PET increased even further. This implies an improved detection of small lesions.

EP-0519

Usefulness Of A Follow Up Study Of PET CT At Around One Year After Curative Surgery For Non- Small Cell Lung Carcinoma

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Purpose: To evaluate the results in asymptomatic patients who a follow-up PET/CT, as an intensive surveillance program, has performed at around one year after curative surgery for non-small-cell lung cancer (NSCLC). **Subjects and Methods:** Between January 2008 and December 2017, this study enrolled 123 patients with NSCLC who had no clinical evidence for recurrence after curative resection and underwent a follow-up PET/CT around one year at our institution. TNM staging was based on American Joint Committee 8th edition. All data were statistically analyzed using SPSS Version 11.0 software (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$. **Results:** One hundred twenty three patients (65 men; mean age, 69.4 years: SD=9.2, range 49–93) underwent a follow up PET/CT to evaluate recurrence around one year after curative surgery. The pathological staging of the tumors was follows: 28 patients had stage IA, 14 stage IB, 8 stage IIA, 46 stage IIB, 27 stage IIIA, respectively, and histologic type of NSCLC was as 18 squamous cell carcinoma, 93 adenocarcinoma and 12 others. None of patients had neo-adjuvant therapy before curative surgery. The mean time from surgery to the follow up PET/CT study was 11.5 months. PET/CT showed positive findings 58.5% in all cases, 33.3% in stage I, 63.0% in stage II, 88.9% in stage IIIA, N0 in 33.3%, N1-2 in 78.3%, pI0-1 in 51.7%, pI2-3 in 79.9%, respectively. Positive sites of PET/CT were 56 locoregionals including three metachronous lung cancers and 25 distant including one colon cancer. There were significant difference between SUVmax of primary lung carcinoma in positive vs in negative case of follow up study, stage I vs II, stage I vs IIIA, lymphnode metastasis: N0 vs N1,2, and pleural invasion: pI0,1 vs pI2,3. Follow up PET/CT showed sensitivity of 96.8%, specificity of 81.4%, PPV of 84.5% and NPV of 96.0% in all stages, 91.7%, 87.1%, 73.3%, 96.4% in stage I, 96.6%, 76%, 82.4%, 95.9% in stage II and 100%, 66.7%, 91.3%, 100% in stage IIIA, respectively. **Conclusion:** Follow-up PET/CT at around one year can be used for early detection of recurrence in asymptomatic

post curative surgery patients of NSCLC, especially stage II and IIIA, N1,2, and pI2,3. Further studies are required to evaluate survival benefit of follow-up study around one year.

EP-0520

Multiple pulmonary nodules detected in patients with previous cancer history: analysis of ^{18}F -FDG diagnostic performance and nodules' characteristics

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Introduction: Multiple pulmonary nodules (MPNs) are frequently detected in oncologic patients during follow-up, still representing a dilemma for clinicians and diagnostic physicians. Indeed, it is difficult to determine their nature because each of them can show differences in growth behavior (disappearance, long-time stability or increase), morphological characteristics, as well as in probability to be malignant (metastases or metachronous lung cancer) or benign (acute or consequences of inflammation related to treatments, other benign conditions). In this setting, ^{18}F -FDG PET/CT performance for characterizing MPNs is less established and often assessed in not strictly-selected oncologic populations. Aims: to evaluate the ^{18}F -FDG PET/CT diagnostic performance and the relationship between malignancy and nodules' characteristics in MPNs detected in a specific oncologic population. **Methods:** We retrospectively evaluated 61 MPNs detected during follow-up in 27 oncologic patients (14M; mean age 69.2 ± 8 years; at least 2 nodules/each) who underwent ^{18}F -FDG PET/CT for restaging. Median disease free-interval (DFI) between previous cancer diagnosis/its recurrence and nodules detection was 6.5 years (range=1–34). Histology or radiological follow-up were used for final diagnosis. ^{18}F -FDG PET/CT diagnostic performance on nodule-based (malignancy criterion: uptake $\geq$ mediastinal activity) and patient-based analysis (malignancy criterion: at least one ^{18}F -FDG-positive nodule), and nodules' characteristics were evaluated. **Results:** 32/61 (52%) nodules were malignant, 29/61 (48%) benign. Overall median SUVmax and size were 1.7 (range=0.8–18.7) and 10mm (range=5–37mm), respectively. On nodule-based analysis, PET classified 26/61 nodules as malignant and 35/61 as benign, providing sensitivity=69%, specificity=86%, diagnostic accuracy=77%, PPV=85%, NPV=71%. Malignant nodules significantly differed ($p < 0.007$) from benign ones in SUVmax and size (median SUVmax=2.9 vs 1.3; median size=12mm vs 8mm, respectively), whereas the two groups did not differ in age, gender, DFI or nodule location (right/left, upper/lower lobe, central/peripheral). According to the final diagnosis, 18/27 patients (67%) were classified "with malignancy" (at least one malignant nodule), 9/27 "without malignancy". On patient-based analysis, PET correctly classified as "positive" 16/18 patients with malignancy (sensitivity=89%), as "negative" 5/9 patients without malignancy (specificity=55%).

Conclusion: Our data indicate that: 1) MPNs in our oncologic population have an intermediate prevalence of malignancy; 2) ^{18}F -FDG PET/CT is useful for ruling in malignancy (few false-positive); 3) the good **patient-based** performance of PET suggests its significant relevance on patient management, allowing to identify the “reference” nodule deserving histological assessment; 4) the diagnosis of PET-negative nodules remains a dilemma (false-negative mainly related to very small size), also because no clinical or location features seem useful to differentiate malignant nodules from benign ones.

EP-0521

The kinetic of ^{18}F -FDG in lung cancer: compartmental models and voxel analysis

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Introduction: The glucose metabolism, represented by the kinetic of ^{18}F -FDG, can be different among tissues as well as between primary tumors and metastases. Aims of our study were: to assess the compartmental model that best describes the kinetic of ^{18}F -FDG in primary lung cancers and in metastatic lymph nodes; to evaluate whether quantitative parameters are different between primary lung cancers and metastatic lymph nodes as well as between adenocarcinomas and other histotypes; and to evaluate the intra-tumor inhomogeneity. **Methods:** Twenty-one patients (7 females, 14 males, mean age 71.0 ± 9.4 years) with primary lung cancer were prospectively evaluated. All patients underwent ^{18}F -FDG PET-CT for staging. Spectral analysis iterative filter (SAIF) approach was used to develop the most appropriate compartmental model; the Akaike information criterion (AIC) to select the best one. Quantitative analysis was performed at voxel level. K_1 , V_d , and K_t were estimated with SAIF approach, Patlak analysis, and the selected compartmental model. Pearson's correlation and non-parametric methods were used for statistical analysis. **Results:** In primary lung cancers, metastatic lymph nodes and normal lung tissues the SAIF approach showed three reversible compartmental models: 3K, 5K, 7K. The AIC indicated 3K model as the best compromise between model fit and complexity in all voxels. Correlation between K_t estimated by Patlak and by 3K model with K_t estimated by SAIF was at global level: $R^2 = 0.97$ and $R^2 = 0.98$, respectively; at voxel level: $R^2 = 0.94$, $R^2 = 0.95$, respectively. Using 3K model, metastatic lymph nodes ($n=24$) showed higher mean and standard deviation values of V_d when compared with lung cancers ($n=23$; $p=1.3 \cdot 10^{-3}$, $p=8.5 \cdot 10^{-5}$ respectively) and higher standard deviation values

of K_t ($p=4.6 \cdot 10^{-3}$). No significant difference in all parameters between adenocarcinomas ($n=9$) and the other histotypes ($n=11$) was found. **Conclusions:** Our data indicate that the one-tissue reversible plus one-tissue irreversible (3K) is the compartmental model that best describes the kinetics of ^{18}F -FDG in primary lung cancers, metastatic lymph nodes and normal lung tissues. Moreover, the quantitative parameters estimated at voxel level show the inhomogeneity of neoplastic tissues: differences in metabolic activity and in vascularization, highlighted among all cancers and within each individual cancer, confirm the wide inter- and intra-cancer variability of primary lung cancers and metastatic lymph nodes. The inhomogeneity is more evident in metastatic lymph nodes compared to primary lung cancer, suggesting that metastasis tend to be less differentiated and with a more chaotic behavior than primary lung cancer.

EP-0522

Influence of CT acquisition and reconstruction parameters on radiomic feature extraction

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Qualitative visual interpretation of computed tomography (CT) images does not extract all of the information contained in the image. Radiomics is the automated extraction of quantitative image-based features which could add diagnostic/prognostic value, with the aim to personalize diagnosis and treatment. However, clinical implementation of radiomics-aided diagnosis has been impeded by differences in CT acquisition and reconstruction protocols that can strongly modify the extracted features. The aim of our study was to investigate the impact of CT acquisition and reconstruction parameters like tube current and slice thicknesses on radiomic feature extraction and their stability. **Material and Methods:** Patients ($n = 16$) with non-small cell lung cancer underwent pre-treatment PET/CT scan and had three distinct CT series were used in this study. PET SUV-based auto-segmentation was used to delineate the primary lung tumor on PET then delineations were cloned to CT. The CT series presented different radiomics extraction problems that would be encountered when using routine imaging in the clinical context: (series_1) Whole body contrast CT (WBCCT) in 2mm slice thickness, (series_2) WBCCT in 5mm slice thickness and (series_3) non-contrast thoracic CT in 2mm slice thickness. In total, 102 radiomic features were extracted from the tumour segment in images using the **pyradiomics** software library. Feature stability was assessed via concordance correlation coefficient (CCC) for variations in acquisition settings. The CCC was calculated between the series in three sets viz. SET_1: between series_1 and series_2; SET_2: between series_1 and series_3; SET_3: between series_2 and series_3. **Results:** Values of radiomic features were affected by slice thickness as well as presence of contrast. The median CCC for each feature was sensitive to changes in the

acquisition settings between CT series. The median and range of CCC values in all three sets are given in Table 1. As expected, shape metrics were among the most consistently transferrable between image acquisition settings, followed by the first-order histogram feature Entropy. Textural features were consistently among the most adversely affected, along with first-order features Energy and 90th Percentile. The top ten least-affected and worst-affected features with regards to their median CCC values across all acquisition settings are given in Table 2. **Conclusions:** Other than shape metrics, measures of first-order entropy were the most reproducible across the CT image acquisition settings. Textural features generally have low transferability between different acquisition settings. Selection of appropriately reproducible radiomic features is essential for developing quantitative image marker models with high external validity.

EP-0523

Lean Body Mass Measured on CT of Pretreatment ¹⁸F-FDG PET/CT is a Prognostic Factor of Non Small Cell Lung Carcinoma Treated by Nivolumab

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Introduction: Immune inhibitors of programmed cell death 1 (PD1) or its ligand (PDL-1), including Nivolumab immunotherapy, are changing the treatment of non-small cell lung cancers (NSCLC). Our aim was to explore in patients treated by Nivolumab for a NSCLC the prognostic value of anthropometric parameters measured on CT of pre-therapeutic ¹⁸F-FDG PET/CT. **Subjects & Methods:** We retrospectively included 47 patients having a NSCLC treated by Nivolumab and who underwent a pre-therapeutic ¹⁸F-FDG PET/CT. Anthropometric parameters were measured by an in-house software, Anthropometer3D, allowing an automatic multi-slice measurement of Lean Body Mass (LBM), Fat Body Mass (FBM), Muscle Body Mass (MBM), Visceral Fat Mass (VFM) and Sub-cutaneous Fat Mass (SCFM) on the CT of the PET/CT. All anthropometric parameters were normalized by the patient's weight used to calculate the dose of Nivolumab. Other clinical and tumour characteristics were also retrieved. The Spearman's rank correlation coefficient (ρ) was computed between anthropometric parameters, and ROC analysis was performed. Overall survival at 1 year was studied using a Kaplan-Meier method and uni/multivariate Cox analysis. **Results:** LBM, FBM and SCFM were highly correlated ($|\rho| > 0.95$), while LBM and MBM were less correlated ($\rho = 0.76$). VFM was relatively uncorrelated to the others anthropometric parameters (maximal $|\rho| = 0.63$). In the ROC analysis, LBM, FBM, SCFM, VFM, body mass index (BMI) and metabolic tumor volume (MTV) had

an AUC significantly higher than 0.5. LBM gave a better accuracy than FBM, SCFM and MBM (0.745, 0.706, 0.723 and 0.702, respectively) and was therefore the only one kept among the correlated parameters. Patients with high LBM (> 0.77 kg/kg), or low BMI (< 25.4 kg/m²) or high MTV (> 86 cm³) had significantly worse prognosis in Kaplan-Meier ($p < 0.001$ and survivors 25% vs 71%, $p = 0.013$ and survivors 38% vs 74%, $p = 0.016$ and survivors 45% vs 63%, respectively). Cox univariate analysis gave the following results : HR: 4.61, $p < 0.001$, HR: 0.62, $p = 0.02$, HR: 2.64, $p = 0.02$, respectively. In a stepwise multivariate Cox analysis combining LBM, BMI and MTV, the only significant parameter was LBM. **Conclusions:** LBM measured by Anthropometer3D on the pre-therapeutic ¹⁸F-FDG PET/CT of patients having a NS-CLC treated by Nivolumab is an important prognosis factor. If these results have to be confirmed on a larger cohort, a dose calculation of Nivolumab taking into account the patient's morphology rather than only its weight could be pharmacokinetically beneficial.

EP-0524

Is the ¹⁸F-FDG diagnostic performance in solitary pulmonary nodules (SPNs) detected in patients with previous cancer history as good as in non-oncological subjects? Experience in 121 cases

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Introduction: Solitary pulmonary nodules (SPNs) detected during follow-up in patients with previous cancer have a high and increased probability of malignancy (up to 85-90%) when compared to non-oncologic subjects (about 60%), both probabilities depending on recruited populations. ¹⁸F-FDG PET/CT is a recognized accurate tool for characterizing pulmonary nodules in a non-oncologic population, whereas its diagnostic performance in oncologic patients is less established and widely variable due to the selected population (also including non-oncologic subjects) and nodule characteristics (solitary/multiples, from few millimeters to masses), all factors affecting the prevalence of malignancy. Aims: to evaluate the ¹⁸F-FDG PET/CT performance for characterizing SPNs in an exclusive oncologic population and the relationship between malignancy and nodules' characteristics. **Methods:** We retrospectively evaluated 121 SPNs in 121 oncologic patients (75M; mean age 69.6±8.5years) who performed ¹⁸F-FDG PET/CT for restaging. Median disease free-interval (DFI) between previous cancer diagnosis/its recurrence and SPN detection was 3 years (range=1-22). Final diagnosis was established by histology or radiological follow-up. ¹⁸F-FDG visual analysis (uptake $\geq$ mediastinal activity), ROC curve analysis for SUVmax and nodules' characteristics were analyzed. **Results:** 106/121 (87.6%) SPNs were malignant (of which 95/106 diagnosed by histology

gy and 11/106 by radiological follow-up), and 15/121 benign (12.4%). The overall median SUVmax was 4.5 (range=0.5–38.0); the overall median size was 16mm (range=5–40mm). PET visual analysis provided sensitivity=82%, specificity=73%, diagnostic accuracy=81%. ROC curve analysis (SUVmax cut-off=2) provided sensitivity=84%, specificity=80% (AUC=0.856; $p=0.0001$). Significant differences ($p<0.001$) in SUVmax and size between malignant and benign SPNs (median SUVmax=5.1 vs 1.4; median size=18mm vs 11mm) were found. Malignant SPNs were predominantly peripheral (78/106) and located in upper lobes (72/106). No significant differences in age, gender, DFI or lung location (right vs left) were found between the two groups. **Conclusion:** Our data, obtained in highly selected population (with previous cancer history and solitary pulmonary nodules), indicate that ^{18}F -FDG PET/CT has good diagnostic performance for SPN characterization, in accordance with reports on non-oncologic populations. PET seems clinically relevant for ruling in malignancy, even when SPN has still small size (just after radiological detection). Moreover, malignant SPNs differ from benign ones for both functional and morphological parameters. In PET-positive SPNs, histological assessment remains mandatory to discriminate between metachronous lung cancer and metastasis and, consequently, to select the appropriate patients' management. In this regard, evaluation of ^{18}F -FDG PET/CT performance for non-invasive characterization of SPN as metachronous lung cancer or metastasis represents an interesting topic of further studies.

EP-0525

Prediction of recurrence using volume-based metabolic index obtained by preoperative FDG-PET for non-small-cell lung cancer

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Aims: To evaluate the predictive values of metabolic parameters acquired using preoperative F-18 FDG-PET/CT in patients with non-small-cell lung cancer (NSCLC). **Materials and Methods:** This study was approved by our Institutional Review Board. A retrospective review of preoperative FDG-PET/CT findings and postoperative pathological records obtained over a 5-year period was conducted. Solid-type NSCLC lesions (diameter ≤ 3 cm), the diagnosis of which was confirmed during surgical resection, were selected. Metabolic parameters, namely maximum standard uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG), were compared to predict postoperative recurrence. Univariate and multivariate Cox proportional hazard model analyses were performed to identify the predictive factors. **Results:** In total, 128 NSCLC lesions of 128 patients (94 males, 34 females; mean age, 69 years) were included. Ninety lesions were adenocarcinomas (ACs), and 38 lesions were squamous cell carcinoma or adenosquamous carcinoma (SCs). During the follow-up periods, 33 patients (24%) experienced recurrence. SUVmax and TLG were significantly higher in the recurrence group than in the no-recurrence group ($p = 0.010$ and $p = 0.042$, respectively). No significant difference was observed between the recurrence and no-recurrence groups in

terms of age, sex, AC/SC, diameter of lesions, and MTV. Univariate analysis indicated that pathological type (SCs), SUVmax, and TLG were correlated with recurrence-free survivals ($p = 0.034$, $p < 0.001$, and $p < 0.001$, respectively). Multivariate analysis revealed that TLG was the only independent prognostic factor (hazard ratio = 1.072, $p = 0.012$). **Conclusion:** SUVmax and TLG calculated using preoperative FDG-PET/CT findings can provide prognostic information for NSCLC patients. TLG, a volume-based index, may become a more useful factor than SUVmax in evaluating the prognosis of NSCLC.

EP-0526

Does F-18 FDG PET/CT have a clinical value for diagnosis and LN staging in lung cancer patients with pneumoconiosis?

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Purpose: To find out whether PET/CT can differentiate (1) progressive massive fibrosis (PMF) from lung malignancy and (2) reactive LN hyperplasia from metastatic LN in patients with pneumoconiosis. **Methods:** This was a retrospective study of 49 patients with pneumoconiosis and suspected lung cancer who underwent PET/CT scans from July 2009 to April 2016. The maximum standardized uptake value (SUVmax), long and short axis diameter (D_L and D_S), ratio of D_L to D_S ($D_{L/S}$), Hounsfield unit (HU) were measured from the site where primary lung cancer or PMF were suspected. For the mediastinal lymph node (LN) analysis, visual and semi-quantitative analysis using SUVmax, D_S and HU from PET and CT were performed for LNs which were confirmed as reactive or metastatic LN by pathology. **Results:** Of the 83 lung masses which were detected from 49 patients, 42 were lung cancer and 41 were PMF. There were significant differences between the lung cancer and PMF in SUVmax (12.3 ± 5.7 vs. 6.3 ± 2.8 , $P < 0.001$), D_S (2.8 ± 1.2 vs. 2.3 ± 1.0 , $P = 0.020$), $D_{L/S}$ (1.4 ± 0.3 vs. 2.2 ± 0.6 , $P < 0.001$) and HU (36.6 ± 9.3 vs. 61.3 ± 19.6 , $P < 0.001$), but not in D_L . The sensitivity, specificity and accuracy were 81.0%, 73.2%, and 77.1% with SUVmax 7.4 as the cut-off value, and 92.8%, 87.8%, and 90.4% for HU with a cut-off value of 45.5, respectively. The specificity increased to 97.6% when assessing malignancy with a combined cutoff value (SUVmax > 7.4 and HU < 45.5). Among the 40 LNs with available pathologic results, 7 were metastasis. Metastatic LNs showed higher SUVmax, larger D_S , and lower HU than reactive LNs. When using combined PET and CT criteria, sensitivity, specificity and accuracy were 85.7%, 93.9% and 92.5 for predicting metastatic LNs. Specificity and accuracy were significantly higher than those of size and HU criteria from CT ($P=0.039$ and $P=0.035$, respectively). **Conclusion:** SUVmax, D_S , $D_{L/S}$, and HU of the lung mass were found to be useful parameters in the differentiation lung cancer from PMF in pneumoconiosis. SUVmax, D_S , and HU of LN were also useful parameters in differentiating metastatic LN from reactive LN. When combining parameters of PET and CT, a diagnostic advantage might be achieved with improved specificity in distinguishing lung cancer from PMF and metastatic LNs from reactive LNs.

EP-0527

Metabolic Parameters Measured By ¹⁸F-fluorodeoxyglucose-positron Emission Tomography/computed Tomography For Predicting The Outcome Of Patients With Non-small Cell Lung Cancer Treated With Pembrolizumab

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Purpose: We evaluated the prognostic value of total body metabolic tumor volume (TMTV) and total lesion glycolysis (TLG) measured using FDG-PET/CT in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) treated with pembrolizumab, a programmed cell death 1 (PD-1) inhibitor. **Materials and Methods:** A total of 132 patients with NSCLC (median age, 68 years; range, 34–89 years) who had undergone FDG-PET/CT prior to pembrolizumab treatment were retrospectively reviewed. All patients received infusions of pembrolizumab every 2 or 3 weeks as one cycle and had undergone baseline FDG-PET/CT within 2 months prior to initiation of pembrolizumab treatment. We determined the maximum standardized uptake values normalized to lean body mass (SULmax), MTV (volume encompassed by a 42% isocontour around the voxel with the highest PET uptake), and TLG (calculated by multiplying MTV by mean SUL). TMTV and TLG values are defined as the sum of MTVs and TLGs of all lesions, respectively. We correlated PET findings with overall survival (OS). **Results:** Of the 132 patients, 35 died during the follow-up period after pembrolizumab treatment. The median OS time was 22 months (range, 0.1–53.6 months). 115 patients were at stage IV and 17 at stage III; 27 patients had brain metastasis at start of pembrolizumab therapy. 41 patients had received prior chemotherapy. Median values for SULmax, TMTV, and TLG were 11.1 g/mL, 53.2 cm³, and 249.43 g/mLcm³, respectively. Number of cycles (>4 cycles), TMTV, and TLG were prognostic for OS ($p < 0.001$, 0.03, and 0.01, resp.) in univariate analyses. Clinical parameters (e.g., age, stage, histology, and presence/absence of brain metastasis) were not found to be significant for OS. In multivariate analysis, the number of cycles (>4 cycles) and TLG were independent prognostic factors for OS ($p < 0.001$ and 0.003; HR 10.03 and 3.02; 95% CI, 4.55–24.46 and 1.44–6.79, resp.). The 1-y OS rates for patients with TLG ≤ 249.43 g/mLcm³ and > 249.43 g/mLcm³ were 83.5% and 59.3%, resp. PD-L1 tumor proportion score (%age of neoplastic cells showing membranous staining of PD-L1) did not correlate with SULmax, TMTV, or TLG (Pearson's correlation coefficients, $r = 0.12$, 0.18, and 0.23). **Conclusion:** TLG on baseline FDG-PET predicted OS in patients with locally advanced or metastatic NSCLC; patients with predicted poor outcome may benefit from alternate, escalated treatment strategies.

EP-0528

Usefulness Of F-18 Fdg PET/CT For The Diagnosis Of Chronic Empyema-associated Malignancy

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Purpose: Chronic empyema-associated malignancies (CEAM) are rare complications of long-standing empyema. Although many CT findings of CEAM have been described, most showed either low positive predictive value or low sensitivity. The purpose of this study was to evaluate the diagnostic criteria and accuracy of ¹⁸F-FDG PET/CT for detecting CEAM in patients with chronic empyema. **Subjects and Methods:** Thirty three patients (mean age, 62.0 $\pm$ 9.5 y, M : F = 26 : 7) who underwent ¹⁸F-FDG PET/CT for suspected CEAM were retrospectively analysed. PET/CT findings were described according to the following criteria; 1) shape of empyema cavity (oval, lenticular, or crescentic), 2) presence of fistula formation (air-fluid level in the empyema cavity), 3) maximum SUV of empyema cavity, 4) uptake pattern of empyema cavity (focal; presence of discrete hypermetabolic foci significantly higher than the activity of surrounding empyema cavity vs. non-focal; diffuse uptake without significant focal uptake) 5) presence of a protruding soft-tissue mass within the empyema cavity, and 6) involvement of adjacent structures (including rib, chest wall, lung, and abdomen). PET/CT findings were compared with final diagnosis based on pathology or clinical follow-up for more than 6 months. **Results:** Six lesions (18.2%, 6/33) were histologically proven to be malignant (diffuse large B cell lymphoma in 3, squamous cell carcinoma in 1, poorly differentiated carcinoma in 1). The presence of fistula formation, maximum SUV of empyema cavity, presence of a protruding soft-tissue mass, and involvement of adjacent structures demonstrated a statistically significant association with CEAM ($p < 0.05$). There were no significant differences in shape of empyema cavity and uptake pattern of empyema cavity. Maximum SUV showed a significantly higher SN, SP, PPV, NPV, and AC over any other criterion. ROC analysis identified highest diagnostic accuracy of maximum SUV to detect of CEAM with sensitivity 100.0% and specificity 96.3% at cutoff 10.8. **Conclusion:** ¹⁸F-FDG PET/CT is useful for differentiating CEAM from benign chronic empyema. The maximum SUV of empyema cavity is the most accurate diagnostic PET/CT criteria for detecting CEAM.

EP-0529

Prognostic Value of Sarcopenia Determined on Pre-therapeutic PET/CT in Patients Treated for Non-Small Cell Lung Cancer by Radiochemotherapy

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Introduction: Sarcopenia is a well-known prognostic factor for patients treated for a non-small cell lung cancer (NSCLC) by surgery or chemotherapy. However, its impact in patients treated by exclusive radiochemotherapy has never been explored. Our

study tries to evaluate the prognostic value of sarcopenia and other anthropometric parameters on this population. **Subjects & Methods:** Clinical (histology, TNM stage, sex, age, WHO score), nutritional (weight, size, weight lost, BMI, albumin serum level, Buzby Index) and anthropometric data were collected for 93 patients treated by radiochemotherapy for a NSCLC. Anthropometric parameters were measured on the CT of the PET/CT by two different methods. The first method was a manual segmentation at level L3, used to define Muscle Body Area (MBA_{L3}), Visceral Fat Area (VFA_{L3}) and Subcutaneous Fat Area ($SCFA_{L3}$). The second method was an in-house software, called Anthropometer3D, allowing an automatic multislice measurement of Lean Body Mass ($LBM_{Anthro3D}$), Fat Body Mass ($FBM_{Anthro3D}$), Muscle Body Mass ($MBM_{Anthro3D}$), Visceral Fat Mass ($VFM_{Anthro3D}$) and Sub-cutaneous Fat Mass ($SCFM_{Anthro3D}$) on the CT of the PET/CT. All anthropometric parameters were normalized by the patient's height² (m²). Sarcopenia was defined on MBA_{L3} by sex-specific cut-off already described: $SMA < 38.5 \text{ cm}^2/\text{m}^2$ for women and $< 52.4 \text{ cm}^2/\text{m}^2$ for men. The primary end point was overall survival time. A receiver operating characteristic (ROC) curve analysis was performed for anthropometric parameters to determine those significant, i.e. having an area under the ROC curve (AUC) significantly higher than 0.5. Univariate and then stepwise multivariate cox analysis were performed for significant parameters. Finally, Spearman's correlation between MBA_{L3} and $MBM_{Anthro3D}$ was assessed. **Results:** Forty-four (44%) patients were sarcopenic. The median overall survival was 26 months. There were 32 deaths among sarcopenic patients (78%) versus 30 deaths among non-sarcopenic patients (61%). The median overall survival was 18 months for sarcopenic patients versus 36 months for non-sarcopenic patients ($p=0.019$). Sarcopenia ($HR=1.806$, $IC95\% [1.09-2.98]$), serum albumin level $< 35 \text{ g/l}$ ($HR=2.203$ [$1.19-4.09$]), Buzby Index < 97.5 ($HR=2.31$ [$1.23-4.33$]), WHO score = 0 ($HR=0.52$ [$0.31-0.86$]) and $MBM_{Anthro3D} < 8.56 \text{ kg/m}^2$ ($HR=2.36$ [$1.41-3.90$]) were the only significant features in univariate analysis. In the stepwise multivariate Cox analysis, only $MBM_{Anthro3D} < 8.56 \text{ kg/m}^2$ ($HR=2.16$, $p=0.003$) and WHO score = 0 ($HR=0.59$, $p=0.04$) were significant. Finally, muscle quantified by MBA_{L3} and $MBM_{Anthro3D}$ were found to be highly correlated (Spearman = 0.90). **Conclusions:** Sarcopenia assessed on the pre-treatment PET/CT is a powerful prognostic factor in patient treated by radiochemotherapy for a NSCLC. The automatic software Anthropometer3D can easily identify patients at risk who could benefit an adapted therapy.

EP-0530

The Impact On TNM Staging Of Incorrectly Diagnosed Thoracic Lymph Nodes Metastatic Involvement In NSCLC Patients Imaged By 18F-FDG-PET/CT

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Purpose: The study attempts to characterize the problem of erroneously determined the N category of the TNM system

among NSCLC patients imaged with the 18F-FDG-PET/CT. **Materials and Methods:** Study included 89 patients and 436 nodal stations diagnosed with 18F-FDG-PET/CT in Department of Nuclear Medicine of UCC in Gdansk and treated operatively with pneumonectomy/lobectomy in the Department of Thoracic Surgery, UCC Gdansk in years 2010-2014. PET/CT results were compared to pathological analysis of operatively excised material, which were used as a "gold standard". **Results:** Among patients in the early stages of NSCLC evaluation of nodal involvement is subject to significant error - in 32.6% of patients N category determined by PET/CT was different from those determined histologically. In 23.6% of all patients N category was overestimated and 9% had an underestimation. In the case of 11 patients (12.4% of total) occurred false positive indication of N2. The most common error in determining the N category was classification of N0 patients to the N1 group, which occurred in 10 cases (11.2% of all patients). In 5 patients (5.6% of all patients) the N2 category was not detected by PET-CT. **Conclusions:** The present study confirms the limited ability of the integrated PET-CT to properly assess the nodal status in patients with potentially resectable NSCLC. In one third of patients the N category of the TNM system was determined incorrectly. Due to the risk of complications and the necessity of hospitalization in determining the N category by invasive methods, the PET/CT scan seems to be the optimal diagnostic choice for candidates for radical surgical treatment, however the invasive verification of positive results should be considered, especially in the presence of a history of inflammatory disorders in the chest.

EP-0531

Do 18F-FDG semi-quantitative parameters correlate with PDL1 expression in pts with advanced lung cancer?

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Purpose/Introduction: to assess whether 18F-FDG PET/CT semi-quantitative parameter correlate with PDL1 expression in patients (pts) with advanced lung cancer. **Subjects and Methods:** among the pts referred to 18F-FDG PET/CT between January 2016 and February 2018, only those with advanced lung cancer and pathological assessment (including PDL1 expression) performed after PET (maximum interval: 1 month) were included. 18F-FDG PET/CT was performed following standard EANM procedures. Each PET/CT scan was retrospectively reviewed by two experienced nuclear medicine physicians (LZ and VA) and semi-quantitative parameters were calculated. In particular, the following indices were measured: SUVmax at the site of bioptical sample/surgical specimen, SUVmax of the whole scan, ratio between the SUVmax of at the site of bioptical sample/surgical specimen and the liver (standard ROI of 5cm on the unaffected liver). Each semi-quantitative index was correlated with PDL1 expression (%). **Results:** overall, 44 pts were included in the analyses. PDL1 was measured on lung surgical specimens in 5 cases while in the remaining pts was determined

on bioptical samples (lung 23, adrenal 1, node 10, liver 1, soft tissue 2, bone 1, pleura 1). PDL1 was negative in 15/44 pts and positive in 24/44 pts. Overall, mean PDL1 was 22.4 ± 13.7 (median=3; range: 0–100). Mean SUVmax at the site that was subsequently biopsied/surgically removed after PET/CT was 12.5 ± 7.0 (median=12.5; range:0–34.3). In 15/44 cases the SUVmax at the site of bioptical sampling/surgical removal was not the highest SUVmax value of the whole scan. Overall, in our series there was no significant correlation between PDL1 and SUVmax at the site of bioptical sample/surgical specimen ($p=0.8$), SUVmax of the whole scan ($p=0.5$), ratio between the SUVmax of at the site of bioptical sample/surgical specimen and the liver ($p=0.8$). **Discussion/Conclusion:** although hampered by the relative small sample size, the retrospective nature of pts selection, the high frequency of bioptical vs surgical pathological analysis, our preliminary data show that there was no significant correlation between PDL1 expression and semi-quantitative parameters. Another potential bias is that the SUVmax might not be representative of the metabolic burden, especially in pts presenting with a voluminous lung mass. Further analyses are on-going to assess the potential predictive value of semi-quantitative indices and PDL1 expression on pts outcome and to evaluate further semi-quantitative indices (i.e. metabolic tumour volume, SUVmean, TLG).

EP-0532

The role of combined ^{68}Ga -DOTATOC PET/CT and ^{18}F -FDG PET/CT in patients with solitary pulmonary nodule

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Background/Aim: ^{18}F -FDG PET/CT (FDG-PET) is widely used to evaluate solitary pulmonary nodule (SPN) but false negative/positive and undeterminate results may occur. ^{68}Ga -DOTATOC PET/CT (Ga-PET) could impact the diagnosis of SPN over FDG-PET, optimizing patient management. **Patients/Method:** Thirty patients (12 male, 18 female, mean age 68) underwent sequentially FDG-PET and Ga-PET for SPN. Nodules were previously classified by CT scan as indeterminate (21), carcinoma (2), amarthocondroma (3), carcinoid (4). FDG-PET scan was considered positive in the presence of any increased uptake with SUVmax value >2.5 . Ga-PET was considered positive if any increased uptake, higher than background, was set out, irrespective of SUVmax. A faint uptake was classified as doubtful. The concordance rate between the two imaging modalities was assessed; finally PET results were compared to follow-up data. **Results:** Of the 30 patients, FDG-PET was positive in 13 and negative in 17 while Ga-PET was positive in 5, negative in 22 and indeterminate in 3. A 57% of concordance rate was found. According to both scans, 3 patients (10%) were classified as positive (surgery confirmed lung carcinoid, grade 2 and 1). Fourteen of the patients (47%) were negative; no one was referred to surgery. Ten underwent CT follow-up, showing lesions stability. Four patients were referred to biopsy, finding 3 amarthomas and 1 non-neoplastic alteration. Thirteen patients (43%) had discordant results. Eight patients positive at FDG/negative at Ga were referred respectively to: CT follow-up (4), showing lesion stability; biopsy (2),

finding 1 amarthocondroma and 1 flogistic alteration; surgery (2), with evidence of 1 amarthocondroma and 1 adenocarcinoma. Two patients positive at FDG/indeterminate at Ga-PET underwent surgery with diagnosis respectively of typical carcinoid G1 and neuroendocrine carcinoma. One patient negative at FDG/indeterminate at Ga-PET had diagnosis of typical carcinoid after surgery. Two patients positive at Ga-PET /negative at FDG were referred respectively to surgery (finding typical carcinoid) and to follow-up, due to important comorbidity. **Conclusions:** in our casistic, the use of combined FDG-PET and Ga-PET improved the overall diagnostic performance compared to a stand alone imaging modality. In discordant case, FDG-PET could be more susceptible of false positive results while ^{68}Ga positivity was strongly associated with neoplastic aetiology. Moreover, nodules classified as positive by both imaging modalities have high probability to be tumoral lesions. Otherwise, nodules classified as negative are strongly associated with non neoplastic aetiology, thus avoiding potentially unnecessary biopsy or surgery.

EP-0533

Mediastinal lymph node staging of non-small cell lung cancer with F-18 FDG PET/CT in a tuberculosis-endemic country

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Purpose: Accurate diagnosis of the mediastinal lymph node staging with F-18 FDG PET/CT in patients with non-small cell lung cancer (NSCLC) is challenging especially in tuberculosis-endemic countries. The aim of this study was to assess the diagnostic performance of F-18 FDG PET/CT in the mediastinal lymph node staging of patients with NSCLC in a tuberculosis-endemic country. **Subjects & Methods:** Between Aug 2010 and Dec 2015, 211 patients (range, 34–85 y; mean age, 66.3 ± 9.2 y) with NSCLC, who underwent F-18 FDG PET/CT for initial staging work-up and followed by lobectomy and thoracic lymphadenectomy were enrolled in this study. After thoracic lymphadenectomy, histopathological diagnosis was performed to determine the mediastinal lymph node metastasis. F-18 FDG PET/CT images were reviewed by 2 experienced nuclear medicine physicians. A Mediastinal lymph node without benign calcification or higher attenuation (Hounsfield unit > 70), which showed greater FDG uptake than mediastinal blood pool was regarded as metastasis. **Results:** Mean SUVmax of the primary tumor in 88 patients with squamous cell carcinoma (13.8 ± 5.4) was significantly higher than in 123 patients with adenocarcinoma (8.3 ± 5.9 , $p=0.005$). A total of 211 patients with 1,216 mediastinal node stations were evaluated. Patients with squamous cell carcinoma (40/88, 45.5%) more frequently showed the mediastinal lymph node metastasis than patients with adenocarcinoma (28/123, 22.8%). On patient-based analysis, the overall sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for detecting lymph node metastasis on F-18 FDG PET/CT were 70.3%, 93.2%, 85.1%, 85.7% and 87.2%, respectively. On lesion-based analysis, mean SUVmax of the metastatic lymph nodes (8.1 ± 5.3) was significantly higher than of benign lymph nodes (2.6 ± 0.1 , $p<0.005$). The sen-

sitivity, specificity, PPV, NPV and accuracy for detecting lymph node metastasis on F-18 FDG PET/CT were 69.1%, 93.3%, 87.5%, 95.3% and 96.7%, respectively. **Conclusion:** SUVmax of the mediastinal lymph node on the initial F-18 FDG PET/CT revealed excellent diagnostic accuracy for mediastinal lymph node staging and might be used as a useful parameter to determine the mediastinal lymph node metastasis in patients with NSCLC in a tuberculosis-endemic country.

EP-0534

Comparison Between Different Semiquantitative Parameters of PET/CT with 18F-FDG for the Characterization of Solitary Pulmonary Nodule

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Purpose: To compare the utility of different semiquantitative methods obtained from PET-CT studies with 18F-FDG for the characterization of solitary pulmonary nodule (SPN) in patients without oncological history. **Subjects & Methods:** Prospective study carried out from July 2015 to December 2017, including patients (total of 51; 15 women, 36 men), with an average age of 69.2 years (range 44 - 87 years), with no oncological history, who underwent a PET-CT scan with 18F-FDG for the characterization of a SPN (≥ 6 mm) seen with another radiological technique. PET-CT was performed at 60min (PET1, whole body) and 150min (PET2, selective imaging of the lungs) after de intravenous administration of the tracer. The semiquantitative variables used to classify the SPN as malignant were: SUVmax PET1 ≥ 1.5 , ≥ 2 and ≥ 2.5 , Δ SUVmax > 0 , Δ SUVmax $> 10\%$. With Δ SUVmax being the percentage difference between SUVmax of the SPN in PET1 and PET2. The final diagnosis was with anatomopathological study or with follow-up (with CT and / or new PET-CT) of at least 1 year. **Results:** The size of the SPN varied between 6-38mm (average 15.6 mm). The anatomopathological studies or follow-up revealed 25/51 malignant lesions, of which: 8 adenocarcinomas, 6 squamous cell carcinomas, 3 carcinoids, 2 lepidic adenocarcinomas, 2 small cell carcinomas; the remaining 4 lesions were considered malignant due to their clinical and/or radiological evolution. 26/51 benign lesions, of which: 1 nocardiosis, 1 hamartoma, and the other lesions were inflammatory-infectious processes of unknown etiology. The statistical parameters calculated for the different semiquantitative methods used to classify the SPN as malignant or benign were sensitivity, specificity, positive predictive value, negative predictive value and accuracy, obtaining the following: SUVmax ≥ 1.5 : 96%, 54%, 70.2%, 93% and 76.5% - SUVmax ≥ 2.0 : 77%, 75%, 77.7%, 66% and 76.5% - SUVmax ≥ 2.5 : 74%, 79%, 80%, 73% and 76.5% - Δ SUV >0 : 85%, 37.5%, 60.5%, 69% and 63% - Δ SUV >10 : 84%, 60%, 68%, 79% and 72.5% **Conclusion:** Δ SUV was not superior to the semiquantitative parameters obtained from PET1 only, for the characterization of solitary pulmonary nodule in non-oncological patients. In our analysis, an SUVmax of less than 1.5 was the best cut-off point to exclude malignancy.

EP-0535

Comparison of a manual and a semi-automatic approach in CT-based 3D quantification of relative lobar perfusion in preoperative patients with lung cancer

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Purpose: Quantification of relative pulmonary lobar perfusion using scintigraphy is an established procedure in calculation of expected lung function after surgery. Published data show that using SPECT-CT and a 3D-technique based on individual patient anatomy pulmonary lobe perfusion fraction can be calculated more exactly than with planar scintigraphy. Software algorithm for quantification such as "PMOD" is based on a more time-consuming manual approach for CT segmentation whereas the "HERMES" software uses a semi-automatic segmentation of the lung CT. Aim was to compare the results of two commercially available software packages (PMOD / HERMES) in a preoperative setting concerning in lung cancer patients with borderline lung function. **Methods:** 30 lung cancer patients referred to routine pre-operative relative lobar perfusion quantification were selected. Ventilation (using Technegas) - Perfusion SPECT-CT (low-dose-CT) was done p.i. of about 150 MBq Tc-99m-MAA (SymbiaT, Siemens), iterative reconstruction with Flash3D algorithm. For the manual 3D approach using PMOD the low-dose CT was manually segmented, the resulting VOIs were transferred to the coregistered perfusion SPECT to calculate relative lobar perfusion. The semi-automatic approach used "HERMES Hybrid 3D Lung Lobe Quantification" for segmentation of the matched low-dose and diagnostic CT (which is usually available in all lung cancer patients); the resulting VOIs were also transferred to the coregistered perfusion SPECT for calculation of relative lobar perfusion. Finally, a correlation analysis of the manual vs. semi-automatic approach was done. **Results:** The semi-automatic approach took 5-10 minutes for a complete evaluation whereas manual segmentation and calculation took about 45 minutes. Relative lobar perfusion values were in lung cancer patients quite similar for both approaches. When correlating all perfusion values the slope of the regression line (semi-automatic vs. manual) was 1.05 with a correlation coefficient of 0.92. **Conclusions:** Using commercially available software excellent correlation was found for relative lobar perfusion values resulting from a manual approach ("PMOD") vs. a semi-automatic approach ("HERMES"). Therefore, the much more accurate 3D-technique for quantification is suitable for routine use with the aim to overcome the old-fashioned planar based analysis. In larger clinical trials it has to be tested whether there are prognostic differences between both 3D-approaches.

EP-0536

Staging ¹⁸F-FDG PET/CT Whole-body Tumor Burden is a Prognostic Indicator in Advanced Non-small Cell Lung Cancer Patients

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Purpose: Evaluate if ^{18}F -FDG PET/CT (FDG-PET/CT) whole-body tumor burden is a prognostic indicator in patients with advanced non-small cell lung cancer (NSCLC). **Materials and Methods:** This retrospective study evaluated 52 baseline FDG-PET/CT scans performed for initial staging of patients with stage III and IV NSCLC (mean age 64.2y; 24 women, 28 men). All patients underwent standard treatment and subsequent clinical follow-up. The studies were performed on PET/CT scanners (Biograph True-Point 64, Siemens Healthcare, USA) 60 minutes after intravenous injection of 4.44MBq/kg of ^{18}F -FDG. The whole-body tumor burden FDG-PET/CT parameters evaluated were: the maximum SUV obtained from all metastatic sites including primary lesion (wbSUV); the maximum SUV of the primary tumor (tuSUV); the metabolic tumor volume from all metastatic sites including primary lesion (wbMTV); the metabolic primary tumor volume (tuMTV); the total lesion glycolysis from all metastatic sites including primary tumor (wbTLG) and of only the primary tumor (tuTLG). Furthermore the following ratios were evaluated: wbSUV/tuSUV; wbMTV/tuMTV; wbTLG/tuTLG. All semi-automatic quantification was performed using the semi-automated multi-foci segmentation tool (MFS, syngo.via MM Oncology, Siemens Medical Solutions USA). The SUVmax = 2.5 was the threshold selected. The variables whole-body tumor burden parameters as well as clinical and pathological variables (age, sex, performance status, histology, TNM stage and treatment types) were correlated to overall survival (OS) and progression-free survival (PFS). **Results:** The median/mean follow-up time was 11.0/11.7 months. The estimated median PFS and OS were, respectively, 9.6 months and 11.6 months. Since all MTV and TLG parameters were highly correlated ($p < 0.0001$) only TLG-based parameters were used for subsequent analyses. In the univariable analyses there was a significant correlation among OS and wbTLG (HR=1.001; 1.000-1.001; $p=0.0361$) and wbTLG/tuTLG (HR=1.705; 1.232-2.362; $p=0.0013$). On multivariable analysis only wbTLG/tuTLG independently correlated with OS (HR=1.660; 1.193-2.310; $p=0.0027$). None of the other tumor burden parameters (wbSUV, tuSUV, tuMTV, tuTLG, wbSUV/tuSUV, wbMTV/tuMTV) or sex, age, performance status, histologic subtype, TNM stage and treatment types) correlated with PFS or OS in advanced NSCLC. **Conclusion:** The relation between whole-body TLG and primary tumor TLG (wbTLG/tuTLG) is an independent prognostic indicator of OS in advanced (stage III and IV) NSCLC. This ratio is stronger than the determination of primary tumor TLG or whole-body TLG in patients with advanced NSCLC. More patients are necessary to confirm our findings.

EP-0537

Role Of ^{18}F FDG PET/CT In Patient Scheduled To Undergo Radical Surgical Resection In Mesothelioma

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Introduction: Mesothelioma is a rare form of cancer. In patients scheduled to undergo radical surgery, a distinction between M0 and M1 tumours is critical in determining possible resectability. The use of FDG-PET to identify metastatic disease or nodal metastases may change patient stage with the potential of

changing treatment management. **Objective:** The aim of our study was to investigate the clinical value of ^{18}F -FDG PET/CT in initial staging of patients with mesotheliomas and its role in the detection of distant lesions that contraindicate radical surgical treatment. **Material and Method:** We retrospectively analysed 15 patients who underwent PET/CT scans from January 2011 to November 2017 as part of the initial staging of a confirmed mesothelioma, where radical surgical treatment was intended. Twelve patients were men (80%). Mean age was 62.9 ± 8.9 yr. Scans were performed 60 minutes after the injection of 4.07 MBq/Kg ^{18}F -FDG. **Results:** PET/CT detected local lesions in 100% of patients. It also detected distant metastases or loco regional involvement in 33 % of patients ($n = 5$). In 3 of them (60%) PET/CT showed distant lymph nodes and bone metastases. In 1 patient (20%) PET detected contralateral pulmonary nodules and bone lesions and in the other patient PET demonstrated extension to the peritoneum. **Conclusion:** ^{18}F -FDG PET/CT upstaged one third of the patients referred for initial staging, avoiding the performance of a highly morbid surgery and allowing a better and earlier treatment plan.

EP-0538

Is a dedicated hybrid lung SPECT/CT camera necessary for pre-interventional quantification of relative lobar lung function?

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Purpose: In patients suffering from lung cancer calculation of relative lung function using perfusion scintigraphy is an established tool to predict post-interventional lung function. Published data has proven the superiority of 3D vs. planar imaging. Data from hybrid SPECT/CT-scanners allow for registration of the low dose CT to the diagnostic CT since a diagnostic CT is used as the best basis for anatomical lobe delineation. Due to still limited availability of dedicated SPECT/CT-cameras, the aim of the study was to test whether - using of a suitable software algorithm and a diagnostic CT - the quantification of perfusion data from SPECT-cameras is as exact as from SPECT/CT-scanners. **Methods:** 61 patients with lung cancer were referred to routine V/P-SPECT/CT with Technegas and $^{99\text{m}}\text{Tc}$ -MAA before surgery. Quantification of the perfusion SPECT data was performed using the software "HERMES Hybrid 3D-Lung Lobe Quantification". In setting A (hybrid approach) perfusion SPECT data and a combination of a coregistered low-dose CT and diagnostic CT were used for quantification, in setting B (non-hybrid approach) only perfusion SPECT data and the diagnostic CT were utilized. Correlation analyses of the resulting relative lobar perfusion between both approaches were performed, additionally processing time was compared. **Results:** 305 lobes were quantified with both approaches. Evaluation time was 6:37 min (hybrid) versus 6:34 min (non-hybrid). Lobar values ranged from 0-55% for hybrid and from 0-58% for the non-hybrid approach, no significant differences were found ($p > 0.9$). Correlation was excellent for both approaches with $R=0.984$ and a slope of the regression line of 1.001 ($p < 0.0001$). **Conclusion:** No relevant dif-

ferences for CT based 3D-quantification of relative lung perfusion in pre-interventional patients with lung cancer were found between approaches comparing a hybrid and a non-hybrid strategy. Using sophisticated software and the generally available diagnostic CT reliable results can be obtained from conventional SPECT-data.

EP-0539

Metabolic and metastatic characteristics of EGFR mutation positive lung adenocarcinoma on FDG PET/CT

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Background: many noninvasive methods have been explored to determine the gene status of the epidermal growth factor receptor (EGFR). However, imaging features related to EGFR mutation positive gene status in adenocarcinoma are still unknown. We evaluate the parameters measured by [18F] fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) might help predict EGFR mutation positive gene status in lung adenocarcinoma. **Methods:** 117 patients with EGFR mutation positive and pretreatment PET/CT between January 2016 and February 2018 were reviewed. Genotyping, abundant genes and metabolic parameters including SUVmax, SUVmean, SUVpeak, SULmax, SULmean, SULpeak, MTV, TLG were evaluated. Statistical significance was assumed at $p < 0.05$. **Results:** the metabolic parameters including SUVmax, SUVmean, SUVpeak, SULmax, SULmean, TLG in EGFR-mutant adenocarcinoma correlates with the genotyping (the p values are 0.005, 0.019, 0.035, 0.025, 0.017, 0.043, respectively). In contrast, no relationship was noted between abundant genes and metabolic parameters. Meanwhile, both the genotyping and abundant genes correlates with the brain metastasis. While, no relationship was noted between them and lymphatic metastasis, bone metastasis, pulmonary metastasis. In conclusion, the genotypings of EGFR-mutant adenocarcinoma patients showed significantly correlations with the metabolic parameters of PET/CT. EGFR-mutant gene characteristics could provide more information for the brain status.

EP-0540

Evaluation of solid pulmonary nodules with dual time point 18F-FDG-PET/CT. Preliminary data

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Purpose: Solid pulmonary nodules (SPN) are one of the major indications for performing PET/CT examination, with high accuracy in characterizing nodules >1 cm as benign or malignant. However smaller nodules, as well as well differentiating and specific histologic types that accumulate FDG in a less degree and inflammatory processes can provoke differential diagnostic problems and lead to further unnecessary examinations. In this study we examined the possible role of delayed PET acquisition

in addition to standard PET in characterizing SPN. **Method- Material:** 17 patients, 7 female average 54y.o., 10 male average 66y.o. were included in the study. 8 presented with SPN ≤1 cm, 6 with SPN 1-2 cm and 3 with SPN >2 cm. 60 min after the IV administration of 18F-FDG PET/CT was performed at a Siemens LSO Biograph PET/CT device. 60 min after the first acquisition, delayed data of pulmonary fields were acquired. The size of the nodule, the uptake of the radiopharmaceutical (SUVmax) at the first and delayed acquisition were evaluated. For all patients histologic confirmation or 6 month surveillance was available. **Results:** In 8 patients with SPN ≤1 cm, mean first SUVmax was 1.7 and mean delayed SUVmax 2.1. 1 nodule did not accumulate FDG at both first and delayed images and proved benign. 1 nodule presented with SUVmax 1.2 at first and 1.5 at second PET, however due to morphologic characteristics of the nodule, the patient was put under surveillance and no further therapeutic action was taken. For 6/8, the delayed SUVmax was higher than the first, with increase 1-1.38 folds and the final diagnosis was adenocarcinoma. In 6 patients with SPN 1-2 cm, mean first SUVmax was 1.97 and mean delayed SUVmax 2.75. In 2 cases delayed SUVmax decreased and patients were put under surveillance, while in the rest 4 delayed SUVmax increased by 1.2-1.9 folds. Final diagnosis for these 4 patients was neuroendocrine tumor for 2 and adenocarcinoma for 2. In 3 patients with SPN >2 cm, mean first SUVmax was 4.8 and mean delayed SUVmax 6.1, raise of 1.28-1.48 folds and final diagnosis was adenocarcinoma. Degree of SUVmax alterations was not correlated with the grade; however this is justified considering the low tumor volume. **Conclusion:** Delayed imaging can contribute to the differential diagnosis of SPN, particularly in small <1 cm pulmonary nodules and in further management of the patients. Although morphologic appearance of the nodule should not be overlooked, increase of FDG uptake is correlated with malignancy, while decrease with benign condition.

EP-0541

Comparison of Dual Energy CT and FDG PET/CT Parameters in Newly Diagnosed Lung Cancer Patients

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Purpose: We assessed the correlation of dual energy CT (DECT) and 18-F FDG PET / CT parameters in patients with lung cancer. **Materials and Methods:** Sixty-eight newly diagnosed and untreated lung cancer patients (58 NSCLC 10 SCLC, 63 man, 5 women, mean age, 64.49 ± 9.25 [standard deviation]) were included. DECT and FDG PET/CT parameters [iodine content (IC) [mg/dL] (maximum iodine content (ICmax), mean iodine content (ICmean) SUVmax, SUVmean, SULpeak] were measured. We also evaluated the correlation between normalized IC, (NIC), [Lesion IC/Aorta ICmean] and normalized SUV (NSUV) [Lesion-SUV /Aorta SUVmean] values. The mean study interval between

FDG PET/CT and DECT was less than 15 days. Statistical analyses were performed using SPSS 19. Pearson correlation was used to analyze between DECT and FDG PET/CT parameters. **Results:** We couldn't find any correlation between SUVmax and ICmax ($r=0.049$, $p=0.7$), SUL peak and ICmax ($r=0.074$, $p=0.5$), SUV mean and ICmean ($r=-0.18$, $p=0.8$). Also there was no correlation between normalized values, between NSUVmax and NICmax ($r=-0.004$, $p=0.9$), NSULpeak and NICmax ($r=0.003$, $p=0.9$), NSUVmean and NICmean ($r=-0.109$, $p=0.4$). We categorized patients into groups as NSCLC and SCLC, but we couldn't find different results. **Conclusion:** In our study, we could not find any correlation between DECT and FDG PET/CT parameters. DECT shows contrast enhancement and perfusion, while FDG PET/CT shows glucose metabolism. Tumor perfusion and glucose metabolism are different physiologic processes. The clinical contributions of these two imaging modalities are different.

EP-0542

Comparison of SPECT/CT to planar based pulmonary lobar perfusion fraction for pre-operative assessment of relative pulmonary lobar function.

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Purpose: Quantification of relative pulmonary lobar perfusion fractions is widely performed prior to pulmonary surgery to provide pre-operative assessments of lung function. Although quantification using planar scintigraphy is often the standard, SPECT/CT quantification may also be used to assess pulmonary function. The objective of this study is to evaluate the difference in relative lobar perfusion fractions when using 3D anatomically based definitions of lung lobes compared to geometrical-based definitions from planar scintigraphy. **Methods:** Technetium-99m SPECT/CT images were collected for five patients, and a semi-automatic segmentation method (SectorAssist™, MIM Software Inc) was used to define the lung lobes on the CT. The 3D SPECT/CT images were used to create 2D projection images to simulate planar lung perfusion images. Whole lung contours were transferred directly from the SPECT/CT to the projected planar images and then split horizontally into lobes. Relative pulmonary lobar perfusion fractions were compared between the 3D and 2D quantification methods. Mean values and absolute differences between the two methods were calculated for each of the lobes and compared with a t-test. **Results:** The mean absolute differences between the 3D and 2D quantification of pulmonary lobe perfusions were as follows, Right Upper Lobe with 6.5%, Right Middle Lobe with 17.4%, Right Lower Lobe with 11.2%, Left Upper Lobe with 3.7%, Left Lower Lobe with 3.5%, Whole Right Lung with 0.5%, and Whole Left Lung with 0.5%. There were significant differences ($p < 0.05$) between the 3D SPECT/CT and 2D planar methods for the right upper, middle and lower lobes. **Conclusion:** Variations in lobar perfusion fractions have the ability to dramatically impact the surgical approach or patient eligibility for lung surgery. The results demonstrate that there can be a significant difference between the results from SPECT/CT and planar images. Semi-automated methods for defining lobes on CT scans allow for the potential

for SPECT/CT to replace planar images for relative pulmonary lobar function assessment.

EP-0543

Single Centre Feasibility Study Exploring The Reproducibility Of Lung Nodule Volumetry In PET/CT Compared To Conventional CT Imaging

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Purpose: To evaluate the reproducibility of pulmonary lung nodule volumetry between PET CT and conventional CT imaging. **Subjects & Methods:** All patients with solid lung nodules who underwent a lung biopsy at a single centre between May 2016 and January 2017 were identified retrospectively. Patients with contemporaneous PET/CT and CT chest imaging were identified (defined as within 28 days of each other). Patients were excluded if the lung lesion was greater than 3cm in size. Using the inspiratory axial dataset, solid pulmonary nodules reported on the CT report were identified. Nodule size was evaluated using the semi-automated Picture Archiving Communication System (PACS) segmentation tool which requires the clinician to place a "seed point" within the lesion of interest. Corresponding nodules were identified on PET/CT images and volumes were similarly calculated. Differences in lung nodule volume and longest axial dimension between PET/CT and conventional CT imaging were compared using Pearson correlation, paired t-test and Bland-Altman statistics. **Results:** A total of 35 patients were included in final analysis. Of these the PACS software was unable to segment the lung nodule on CT images in 14 patients (40%). The volume segmented was not visually concordant between PET/CT and CT images in 2 patients (6%). 22 lung nodules identified in 19 patients were included for statistical analysis investigating concordance in volume and longest axial dimension. PET/CT and CT demonstrated good linear correlation and we did not find any statistically significant difference in values for nodule volume ($r=0.98$, $p=0.057$) or longest axial dimension ($r=0.93$, $p=0.44$). The variability in lung nodule volume and longest axial dimension as determined by PET/CT compared to CT ranged from -1119 to +1768 mm³ (-54 to +89%) and -5 to +4 mm (-29 to +24%) respectively. **Conclusion:** Volumetry as determined by the semi-automated segmentation tool on PET/CT when successful (54%) demonstrates good correlation and agreement with that of conventional CT imaging. However, there is substantial variation between PET/CT and CT in both nodule volume ($\pm 90\%$) and longest axial dimension ($\pm 30\%$). Whether such variability is acceptable depends on clinical context.

EP-0544

Correlation Between Histological Architecture On Biopsy And 18F-FDG PET-CT Findings In Primary Lung Adenocarcinoma

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Introduction: Lung cancer is the leading oncological cause of death worldwide. Histological subtype is known to be an important prognostic indicator in lung adenocarcinoma. The order of clinical prognosis from most to least favorable is: lepidic, papillary, acinar, solid and micropapillary. Here, we aimed to explore any potential relationship between lung adenocarcinoma histological subtype as determined on biopsy and the maximum standardized uptake values (SUVmax) within the malignant lesion on 18F-FDG PET-CT imaging. **Subjects & Methods:** All patients at a single center who underwent a lung biopsy diagnostic of a primary lung adenocarcinoma between January 2015 and August 2017 were identified retrospectively. The full histological biopsy reports were screened by a clinician for the identification of any specific architectural subtype within the biopsy sample. Biopsies which specified histological architecture were categorized into 3 groups: lepidic (lepidic only architecture), lepidic mixture (a lepidic component in combination with any other histological architectures) and non-lepidic (any histological architecture or combination thereof without a lepidic component). SUVmax values for each biopsied lesion were extracted from contemporaneous ¹⁸F-FDG PET/CT imaging. Mann-Whitney U analyses were used to assess the association between SUVmax by histological category. **Results:** 128 biopsy samples were included for final analysis (40 lepidic, 29 lepidic mixture and 59 non-lepidic). Across all samples median SUVmax was 9.3 (interquartile range: 2.9–11.6). In pairwise analyses, SUVmax were significantly lower in lepidic biopsies compared to lepidic mixture biopsies (2.6 vs 5.6, $p < 0.001$), and non-lepidic biopsies (2.6 vs 11.0, $p < 0.001$). **Conclusion:** In this retrospective analysis, we demonstrate a statistically significant association between lung adenocarcinoma histological subtype as identified on lung biopsy and SUVmax values on PET/CT imaging. SUVmax may be a potential predictor of lung adenocarcinoma histology and as a corollary may provide an indication of clinical prognosis.

EP-0545

Clinical and prognostic impact of restaging 18F-FDG PET/CT in SCLC: a multicentric study

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Purpose: The aims of the study were to 1) assess the impact of 18F-FDG PET/CT on the prediction of the overall survival (OS), 2) evaluate the agreement between 18F-FDG PET/CT and CT for the detection of metastatic lesions and 3) compare metabolic data in smokers and non-smokers, in a cohort of patients affected by small-cell lung cancer (SCLC). **Materials and Methods:** 108 patients were evaluated from a multicenter database (median age 64 years, range: 45–86; M:F=2.8). All patients underwent 18F-FDG PET/CT for restaging purposes after pathological confirmation of SCLC. Clinical information including smoking history, PET/CT and contrast enhanced CT findings (performed within 1 month from each other) were recorded. OS was assessed by means of Kaplan-Meier curves. The diagnostic agreement between the imaging modalities was evaluated by comparing the number of metastatic lesions detected by each modality on a patient-based analysis. Mann-Whitney Test was used to compare metabolic parameters [i.e. MTV, TLG and SUVratio (SUVmax/SUVmax blood pool)] between smokers and non-smokers. **Results:** After 5 years follow-up, 74% of patients (n=91) were dead. Patients with metastatic lesions at PET/CT showed a significant shorter OS than the counterpart ($p=0.02$). In 28/108 patients who underwent both PET/CT and CT, the overall agreement was 64%; in 5 cases PET detected more metastatic lesions than CT, whereas in 5 cases depicted less lesions. TLG, MTV and SUVratio resulted significantly higher in patients with no-smoking history ($p < 0.05$), despite they showed a longer OS (respectively, 40.8 ± 31.22 months for non-smokers and 14.62 ± 12.54 months for smokers). **Conclusions:** Metastatic detection at PET/CT has a strong influence on OS of patients with SCLC. FDG PET/CT and CT seem to be complementary imaging modalities in patients with metastatic SCLC. Nevertheless, PET/CT allow the evaluation of different metabolic in smokers vs. non smokers subjects; further investigations, possibly on a larger cohort of subjects, could explain those relevant biological features influencing the survival of SCLC patients with no-smoking history by means of PET/CT.

EP-0546

Quantitative and anatomical assessment of lung perfusion with ^{99m}Tc-MAA SPECT/CT in emphysema and lung cancer patients

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Purpose/Introduction: Predicting the postoperative lung function is critical in assessing patient's operability prior to lung resection. A current practice is to use planar (2D) lung perfusion scan and spirometry to predict the post-surgical outcome. The aim of this single centre, prospective, cohort study is to assess and compare the accuracy, reproducibility and potential clinical value of quantitative lung perfusion SPECT/CT over

the 2D method. **Subjects & Methods:** Patients with suspected/known lung cancer or with advanced emphysema were referred for preoperative lung perfusion scan and spirometry. Planar and SPECT/CT images were acquired immediately after ^{99m}Tc -labelled macroaggregated albumin (^{99m}Tc -MAA) administration (Intevo, Siemens). Regional lobar perfusion (%) was assessed by two observers with the 3D-anatomical quantitative method (CT Pulmo 3D and xSPECT-Quant, Siemens) and compared to the established 2D-projection method using Student's matched-pair t-test. The accuracy of measurement was tested against computational and physical anthropomorphic chest phantom. The interobserver variability was assessed using Pearson, Bland-Altman and intraclass correlation methods. Effect of respiratory motion on quantification was tested using gated list-mode SPECT data. **Results:** Among the 106 patients enrolled from 10/2016 to 10/2017 (67.8 ± 10.2 years old), 40 were women, 66 men; 61 were referred for suspected or proven lung cancer, 38 for severe emphysema and 7 for other indications. As expected, the left-to-right split function was similar, however, at the lobar level, there was a very significant measurement difference between the 2D and the 3D method. Compared to 3D, 2D systematically underestimated the regional perfusion of the upper lobes (negative bias) and consistently overestimated it in the lower lobes (positive bias). Absolute mean bias [$\pm$ uncertainty at 95% confidence]: $-30\% \pm 8$ and $-33\% \pm 7$ for the left and right upper lobes and $+25\% \pm 4$ and $+19\% \pm 4$ for the left and right lower lobes, respectively ($p < 0.001$). The mean absolute difference of lobar perfusion (measured in %-point of the total perfusion) between reader 1 and 2 was $0.7\% \pm 0.2$ ($r^2 = 0.972$, $p < 0.001$) and $4.1\% \pm 0.5$ ($r^2 = 0.743$, $p < 0.001$), while the pooled intraclass correlation coefficient ICC(2,1) was 0.99 ± 0.01 and 0.86 ± 0.03 for the 3D- and 2D-methods, respectively, $p < 0.001$. **Discussion/Conclusion:** 3D Quantification of lung perfusion is feasible in clinical practice, more accurate at the lobar level and shows superior interobserver agreement compared to the routinely used 2D-method. Further prospective clinical studies are warranted to validate its clinical value and impact on management.

EP-0547

Patient characteristics of unexpected N2 stage lung cancer by CT & PET/CT

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Introduction: Clinical nodal staging is important in non-small cell lung cancer patients, which can make decision of lung operation. Conventional CT & PET/CT are well-known modality for staging non-small cell lung cancer. Sometimes, unexpected mediastinal lymph node metastasis is found in operation field, without any evidence of imaging modality. The aim of this study is find out patient characteristics of unexpected N2 stage lung cancer by CT & PET/CT. **Methods:** We enrolled 152 lung cancer patients, who registered chest surgery division of Chungnam national university hospital in 2006-2017. All the patient underwent both contrast-enhanced chest CT & PET/CT for lung cancer staging. All the patient was pathological-

ly confirmed for mediastinal lymph nodes in operation field. **Results:** A total of 13 of the 152 patients were found to have mediastinal lymph node metastasis. Primary mass maximum standardized uptake value, long axis diameter, short axis diameter is 10.4 (range : 5.1-17.4), 4.2 (range : 2.2-6.2cm), 3.0 (range : 2.0-4.7cm), respectively. Pathologic type of N2 patients was 10 adenocarcinoma (4 papillary type, 2 acinar type, 4 mixed type), 2 adenosquamous carcinoma, and 1 squamous cell carcinoma. 2 of 13 patients shows increased glucose metabolism in mediastinal lymph nodes, with internal calcification. **Conclusion:** We found the characteristics of unexpected N2 patients in non-small cell lung cancer. Unexpected N2 patients shows high SUVmax, higher 2cm size, and adenocarcinoma-dominant pathologic type. For further evaluation, subgroup analysis is needed.

EP-0548

FDG PETCT in DIPNECH

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Introduction: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a possible pre-malignant invasive condition. Patients with solitary pulmonary nodules undergo ^{18}F -fluoro-deoxy-D-glucose (FDG) positron emission tomography combined with computed tomography (PETCT) scanning. Multiple case studies have described DIPNECH lesions with variable FDG uptake. Our aim was to investigate the FDG PETCT appearance of multiple DIPNECH lesions in patients with pathologically confirmed disease with FDG PETCT scans performed prior to resection. **Method:** A retrospective study of patients presenting with pathological confirmed DIPNECH on resection for FDG positive lung nodules were studied. We present preliminary data of the first 4 patients. Detailed analysis of all identifiable pulmonary nodules was performed with recording of the position in the lung (lobe, segment and aspect), size, shape and character on the non-breath-hold CT component of the PETCT. The presence or absence of FDG uptake on the CT attenuated corrected images (CTAC) PETCT images with ultra-high definition (ultra HD) reconstruction was recorded, guided by the co registered imaging, taking into account any respiratory mis-registration. **Results:** Three female and one male patient were investigated with age range 65-71 years. A total of 91 nodules were seen in the four patients. The mean size of the nodules recorded was 8mm (range 3-50mm, mode 5mm). The FDG uptake was measured in those lesions with qualitatively identifiable FDG on the CTAC lung images on the PET and coregistered images. We recorded the maximum standardised uptake value adjusted for body weight (SUV max). The mean SUV max for the identified nodules was 3.2 (range 0.9-7.2, standard deviation 2.2, mode 1.4). The relationship between the size of a nodule and its FDG uptake was established using scatter plot and Spearman coefficient rank and this showed a value of 0.86. **Conclusion:** We demonstrate detectable FDG uptake in all presumed lesions measured over 10 mm in size. Our literature search demonstrated only case studies, describing variable uptake in DIPNECH with common assertion that DIPNECH is a generally FDG neg-

ative pathology. We show that DIPNECH is a reliably FDG positive pathology when large enough and only size limits the detectable nature of the FDG uptake. A limitation of our study is that we have selected FDG positive resected disease, but the consistent appearance and correlation of size/SUV max in the remaining and stable underlying and variable sized focal lung lesions would still support our hypothesis.

EP-43

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology ->
Melanoma, malignant

EP-0549

Role Of 18 F FDG PET/CT In Anorectal Melanoma

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Purpose: To evaluate diagnostic role of 18 F FDG PET/CT in initial staging and restaging of anorectal melanoma. **Subjects and Methods:** This was a retrospective observational study, patients for initial staging and with clinical or radiological suspicion of disease recurrence referred for PET/CT from Jan-2006-Dec-2016, were included in the study. Diagnostic performance of PET/CT was evaluated for baseline staging and disease recurrence. Any area with intensity greater than background that could not be identified as physiological activity on PET images or which on CT correlation did not fit into benign (infective/inflammatory/degenerative) was considered to be suggestive of tumor on the PET study. PET/CT findings were correlated with histopathology results. When tissue diagnosis was not available, clinical or radiological follow-up was used as reference standard.

Results: Total 61 patients who were referred for initial staging were included. PET/CT correctly detected primary lesion in 57 cases (93.44%), regional nodes in 46 cases (75.4%), non-regional nodes in 22 cases (36%) and distant metastases in 25 cases (41%). PET/CT was false negative in 2 cases which on surgical histopathological report revealed submucosal anorectal lesion. The sensitivity, specificity, positive predictive value, negative predictive value for primary lesion, regional nodes, non-regional nodes and distant metastases were 96.61%, 100%, 100%, 50%; 97.87%, 100%, 100%, 93.33%; 100%, 100%, 100%, 100% and 100%, 100%, 100%, 100% respectively. Total 24 patients were included for suspected recurrence/restaging. All the patients were treated previously by surgery, radiotherapy, or chemotherapy. PET/CT detected disease recurrence in 20 patients (83.3%). 10 patients had recurrence at the primary site, 8 of whom also had distant metastases and 2 had only loco-regional metastatic nodes. In remaining 10 patients, there was no primary site recurrence, however, 2 patients had loco-regional nodal and distant metastases while 8 patients had only distant metastases. Histopathological confirmation was available in 6 patients whereas imaging and clinical follow-up confirmed recurrence in remaining patients. PET/CT was negative for recurrence in 3 patients. PET/CT was false negative in 1 patient

which missed liver metastasis. Sensitivity, specificity, positive predictive value and negative predictive value of PET/CT was found to be 95%, 100%, 100%, 75% respectively with accuracy of 96%. **Conclusion:** 18 F FDG PET/CT demonstrates high diagnostic accuracy in the initial staging and detection of recurrent disease in cases of anorectal melanoma. Therefore, we strongly recommend 18 F FDG PET/CT, a whole body imaging modality, to be performed in such cases.

EP-0550

Role of ^{99m}Tc - α -MSH Scan in Diagnosis of Malignant Melanoma

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Purpose/Introduction: As the metastatic melanoma has very poor outcome with less than one year average survival after metastatic dissemination, it is highly important to diagnose this malignancy in early curable stages. While in vitro and in vivo animal studies using radiolabeled α -MSH are very promising, there is no human study to address the detectability rate of this new imaging technique. This study is aimed to determine the diagnostic value of ^{99m}Tc - α -MSH in malignant melanoma. **Subjects & Methods:** 21 patients were included in this prospective study. 20-30 mCi of ^{99m}Tc - α -MSH was administered intravenously and whole body scans were performed in anterior and posterior projections, 20min, 2h and 4h post injection with a dual-head gamma camera equipped with a LEHR collimator using a 256×1024 matrix centered on 140 keV with 20% window. Both qualitative and semi-quantitative assessments were done. The gold standard was pathology in addition to patient's conventional imaging results. **Results:** No minor or major side effects was seen after ^{99m}Tc - α -MSH application. Foot was the most common location of primary tumor constituted of twelve out of 21 primary locations following with scalp, hand, eyelid, nasal mucosa, arm and trunk. The sensitivity, specificity, NPV and PPV were 75%, 80%, 50% and 92% for primary lesion and 25%, 100%, 68% and 100% for distant metastasis, respectively. **Conclusion:** Our preliminary results are promising to suggest this targeted imaging modality as a new complementary method in management of malignant melanoma showing a high sensitivity with this modality in primary lesions as well as lymph node involvements. We recommend further evaluation on diagnostic value of ^{99m}Tc - α -MSH with larger patient population and a head to head comparison with ^{18}F -FDG PET/CT in future studies.

EP-0551

Benign lymphoid tissue changes as response to immunotherapy in metastatic melanoma patients: an ^{18}F -FDG PET/CT study

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Aim: Owing to their unique anti-cancer mechanism, partly involving cytokine release by activated T cells, immunotherapeutic agents are associated with cumulative, dose dependent, immune-related adverse events (irAEs). An association between irAEs and the clinical benefit of immunotherapeutic agents has been suggested. We aimed to evaluate lymphoid tissue changes in response to immunotherapy in metastatic melanoma and in correlation with the patients' best clinical response (BCR). For this reason the glucose metabolism in the mediastinal and hilar lymph nodes as well as in the spleen was studied by means of dynamic ^{18}F -FDG PET/CT in a group of metastatic melanoma patients receiving ipilimumab. **Materials and Methods:** 41 metastatic melanoma patients receiving ipilimumab were enrolled in the study. ^{18}F -FDG PET/CT scans were performed before the start of ipilimumab treatment (baseline PET/CT), after two cycles of treatment (interim PET/CT) and at the end of treatment after four cycles (late PET/CT). Data analysis was focused on the mediastinal and hilar lymph nodes and the spleen. The lymph nodes were evaluated visually/qualitatively. Spleen glucose metabolism was assessed by means of semi-quantitative evaluation, based on standardised uptake value (SUV) calculations, and quantitative analysis of the dynamic ^{18}F -FDG PET data based on two-tissue compartment modelling. Patients' best clinical response (BCR) was assessed at a median of 21.4 months (range: 6.3 - 41.9 months) and used as reference. **Results:** According to the BCR reference, 31 patients showed disease control (DC) and 10 patients showed progressive disease (PD). Qualitative evaluation of the mediastinal/hilar lymph nodes revealed that 3 patients in the interim PET/CT (7.3%) and 3 patients in the late PET/CT (7.3%) demonstrated a sarcoid-like lymphadenopathy as response to treatment (LN-positive). All patients classified as LN-positive responded to ipilimumab therapy with DC. Regarding spleen glucose metabolism, linear mixed model analysis revealed no statistically significant differences between the DC and PD groups regarding both semi-quantitative ($\text{SUV}_{\text{mean}}/\text{SUV}_{\text{max}}$) and quantitative ($V_{\text{g}}, K_1, k_3, K_2, \text{FD}$) baseline spleen-related parameters. Moreover, no significant changes took place in each group as response to treatment. **Conclusion:** Based on our findings, 7.3% patients in the interim and late PET/CT showed a sarcoid-like reaction as response to treatment. All these patients showed DC according to the BCR reference, supporting the described association between incidence of irAEs and the clinical

benefit of anti-CTLA-4 therapy. On the other hand, our results show a poor performance of quantitative ^{18}F -FDG PET analysis of the spleen in predicting clinical benefit to ipilimumab.

EP-0552

^{18}F -FDG PET/CT longitudinal studies in patients with advanced metastatic melanoma for response evaluation of combination treatment with vemurafenib and ipilimumab

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Aim: To assess the role of ^{18}F -FDG PET/CT in evaluation of the clinical response in the combination treatment of vemurafenib and ipilimumab in a group of 16 BRAF-positive, metastatic melanoma patients with very advanced disease (AJCC stage IV). **Materials and Methods:** After clinical improvement under vemurafenib monotherapy in most patients, four cycles of ipilimumab were additionally administered. Whole-body ^{18}F -FDG PET/CT was performed before the start of the combined ipilimumab/vemurafenib treatment, after two cycles of combined treatment, as well as after completion of the combined administration. The patients' best clinical response after completion of the combined treatment was used as reference. PET/CT-based response evaluation to combination treatment was performed according to the European Organization for Research and Treatment of Cancer (EORTC) 1999 criteria for PET as well as the recently proposed PET Response Evaluation Criteria for Immunotherapy (PERCIMP). **Results:** According to their best clinical response, the patients were classified in two groups: those showing clinical benefit (CB) including stable disease, partial response and complete response (8 patients), and those showing no clinical benefit (no-CB) including progressive disease (8 patients). Similar to the best clinical response-based classification, the patients were dichotomized in two groups based on the PET/CT findings: those showing metabolic benefit (MB), including patients with stable metabolic disease (SMD), partial metabolic response (PMR) and complete metabolic response (CMR), and those demonstrating no metabolic benefit (no-MB), including patients with progressive metabolic disease (PMD). In total, 13/16 patients (81.3%) were correctly classified by EORTC, while 15/16 patients (93.8%) were correctly classified by PERCIMP. Eight patients had PET/CT findings of newly emerging, immune-related adverse events (irAEs) as response to combined treatment, with colitis and arthritis being the most frequent ones. Interestingly, seven of these patients showed CB. **Conclusion:** ^{18}F -FDG PET/CT is a valuable tool for stratification of patients receiving combination treatment of vemurafenib/ipilimumab into responders and non-responders. Interestingly, the appearance of irAEs might correlate with benefit to immunotherapy and lead clinical decision to discontinue targeted treatment.

EP-0553

Role of SPET/CT in radio-guided research of Cutaneous Melanoma patients with unexpected sentinel nodes

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Aim: one of the main prognostic factor in Cutaneous Melanoma (CM) is the lymph nodal metastasis. Lymphoscintigraphy is the most important investigation allowing the study of lymphatic drainage pathways, not always predictable. It detects the sentinel node, intended as the first lymph node (LN), located in a basin receiving lymphatic fluid from a specific cutaneous region. These basins can be in “classic” or in “unexpected” regions. Some authors proposed the nomenclature of “interval” LN, intended as LNs identified between the cutaneous region and the “classic” basin, and they have demonstrated that the “interval” LNs have the same chance of being the site of metastatic invasion as in classic basins. The aim of this study is to evaluate the role of SPET/CT in identifying “unexpected” locations of sentinel nodes.

Materials: 128 patients (59 F and 69 M) underwent lymphoscintigraphy from April 2017 to April 2018. 99mTc- human serum albumin (Nanocoll, GE Healthcare, USA) was injected intra-dermal at the dose of 18-37 MBq in 0.2-0.4 ml. According to surgical time, one or two days protocol and site of injection, a dynamic acquisition followed by planar and SPET/CT was performed in all patients using Discovery NM/CT 670 Pro (GE Healthcare, USA). All patients has a confirmed histologic diagnosis of CM performed on the previous excision of suspected skin lesion.

Results: A total of 128 lymphoscintigraphy were performed. The sites of the lesions were as follow: back in 39 pts (30%), chest in 12 pts (9%), abdomen in 9 pts (7%), head and neck in 11 pts (9%), upper limbs in 19 pts (15%) and lower limbs in 38 pts (30%). Unexpected lymphatic drainage was detected in and 11 pts (9%) with final evidence of interval LNs. SPET/CT detected the exact location of all interval LNs. 13 lymph node biopsies performed in the 11 pts with interval LNs, resulted positive for metastatic nodal invasion in 3 of them. **Conclusions:** SPET/CT is an important tool for anatomically accurate detection of Sentinel Nodes in “unexpected” regions. SPET/CT images are better the planar ones, thank to the anatomic information, that can affect positively the LN's research and excision, improving at the same time operators' confidence.

EP-0554

Time to Procedure, Nuclear Imaging and Clinicopathological Characteristics as Predictive Factors for Sentinel Lymph Node Metastasis in Cutaneous Melanoma

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Objective: Sentinel lymph node (SLN) biopsy is widely accepted staging procedure for cutaneous melanoma patients who are at risk of clinically occult nodal metastases. Numerous predictive factors for regional lymph node metastases have been identified, however, few have been found to be reproducibly

significant. Time to procedure was also found to be predictive of SLN positivity but this was not confirmed in other studies. In our study, predictive factors for metastatic involvement of SLN were analyzed. An impact of time interval to procedure on the rate of SLN positivity was also explored. **Methods:** Data analysis was done in 407 cutaneous melanoma patients who underwent lymphoscintigraphy and SLN biopsy at our Institution from 2010 to 2017. To delineate the relation of each variable (demographical, time to procedure, clinical and pathological variables as well as the presence of in-transit nodes, number of draining basins and SLN localization on scintigraphy) with positive SLN status, we used univariate logistic regression with odds ratios representing effect size. **Results:** Metastatic involvement SLN was found in 78/396 (19.6%) patients. Detection rate was 97.3%. Time to procedure was not associated with higher SLN positivity rate ($p>0.05$). In univariate analysis, Breslow thickness ($p<0.001$), nodular histology ($p<0.001$), primary ulceration lesion ($p=0.003$), and lymphovascular invasion ($p=0.017$) were strongly correlated with SLN positivity as well as the gender ($p=0.04$). In multivariate analysis Breslow thickness was found to be only significant independent predictors of SLN status ($p<0.01$). The remaining variables, including SLN nuclear imaging characteristics were not significantly associated with SLN status ($p>0.05$). **Conclusion:** Time to procedure was not found to be associated with higher SLNB positivity rates. Breslow thickness was consistently found to be significant independent predictor of SLN status.

EP-0555

Evaluation of early response to immune checkpoint inhibitors by 18F-FDG PET/CT in nine patients.

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Purpose: Pembrolizumab (Opdivo) and nivolumab (Keytruda) are highly selective monoclonal antibodies against the programmed cell death receptor 1 (PD-1), recently approved for the treatment of patients with advanced or metastatic melanoma. ¹⁸F-FDG PET/CT has demonstrated very satisfying results in detecting melanoma metastases in general. The aim of the study was to evaluate the early response to anti-PD1 by using ¹⁸F-FDG PET/CT. **Materials and Methods:** In 9 patients (pts) suffering from unresectable metastatic melanoma, scheduled for anti-PD1 treatment, PET/CT scanning was performed before the start of treatment (baseline PET), after 1 to 4 cycles of treatment to evaluate early response. 5 pts treated by pembrolizumab and 3 pts by nivolumab. 3 early PET were realized after 1 cycle, 3 early PET after 2 cycles, one early PET after the 1st cycle and 2 PET immediately after the 4th cycle. The follow-up was realized by PET/CT, other imaging modality and clinical follow-up during 2 years. The evaluation of patient response to treatment

was based on the European Organization for Research and Treatment of Cancer EORTC 1999 criteria. **Results:** 4 patients had shown early partial metabolic response on early PET: 2 of them had complete remission on follow-up, 1 progressed then showed partial metabolic response, and 1 progressed and died. 3 patients showed progressive metabolic disease on early PET/CT which was confirmed later and the 3 patients died. 1 patient showed stable metabolic response then progressed and died. 1 patient had shown progression after 2 cycles then a complete metabolic response at 6 months on PET and during more than two years after beginning of the treatment (PET/CT was realized every 3 months). The early FDG PET/CT pattern was very suspicious of a pseudoprogression (wrongly classified by EORTC). **Conclusion:** Early ^{18}F -FDG PET/CT can help as a biomarker to evaluate the final treatment outcome in melanoma metastatic patients. In particular, the appearance of new lesions was predictive of progressive disease. The response evaluation of early ^{18}F -FDG PET/CT after anti-PD1 treatment should be investigated further in larger prospective series.

EP-0556

$^{99\text{m}}\text{Tc}$ -Tilmanocept. First experiences and practical approach in melanoma sentinel node biopsy in a two-day protocol

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Aim: Although approved for clinical use by FDA and EMA in 2013 and 2014, respectively, $^{99\text{m}}\text{Tc}$ -Tilmanocept has been introduced in European countries since mid-2017. The aim of this study is to describe our preliminary results with this “next generation” radiotracer in melanoma patients scheduled for sentinel node (SN) biopsy. **Materials & Methods:** We prospectively analysed 11 patients who underwent SN biopsy using $^{99\text{m}}\text{Tc}$ -Tilmanocept as radiotracer. Median age was 55 (range: 34–72). Mean Breslow thickness was 1.6 mm (range 0.8–3.7). Nine patients presented at least 1 mitosis/mm² (range 0–16). Four melanomas were located in thorax, 5 in lower limbs and the remaining 2 in head (scalp and right ear, respectively). All of them were injected with 50 microgr $^{99\text{m}}\text{Tc}$ -Tilmanocept with a median dose of 90 MBq (range 46–140 MBq) in a volume of 0.4 ml. After tracer injection, all patients underwent lymphatic mapping within 4h. Operating room procedure started after 21–25 hours of tracer injection (two-day protocol). A conventional hand-held gamma probe and a portable gamma camera were used to locate the SNs. **Results:** SN visualization was possible in all 11 patients. Dynamic study showed lymphatic channels in 7 out of 11 patients (63%). Early planar images (15–30 min after injection) visualized lymphatic ducts in 10 of 11 patients (91%) and at least 1 SN in all cases. Pre-operative images demonstrated 29 hot spots (2.6 per patient). During surgery, 22 SNs were retrieved, 5 were considered as second-echelon nodes and 2 were located in pelvic area and were not pursued. In our two-day protocol, when injected dose was below 90 MBq (3 patients), SNs showed low radioactiv-

ity during surgery, and therefore, time to intraoperatively locate them was higher. However, when dose was increased between 90–111 MBq, no detection problems were reported by surgeons and surgical time was shortened. There were no adverse events. The 2 cases in the head and neck area were positively rated by surgeons because the easiness to depict the nodes in this complex area. Although the surgery time was longer than in other areas, every SN was well depicted even when located near the injection site. **Conclusions:** $^{99\text{m}}\text{Tc}$ -tilmanocept successfully identified SNs in less than 30 minutes in our melanoma cases. However, its results can be hampered if a dose below 90 MBq is used in a two-day protocol. In our experience, although all cases were located, a slight dose increment allows a more comfortable procedure in operating room.

EP-0557

Which Melanoma 18F-FDG-PET Studies Should Include Lower Limbs?

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Introduction: To evaluate the utility of including lower limbs in the 18F-FDG-PET studies for the staging and follow-up of melanomas. **Subjects and Methods:** A retrospective and descriptive study was carried out, reviewing all 18F-FDG-PET studies of melanomas, both for staging and / or follow-up, performed in our center from November 2011 to December 2017. All of them included lower limbs. We assessed the presence of findings in lower limbs in relation with the primary tumor location, and if these findings produced modifications in the patient's management. **Results:** We reviewed 271 studies corresponding to 148 patients (77 men and 68 women), with an average age of 58.6 years, with diagnosis of melanoma (57 of 271 were located in the lower limbs). Of the 271 studies conducted, findings were found in the lower limbs in 33 of them (12.1%), changing the management of the patient due to recurrence or local dissemination in 7 studies (2.6%), corresponding to 4 patients. Of these 7 studies, 6 corresponded to a melanoma of the lower limbs, and 1 of them to a patient with metastatic inguinal adenopathies of unknown origin that turned out to be melanoma in the lower limbs. **Conclusion:** The results obtained in our center indicate that performing the full body on melanoma 18F-FDG-PET studies including lower limbs, provides relevant findings in patient management when the melanoma is located in the lower limbs. Because of that, our center only includes lower limbs in patients with melanomas located in this site.

EP-0558

How Previous Risk Factors in Malignant Melanoma Relate to the Result of Sentinel Lymph Node Biopsy

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Aim: To check that sentinel lymph node biopsy (SLNB) in melanoma is done according to the American Joint Committee on Cancer's recommendations and to assess the previous malignancy features of melanoma to relate them with the outcome of the SLNB. **Subjects & Methods:** We studied 65 consecutive patients, who underwent SLNB after exeresis and diagnosis of malignant melanoma in any location, all of them surveilled by the Tumors Committee from our hospital. They underwent SLNB between July 2015 and December 2017. We studied the mitotic index (≤ 1 vs > 1), ulceration (yes vs no) and Breslow thickness (thin ≤ 1 mm vs intermediate/thick > 1 mm) as dichotomous qualitative variables for their assessment as risk factors for lymph node metastasis in SLNB. **Results:** Of the 65 patients, 30 were men, 35 were women and they had an average age of 63. Only 7 out of the 65 (10.7%) patients studied didn't meet the requirements of thickness, mitotic index, ulceration and/or Clark proposed in the text of reference. Prevalence of metastasis in sentinel lymph node was 18.46% (12/65). All 12 patients with positive SLNB had intermediate or thick Breslow, 7 out of 11 had mitotic index over 1 and 5 out of 12 were ulcerated. After analysing the features of the melanomas as risk factors we obtained: in thin melanoma, no patient had a positive sentinel node (risk 0% IC95%: 0-17, 0/18 affected) while 25.53% (IC95%: 15.2-39.5) of intermediate/thick melanoma were affected (12/47), with statistically significant difference ($p < 0.3$). When analysing ulceration, we observed the risk of a positive outcome of the biopsy was 27.7% (IC95%: 12.5-50.8) (5/18) when the melanoma was ulcerated and 14.9% (IC95%: 7.4-27.7) (7/47) when it wasn't, without reaching statistical significance ($p = 0.4$). Melanomas with mitotic index ≤ 1 showed 16% (IC95%: 6.4-34.6) (4/25) of affected nodes, while those with mitotic index > 1 had 15% (IC95%: 9.5-34.2) (7/37). **Conclusions:** 1. The request for SLNB mostly complies with the requirements proposed by the American Joint Committee on Cancer (58/65). 2. Thin melanoma predicted a SLNB negative result (0% risk) in our population, although this might not be applicable to other populations. 3. Ulceration increases the chances of a positive SLNB, but not as strongly as thickness, we did not get statistically significant results. 4. Mitotic index isn't suitable for the prediction of the result of the biopsy, which is consistent with its removal as a staging criterion for T1 tumors.

EP-0559

FDG-PET/CT in the Evaluation of High-Risk Squamous Cell Carcinoma of the Skin

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Aim: Cutaneous squamous cell carcinoma (cSCC) is a common malignancy, especially in elder individuals with a history of sun exposure. Though usually indolent, certain high-risk factors (HRF) can determine a locally aggressive behavior, and even distant dissemination. This work aims to evaluate the role of FDG-PET/CT in assessing disease extension in patients with high-risk cSCC, and to correlate patients' outcome with metabolic activity of the lesions. **Material & Methods:** Retrospective evaluation of FDG-PET/CT studies performed in 29 patients (26 men, median age 79 years) with high-risk cSCC; 12 (41%) were referred for initial staging (IS) and 17 for recurring disease (RD). HRF analyzed were: size and location of the primary tumor, degree of differentiation (G), presence of perineural and vascular involvement, and immune status. We evaluated the ability of FDG-PET/CT to detect the primary lesion (if present), lymph node involvement (N) and distant metastasis (M), comparing image findings with histology or follow-up, and assessed the relationship between SUVmax and outcome. **Results:** Size of cutaneous lesions was 0.9-19 cm (median 3.5 cm). In 13/29 patients (45%) the primary lesion was in a high-risk area (H), 8 of whom were referred for IS. Among those referred for RD, 13 had a cutaneous relapse (7 in an H area). Four lesions were G1, 19 G2, 1 G2 with areas of G3, and 5 G3. Seven patients (24%) had perineural invasion, 1 (3%) had vascular involvement, and 7 perineural and vascular invasion; in one patient it could not be assessed. Immunologically, three patients had a concurrent chronic lymphocytic leukemia, one had a renal transplantation, and one an idiopathic thrombocytopenic purpura. FDG-PET/CT detected all present cutaneous lesions (17). Overall, 17/29 patients (59%) had N (6 at IS), and 5/29 (17%) M (2 at IS). Two patients did not have lesions at FDG-PET/CT. Sensitivity and accuracy of FDG-PET/CT was, respectively, 100% and 96.2%. During evolution, 5/12 IS patients (42%) relapsed (3-12 months), all with the primary in a H area. At follow-up (median 25 months), 8 patients are free-of-disease and 21 died (72%, 16 due to disease complications). In a per-patient basis, median SUVmax of the most hypermetabolic lesions in deceased patients was 13.8, and 7.5 in patients who are still alive. **Conclusion:** FDG-PET/CT is a sensitive technique to detect lesions in cSCC, identifying unsuspected sites of disease. Deceased individuals tend to have highly hypermetabolic lesions, though more patients are needed to establish a prognostic significance.

EP-0560

Sentinel lymph node detection in malignant melanoma - planar vs SPECT/CT technique

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Introduction: Sentinel lymph node (SLN) biopsy is a part of standard procedure in the evaluation of the status of the lymph nodes in early stage (N0, M0) malignant melanoma. Two techniques: planar (two dimensional) and SPECT/CT (three dimensional) are widely used for SLN detection. **Aim:** To compare the diagnostic value of planar vs SPECT/CT technique for SLN de-

tection. **Material and Methods:** 40 patients (13 females - 32,5% and 27 males - 67,5%), 50±19 years, staged T1b/T2 (1–4mm Breslow tumor size), N0, M0 were included. All patients were imaged with both planar and SPECT/CT study. **Results:** The detection rate was 100% with both modalities, but the planar technique detected 51 SLNs, and the SPECT/CT detected 68 SLNs. SPECT/CT detected additional drainage pathways in 11 (27,5%) patients. In 3 (7,5%) patients, positive SLNs were detected only with SPECT/CT technique. SPECT/CT presented better spatial resolution, better detection rate with deeper positioned SLNs and SLNs with lower radioactivity counts, attenuation correction and anatomic information (CT included). **Conclusion:** SPECT/CT technique presented statistically significant advantage over the planar technique in SLN detection in malignant melanoma.

EP-0561

A Meta-analysis To Evaluate The Diagnosis Value Of PET/CT Or PET And CT For Diagnosis Of Melanoma

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Aims: The study aims to perform a meta-analysis to compare the diagnostic performance of PET/CT or PET and CT in diagnosis of melanoma. **Methods:** Articles of PET/CT or PET and CT on melanoma published in English from January 1990 to September 2018 was searched in the PubMed, EMBASE, Cochrane Library, Web of Science, and EBSCO databases to identify eligible studies on PET/CT or PET and CT of melanoma. QUADAS was used to evaluate the methodological quality of the included studies. Pooled sensitivity, specificity, and diagnostic odds ratios (DOR) were calculated both on a per-patient basis and on a per-lesion basis. Summary receiver operating characteristic (SROC) curves were also drawn to obtain the area under curve (AUC) and Q* value. **Results:** Fifteen articles consisting of 30 studies were included in the analysis. On a per-patient basis, the pooled sensitivity of PET/CT (66%) was significantly higher than that of CT (58%), and the pooled specificity of PET/CT (92%) was markedly higher than that for CT (85%). **Conclusions:** This meta-analysis indicated that FDG PET/CT was better than CT on a per-patient basis for diagnosis of melanoma. Key Words: Melanoma, Positron emission tomography with computed tomography, Computed tomography, Meta-analysis

EP-44

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Other urological, malignant

EP-0562

Role of FDG-PET/CT in the detection of recurrence or residual disease in testicular neoplasms

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Aim: To assess the utility of FDG-PET/CT (PET) in the detection of recurrence or presence of residual disease in testicular neoplasms. **Material and Method:** Retrospective analysis of PET studies performed in 34 patients (17 seminoma and 17 NSGCT, median age 36 y.o.), with radiological / serological suspicion of recurrence or persistence of disease after treatment. We studied the location and metabolic activity of the lesions (PET+/PET-), its correlation with the serum levels of alpha-fetoprotein (AFP) and beta-HCG (B-HCG) and the subsequent follow-up of the patients. **Results:** Twenty-one patients (61%) were PET+, one of them false positive due to reactive lymph nodes. The tumor detection rate was slightly higher in patients with altered tumor markers (TM) (7/11, 63%) compared to those with normal TM (NTM) (13/23, 56%) and higher in patients with NSGCT (12/17, 70%) than in seminoma (9/17, 52%). In 17 patients the recurrence was lymphatic, in 1 visceral and in 3 both lymphatic and visceral. The median SUVmax of the lesions detected was SUVmax: 6.7 en NTM versus SUVmax: 4.5 in TM, and higher in patients with seminoma (SUVmax: 8) than in those with NSGCT (4.2). At the follow up, 27/34 patients (79%) were free of disease; 76% (16/21) of the PET+ and 92% (12/13) of the PET-. Only two of the PET- patients have subsequently presented recurrence (follow-up 9 to 51 months). The figures are similar in the groups of MT (81%, 9/11), NTM (82%, 19/23), seminoma (88%, 15/17) and NSGCT (76%, 13/17). Only one patient was exitus; a PET+ patient with NTM. **Conclusion:** In our preliminar study, FDG-PET/CT was useful for detection of recurrence or residual disease in testicular neoplasms, although there was no clear correlation between its performance and the alteration of tumor markers. Disease-free survival was high, especially in PET- patients.

EP-0563

Diagnostic Value of ¹⁸F-FDG PET-CT in diagnosis of recurrent testicular tumors (seminoma and non seminoma)

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Aim: To assess ¹⁸F-FDG PET-CT contribution in the evaluation of suspicion on tumoral recurrence of testicular tumors. **Materials and Methods:** We retrospectively evaluate 24 patients, from 23 to 59 years old (mean age at diagnosis 35 years) investigated for suspected testicular cancer recurrence. Inclusion criteria were elevation of tumor markers (alpha-fetoprotein and human chorionic gonadotropin) and/or suspicious CT findings. ¹⁸F-FDG PET - CT was performed using a standard protocol. All the patients were followed a minimum of 2 years. Final diagnoses were based on clinical evolution at follow up and/or histological data at follow-up. **Results:** At diagnosis, 12 of 24 patients were anatomopathologically classified as seminoma and 12 as non-seminomatous tumors. In seminoma group, 4

PET-CT studies demonstrated pathological FDG uptake: 3 studies were considered TP and 1 was a FP (it was considered inflammation). PET-CT showed no pathological FDG uptake in 8 cases; all of them were considered TN (no evidence of disease during the follow-up or negative histological examination). We got a positive predictive value of 75% and a negative predictive value of 100%. In non-seminomatous group, we obtained similar results. PET-CT showed pathological FDG uptake in 4 cases (3 were considered TP and 1 FP due to an infectious disease with positive microbiological culture). As in the previous group, 8 PET-CT studies did not prove presence of disease (TN). We got a positive predictive value of 75% and a negative predictive value of 100%. In 79% cases PET-CT was considered clinically helpful and contributory to therapeutic attitude: in 6/24 positive PET-CT induced to start chemotherapy and in 13/24 negative PET-CT allowed to maintain an expectant attitude avoiding aggressive measures. **Conclusion:** PET-CT is a noninvasive diagnostic tool useful for the diagnosis of patients with suspected testicular tumors recurrence. In our series, we did not find differences between both seminoma and non-seminomatous PET-CT results.

EP-0564

Prognostic Value of Functional Volumes Determination using SPECT Data for Estimation of Kidney Tumors

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Introduction: During the processing of SPECT data the volume of functional tissue of organ can be received by calculation of total sum functional voxels after correct cutting background. The value of this volume can be compared with “geometrical” volume which includes all voxels inside organ outline, with the value of normal volume based on a patient's anthropometrics. **Aim:** To evaluate usefulness of functional volume for differential diagnosis of kidney tumors. **Methods:** For kidney investigations we used 99mTc-DMSA 370 MBq intravenously. Our results are based on the examination of data on 97 patients (includes 65 renal cell carcinomas and 32 renal cysts). Data analysis was performed for all clinical groups considering histological study which included size of the tumors and data about infiltration growth of the renal carcinoma. The following indicators were used: ratio of functional volumes and specific activity of affected and contralateral kidneys. **Results:** In cases of tumors with infiltrating growth there was a decrease in the ratio of the volumes of the affected and contralateral kidneys to the value 0.71 ± 0.08 and a decrease in the ratio of the respective specific activities to 0.71 ± 0.07 . In cases of tumors without infiltrating growth, these values were 0.88 ± 0.05 and 0.99 ± 0.06 , respectively. The decrease in these parameters was due to the inhibition of the functioning of the elements surrounding the tumor. The developed scheme makes it possible to classify different kidney images into classes characteristic of tumors with the presence and absence of infiltrating growth with an accuracy of 90%. In addition, if there is a tumor in one kidney with infiltrating growth, the contralateral kidney has an increased volume compared to the volume of the

kidney of this patient according to anthropometry. **Conclusion:** The value of the functional volume according to SPECT, allows to get important information about the state of functioning parenchyma of the kidney in tumors. The data used in the selection of indications for conserving surgery.

EP-0565

Comparison of ^{18}F -FDG PET-CT scan with CT scan in detection of metastasis, recurrence and assessment of response to cytostatic therapy in patients with renal cell carcinoma

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Introduction: Renal cell carcinoma (RCC) is highly angioinvasive with widespread haematogenous and lymphatic metastases (lung, liver, lymph nodes, bone, brain). RCC localized in kidney are treated with surgery and have favourable prognosis, but 20–40% later develop metastases and 5-year survival decreases to <10%. Furthermore, 25–30% patients already have metastatic disease at time of diagnosis. Early detection of local recurrence/metastatic disease is the primary goal of postoperative surveillance for RCC. **Materials & Methods:** A retrospective and prospective study of diagnostic efficacy (Oct 2013 - April 2017) included 76 patients with suspected metastatic RCC or post surgery histopathology RCC. ^{18}F -FDG PET CT findings were compared with those of CT scan for characterization of loco-regional and distant metastatic lesions. Findings were correlated with gold standard histopathology or/and follow-up studies, if and when available. The sensitivity, specificity and accuracy of CT scan and PET-CT findings were calculated ($p \leq 0.05$). **Results:** 76 patients of RCC (60 male) were included in the study. Of total 176 lesions, CT scan detected 157 lesions with metastasis/recurrence (154 - true positive and 3 false positive). The 22 lesions not detected on CT scan were positive on PET-CT scan and confirmed on histopathology or/and follow up imaging. Therefore, CT scan had sensitivity, specificity, PPV, NPV and accuracy of 70%, 81.2%, 93.3%, 41.9%, and 72.37%, respectively. All 176 lesions were detected by ^{18}F -FDG PET/CT scan for recurrent disease (no false positive/false negative lesions). Thus, FDG PET/CT had sensitivity, specificity, PPV, NPV and accuracy of 100%, 100%, 100%, 100%, and 100%, respectively. Sensitivity, specificity and accuracy of the FDG PET/CT were statistically significantly superior to those of conventional CT scan ($p < 0.05$). 18 of 76 patients were followed up (available baseline and follow up PET-CT scans) on cytostatic therapy for metastatic RCC with both PET-CT scan (PERCIST criteria) and CT scan (RECIST criteria) at baseline and after 6 months to evaluate therapeutic response. There was discordance found in 3 of 18 patients in evaluating therapeutic response on both modalities favouring PET-CT scan (PERCIST criteria) over CT scan. **Conclusion:** ^{18}F -FDG PET/CT imaging appears more accurate than conventional CT scan in patients with RCC for detection of metastasis and recurrence. For cytostatic therapy response assessment, PET-CT scan proved a better modality over CT scan as seen by discordance observed in almost 16% patients which further corroborated on follow up imaging.

EP-0566**The contribution of 18F-FDG-PET/CT in restaging testicular cancer patients**

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Purpose: Although testicular cancer is a common cancer, affecting as well younger male, its prognosis remains excellent with 5 year survival rate over 90%. CT is the image of choice for staging and restaging the disease. However, CT has the limitation of anatomical imaging and the criterion of size when evaluating residual enlarged lymph nodes. On the other hand, chemotherapy is not innocent of complications and attention should be paid when administered especially in young patients. The aim of this study is to examine the role of PET/CT in evaluating treatment response in testicular cancer patients. **Method-Material:** 83 patients 17- 56 y.o suffering from testicular carcinoma underwent 86 PET/CT examinations for restaging their disease after treatment and evaluation of therapy response. 60 min after the IV administration of 18F-FDG, PET/CT was performed at a Siemens Biograph LSO device. PET images were reconstructed at three levels, corrected for attenuation and fused with CT. All patients had previously been restaged by conventional imaging (CT). Comparison of the two imaging modalities took place. Patients were followed up for 1 year. **Results:** PET/CT was positive in 27/86 cases and negative in 57/86. In 23/27 cases both PET and CT were positive; however PET revealed more metastatic lesions in 4 cases, concerning lymph node invasion. In 4/27 cases CT was negative while PET showed residual disease, 1 osseous and 3 lymph node metastasis. 27/57 cases both PET and CT were negative and in 30 cases CT was either positive or equivocal (small pulmonary lesions, lymph nodes slightly enlarged) while PET was negative for hypermetabolic lesions. In 2/86 cases both PET and CT showed equivocal findings. **Conclusion:** PET/CT is a whole body imaging modality, can be helpful in estimating treatment response and evaluating residual lesions on CT, since functional alterations precede the anatomical ones. However, attention should be paid at small pulmonary nodules that do not present hypermetabolic activity.

EP-45**e-Poster Area**

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology ->
Prostate, malignant

EP-0567**Strategies for Prevention of Potential Salivary Gland Toxicity after PSMA Radioligand Therapy: a Case Series of Locally Injected Pharmaceuticals**

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Purpose/Introduction PSMA-targeted radioligand therapy (RLT) using Lu-177 labelled PSMA small molecules (Lu-177 PSMA) in patients with metastatic castration-resistant prostate cancer (mCRPC) generally does not result in a clinically relevant impairment of the salivary gland (SG) function. However, RLT applying alpha emitters like Ac-225 labelled with PSMA ligands (Ac-225 PSMA) may cause severe xerostomia, which might even become a dose-limiting toxicity. Based on a detailed search of literature and interdisciplinary collaboration, different approaches using locally injected substances in the SG were investigated and their protective potential as well as undesirable side effects were studied. **Subjects & Methods:** Overall, in 10 patients with mCRPC, all progressing under Lu-177 PSMA-RLT and considered for Ac-225 PSMA-RLT, 3 substance classes were used for multifocal, ultrasound-guided injections into the SG parenchyma after detailed informed consent. One patient underwent Ga-68 PSMA PET/CT and dynamic salivary gland scintigraphy (SGS) before and 45 days after injecting 80 units of botulinum toxin A into his right parotid gland. In 3 patients, 0.4-0.6 mg of the short-acting, antimuscarinic Glycopyrronium bromide was injected unilaterally in the parotid and submandibular gland, followed by Ga-68 PSMA PET/CT imaging 45 min - 5 hours post injections. Local anaesthetics, either in combination with vasoconstrictor (Prilocaine plus epinephrine) or without (Mepivacaine only) were injected and the effect on the SGS in 1 patient and the potential uptake reduction in the SG in post-therapeutic scintigraphies after Lu-177-PSMA in 2 patients and in Ga-68 PSMA PET/CT 30 min post-injection in 1 patient were analysed. **Results:** The patient injected with botulinum toxin A demonstrated a SUV-decline in the ipsilateral parotid gland by up to 64% when compared with the baseline PET/CT and by 60% compared with the non-injected parotid gland. No adverse events were noted in follow-up of currently 6 months. In the Ga-68 PSMA PET/CT studies after Glycopyrronium bromide injections, however, none of the treated SG exhibited any significant decline in tracer uptake. Injection of Prilocaine/epinephrine or Mepivacaine did not reveal any significant difference in tracer uptake in the Ga-68 PSMA PET/CT, the dynamic SGS or on post-therapeutic Lu-177-PSMA scintigraphy. **Discussion/Conclusion:** Among the pharmaceuticals reported in this case series for local injection in salivary glands in an attempt to reduce the potential sialotoxicity from Ac-225 PSMA-RLT, so far only botulinum toxin A demonstrated a partial, but very distinct decrease of tracer uptake. Blocking the specific radioligand accumulation might be another promising approach, which needs to be studied further.

EP-0568**⁶⁸Ga-PSMA PET/CT In Patience With Biochemical Recurrence And A PSA Value Of ≤ 2ng/ml: A Prospective Review Of Its Diagnostic Performance**

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Introduction: Treatment with curative intent for prostate confined prostate cancer results in excellent survival rates however up to one third of these patients will re-present with biochemical recurrence in the form of a detectable rising serum PSA. The success of salvage therapy is dependent on the early identification of the site recurrence whilst PSA values are still low. Imaging with Prostate-specific membrane antigen (PSMA) ligands are rapidly emerging as a significant step forward in the management of prostate cancer, based on the fact that Prostate-specific membrane antigen (PSMA) is a type II transmembrane protein with high expression in prostate carcinoma cells. The aim of this study was to determine the diagnostic performance of ^{68}Ga -PSMA PET/CT in patients with biochemical recurrence with a PSA of $\leq 2\text{ ng/ml}$. **Subjects & Methods:** 49 Prostate cancer patients prostate (mean age 63.6 ± 8 , range 47–87 years) presenting with abnormal PSA (mean PSA $0.81 \pm 0.55\text{ ng/ml}$, range 0.07–2) underwent contrast-enhanced ^{68}Ga -PSMA PET/CT. PET/CT findings were evaluated qualitatively and semiquantitatively (SUV-max) and compared to the results of histology, Gleason score, CT scan and bone scintigraphy. **Results:** 18 of the 49 (36.7%) patients demonstrated a site of recurrence on ^{68}Ga -PSMA PET/CT. The detection rates for PSA levels 0– <0.5 , 0.5 – <1 , 1 – 2 were 16.7%, 46.2%, and 59% respectively. Solitary sites of recurrence were identified in 11 (61%) patients of whom 9 (18.4%) were prostate confined. Treatment received before biochemical recurrence and the outcome from the scan was significantly associated ($p < 0.001$), where all 8 patients who received radiotherapy (brachytherapy or EBRT or both) alone had a positive PSMA scan result whilst 5 (16.7%) of the patients who had undergone prostatectomy demonstrated local recurrence. Lowest detected PSA value was at 0.15 ng/ml . **Conclusion:** Detecting sites of recurrence at PSA values as low as 0.15 ^{68}Ga -PSMA PET/CT demonstrated excellent diagnostic performance. This will significantly impact the way these patients could be managed.

EP-0569

qPSMA: First semi-automatic tool for whole-body tumor burden assessment in prostate cancer PET imaging and preliminary evaluation for PSMA-targeted radioligand therapy

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Aim: PSMA-targeted radioligand therapy (RLT) is increasingly used in patients with metastatic castration resistant prostate cancer (mCRPC). Whole-body tumor burden is an established prognostic factor in different malignancies. Our aim was to develop a tool to assess whole-body tumor burden in PSMA-targeted PET-imaging and to evaluate its value in a proof-of-concept study in mCRPC patient undergoing ^{177}Lu -PSMA I&T RLT. **Material and Methods:** We developed qPSMA, a semi-automatic Python-based software that allows segmentation of soft-tissue and bone lesions using ^{68}Ga -PSMA-11 PET/CT. Organs with physiological uptake are automatically segmented as nor-

mal uptake. Bone lesions are automatically selected based on a fixed threshold determined in a prior study. An automatically liver-based scan-individualised threshold is used to compute soft-tissue lesions. Outcome parameters were PSMA-positive tumor volume (PSMA-TV) and total lesion PSMA (PSMA-TL), similar to MTV and TLG used in FDG-PET quantification. PSMA-TV and PSMA-TL can be determined for the whole body (wbPSMA-TV, wbPSMA-TL) and separated for bone and soft-tissue lesions (bonePSMA-TV, bonePSMA-TL and stPSMA-TV, stPSMA-TL). We analysed clinical data and PSMA-TV and PSMA-TL in 24 mCRPC patients who underwent ^{177}Lu -PSMA-I&T RLT pairwise prior and after 2 cycles of RLT. Initial PSMA-TV and PSMA-TL and change in PSMA-TV and PSMA-TL were compared to best PSA response, PSA response, PSA progression-free survival (PSA-PFS) and overall survival. **Results:** Mean wbPSMA-TV, bonePSMA-TV, stPSMA-TV were 851 ± 845 , 796 ± 869 and $91 \pm 200\text{ ml}$ prior and 689 ± 854 , 781 ± 893 and $39 \pm 54\text{ ml}$ after PSMA-targeted RLT, respectively. Mean wbPSMA-TL, bonePSMA-TL, stPSMA-TL were 7009 ± 7102 , 6364 ± 7307 and $645 \pm 869\text{ ml}$ prior and 5107 ± 5211 , 4834 ± 5197 and $344 \pm 503\text{ ml}$ after 2 cycles PSMA targeted RLT, respectively. Mean (range) of changes in PSA-value, wbPSMA-TV and wbPSMA-TL were $+39\%$ (-98% to $+594\%$), $+31\%$ (-96% to $+346\%$) and $+5\%$ (-98% to $+262\%$), respectively. Statistical significant high correlations were present between changes in PSA-value and wbPSMA-TV ($r=0.82$, $p < 0.0001$) and wbPSMA-TL ($r=0.82$, $p < 0.0001$). Statistical significant moderate correlations were observed between PSA-PFS and pre-treatment wbPSMA-TL ($r=0.51$, $p=0.0097$) and wbPSMA-TV ($r=0.43$, $p=0.0340$). Moderate but not statistical significant inverse correlations were present between overall survival and wbPSMA-TV ($r=-0.38$, $p=0.0599$) and wbPSMA-TL ($r=-0.34$, $p=0.0963$). **Conclusion:** Semi-automatic analysis of total, osseous and soft-tissue whole-body tumor burden in ^{68}Ga -PSMA-11 PET is feasible. PSMA-TV and PSMA-TL are promising quantitative biomarkers during PSMA-targeted RLT with significant correlations to PSA changes and PSA progression-free survival. Despite not statistically significant in this small proof-of-concept analysis a trend towards a lower overall survival in patients with high PSMA-TV and PSMA-TL warrants future analyses to evaluate its role as prognostic marker.

EP-0570

Hematological toxicity of Ra-223-dichloride therapy in dependance of bone marrow reserve

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Introduction: Ra-223-dichloride (Xofigo®) therapy is known as a minimally myelosuppressive treatment targeting bone metastases in mCRPC. The aim of the study is to analyze the bone marrow scan (BMS) as prognostic and predictive factor. **Subjects & Methods:** In 79 patients (74 > 60 and 5 < 60 years), a BMS with 492 – 667 MBq Tc-99m Scintimun® was done approximately a month prior therapy. Uptake ratio (UR) was calculated by drawing irregular regions of interest around the sacroiliac and background area, respectively. The cut-off value ($\text{UR}=8$) representing

the median and predetermined by us, the standard value range published in the literature and automated Bone Scan Index (BSI) were compared with our collected clinical data. SPSS 24 was used to evaluate prognostic and predictive factors by univariate and multivariate analyses. **Results:** 35 patients (47.3%) >60 years exhibit an UR located within the UR-standard range of 4.4–11.0. Based on the threshold, the pre-therapeutic levels of neutrophil granulocytes (NG) for the cohort with an UR<8 were decreased by 18% ($p=0.022$). The NG-decrease before the third cycle was 33% ($p=0.013$). These results were applicable to values of erythrocytes, leukocytes and hemoglobin. The decline of NG before the 6th cycle amounted to 53% in terms of UR<4 ($p=0.022$). Kaplan-Meier curves showed a survival benefit of 7.3 months for the collective with UR>8 vs. UR<8 (95% CI: 13.43–26.13; $p=0.275$). Stratification by cut-off and analysis in terms of the baseline-alkaline phosphatase (AP) resulted in a survival advantage of 10.4 months for a baseline-AP<129 U/l compared with a baseline-AP>129 U/l in terms of UR>8, respectively. With regard to an UR<8 the advantage of overall survival (OS) was 4.7 months for a baseline-AP<129 U/l ($p=0.019$). A BSI<1 together with an UR>8 achieved the longest median OS of 21.1 months, compared to UR<8 and a BSI>1 with 11.1 months ($p=0.379$). Cox regression analysis showed a 1.5-fold higher treatment success with UR=10 compared to UR=5 ($p=0.033$). Other significant factors affecting the OS were number of therapy-cycles ($p<0.001$) and antiandrogenic therapy ($p=0.006$). The method revealed very good intraobserver agreement with an intercorrelation coefficient by 0.991 ($p<0.001$). **Conclusion:** In summary, patients with UR>8 prior Xofigo® developed a lower expression of hematologic toxicity and a noticeable survival advantage. Understanding baseline and risk factors associated with myelosuppression may assist clinicians in avoiding severe adverse effects with Ra-223 and other radionuclide therapies like PSMA-therapy. BMS could be a valuable tool for clinicians with respect to radioendotherapy and improve outcome.

EP-0571

11C-choline PET/CT in the Detection of Prostate Cancer Relapse in 260 Patients after Radical Treatment

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Purpose: To investigate the usefulness of 11C-Choline PET/CT in the detection of recurrent prostate cancer (PCa) in patients after radical treatment with biochemical relapse. **Materials and Methods:** This retrospective analysis included results of 11C-Choline PET/CT examinations performed in 260 PCa patients with rising PSA after radical treatment. The mean PSA value in the group was 2.1 ± 2.6 (0.2–9.7) ng/ml. Examinations were done on PET/CT scanner (Biograph-64, Siemens) 10 min after 11C-Choline injection (400–550 Mbq). **Results:** Overall, PET/CT detected PCa relapse in 58% (151/260) of cases: in 53% (102/193)

after radical prostatectomy and in 73% (49/67) after radiation therapy. The mean PSA value in PET-positive cases was statistically higher than in PET-negative ($p<0.05$): 3.1 ± 2.1 (0.2–9.7) vs 1.7 ± 1.5 (0.2–4.6) ng/ml. The majority of PET-negative patients - 71% (77/109) had low PSA levels (<2 ng/ml). PET/CT results were positive in 43% (59/136) patients with PSA of <2 ng/ml, in 68% (59/87) with PSA of 2–5 ng/ml, and in 89% (33/37) with PSA of >5 ng/ml. Local relapse was detected in 50% (76/151), distant metastases - in 29% (43/151), both local and distant metastases - in 21% (32/151) of cases. Lymph node metastases were detected in 39% (101/260) of all patients included in the analysis, of which 28% (28/101) had lesions in lymph nodes of normal size (median 7 mm). Of all PET-positive patients bone metastases were detected in 30% (46/151), of which 63% (29/46) had isolated skeletal involvement. Importantly, that 28% (13/46) of PET-positive patients with bone metastases had no structural abnormalities on CT images (CT-negative cases), corresponding to isolated involvement of bone marrow. And 61% (6/13) of these CT-negative patients had single lesions. The mean PSA value in patients with bone metastases was 3.6 ± 2.2 (0.4–9.1) ng/ml, median - 3.0 ng/ml. According to 11C-Choline PET/CT results oligometastatic PCa recurrence was revealed in 39% (102/260) of all patients, of which 63% (64/102) had local relapse only. Distant oligometastatic lesions were detected in 37% (38/102), of which 16% (6/38) were presented by normal-size lymph nodes and 21% (8/38) - by early bone marrow metastases. 52% (79/151) of PET-positive results were confirmed by data of repeated PET/CT examinations. **Conclusion:** 11C-Choline PET/CT allows to differentiate patients with local and distant metastases in one study, as well as identify oligometastatic process, metastases to lymph nodes of normal size and bone marrow. PET/CT results play crucial role in determining the further personalized treatment.

EP-0572

Can SUVmax Values of 68Ga-PSMA PET/CT scan Predict the Clinically Significant Prostate Cancer

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Introduction: According to the European Association of Urology guidelines 10–12 core systematic transrectal-ultrasonography guided prostate biopsy (TRUSBx) is standard of care for the primary diagnosis and risk stratification of prostate cancer. It has been reported that 20%–30% of clinically important cancers are missing due to anterior or apical localization leading in inaccurate grading and staging. We know that intensity of PSMA

expression is increasing as the tumor grade increases. The aim of the study was to evaluate the correlation of tracer uptake to gleason score(GS) obtained from definitive pathology report in patients who underwent radical prostatectomy and who had 68Ga-PSMA PET/CT scan prior to operation performed for primary staging. **Methods:** We retrospectively evaluated 141 patient who had 68Ga-PSMA PET/CT imaging for a purpose of primary staging and who underwent radical prostatectomy. All patient had a diagnosis of prostate cancer based on 10-24 quadrants TRUSBx. All patients had histopathology analysis including GS sum and grade groups(GG) in biopsy and postoperative tissue specimens and a PSA measurement within maximum of 28 days prior to 68Ga-PSMA scan. The highest SUVmax value from whole prostate gland is assumed to be the highest site of PSMA expression and recorded for further evaluation. **Results:** There were 141 patients with a mean age of 64.6 ± 6 . When we compared the final pathology reports with biopsy results we observed 49% change in GG (%41 upgrading, %11 downgrading) which was significant ($p < 0.001$). According to pathology reports 21% ($n=16$) of patients moved from low-risk (GG1+2) to high-risk level (GG3+4+5) and 10% ($n=6$) patients moved from high-risk to low-risk level. Mean SUVmax value was 13.2 ± 11.7 with a median of 8.8. The mean SUVmax values for GG3 (13.3 ± 8.5) was significantly higher than GG2 tumors (7.4 ± 4.6), ($p < 0.001$). The mean SUVmax values of high-risk patients according to final pathology reports were significantly higher than those of low-risk patients, which were 18.9 ± 12.1 and 7.16 ± 6.2 , respectively ($p < 0.001$). ROC curve analysis of SUVmax (AUC: 0.85, 95% CI, 0.79–0.91) showed a cut of value of 9.1 giving a sensitivity and specificity of 78% and 81%, respectively. PSA values for low risk patients were significantly lower than high risk patients (12.8 ± 14.3 ng/ml and 23.0 ± 24.5 ng/ml), ($p < 0.001$). There wasn't any correlation between PSA and GG ($P=0.21$). **Conclusion:** SUVmax values significantly correlate with the GG of the primary tumor. The accumulation sites may potentially predict the clinically significant cancer. The accumulation sites of the tracer may potentially serve as a target for biopsy sampling in conjunction with mpMRI in selected patients.

EP-0573

Contribution of 68Ga-PSMA-11 PET/CT imaging in Gleason Score 3+3=6 Prostate Cancer

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Introduction: 68Ga-PSMA-11 PET/CT imaging, which has come into use in recent years for detection of prostate cancer (pCa) that relapses and metastases, is an effective imaging procedure. Recent studies demonstrated that 68Ga-PSMA PET/CT imaging has indications of staging and biopsy guidance but it is not being used routinely for pCa patients with gleason score(GS) 3+3=6. The purpose of our study is to evaluate contribution of 68Ga-PSMA-11 PET/CT imaging for GS6 patients. **Methods:** Pathologically proven 127 pCa patients with GS6 and their 154 68Ga-PSMA PET/CT scans are included. PSMA-PET/CT was per-

formed and evaluated at a single center. Patients are divided into two major groups: Group A includes 36 patients (70.2 ± 7 years) who underwent radical prostatectomy and their 52 PSMA-PET/CT scans and Group B includes 91 patients (68.8 ± 8.9 years) who were diagnosed only via biopsy and 102 PSMA-PET/CT scans. For each imaging, primary/relapsed lesion, lymph nodes (LN), bone and visceral metastases were evaluated separately. Correlation of the lesions was made by previous PSMA PET/CT scans and other procedures if it is available or via PSA values if it is not. **Results:** In assessment of Group A patients, no lesions were detected in 16 of 36(%45) patients and 20(%55) patients had one or more positive PSMA lesions. 3(%8) patients had local relapse, 14(%38) patients had LN metastases, 11(%30) patients had bone metastases and only 1 of them had liver metastasis. 52 PSMA-PET/CT imaging of Group A patients (average PSA: 4.7 ± 12.1) were evaluated separately: 34(%65) imaging detected at least a lesion of relapse or metastases and no lesions were detected on 19(%35) imaging. In assessment of Group B patients, no lesions were detected in 18 of 91(%20) patients. 51(%56) patients had a primary lesion but no metastatic lesions detected. 22(%24) patients had one or more metastatic lesions: 16(%17) patients had bone metastases, 17(%18) patients had LN metastases and 4(%4) patients had visceral organ metastases. 102 PSMA-PET/CT imaging of Group B patients (average PSA= 61.6 ± 230) were evaluated separately: 29(%28) imaging detected one or more metastatic lesions. 52(%51) imaging detected only primary lesion. 21(%21) imaging had no PSMA positive lesions. **Conclusion:** 68Ga-PSMA-PET/CT CT imaging is routinely used for prostate cancer patients with gleason score 7 or more. We found that 68Ga-PSMA-PET/CT is an effective imaging procedure for prostate cancer patients with GS 3+3=6, who are clinically suspected as having relapse or metastasis.

EP-0574

Standardized uptake value atlas: physiological and abnormal ⁶⁸Ga-RM2 uptake in patients with prostate cancer

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Object: To describe the distribution and range of physiological uptake of ⁶⁸Ga-RM2 in patients with prostate cancer and to evaluate the spectrum of abnormal uptake using standardized uptake values (SUVs). **Materials & Methods:** We retrospectively reviewed images of 29 prostate cancer patients who performed either an ⁶⁸Ga-RM2 PET/CT for primary diagnosis and staging ($n=7$) or ⁶⁸Ga-RM2 PET/MRI for a biochemical recurrence ($n=22$). Two nuclear medicine physicians evaluated images using an AW workstation (GE Healthcare). SUVmax and SUVmean were measured in 24 normal anatomical structures for each patient. ⁶⁸Ga-RM2 uptake values of each organ was classified as "none" if SUVmean value was less than of the aortic blood pool, "mild" if SUVmean was greater than SUVmean of aortic blood pool, but less than 2.5, "moderate" if SUVmean was between 2.5 and 5 and "intense" if SUVmean was greater than 5. Areas of focal increased ⁶⁸Ga-RM2 uptake were also collected. **Results:** The highest ac-

tivity was observed in bladder and renal collecting system, related to urinary excretion of radiotracer. The highest physiological uptake was present in the pancreas (SUVmax 64.08 ± 16.85). Uptake in the kidney cortex, duodenum and esophagus was mostly classified as mild (average SUVmax of 3.56) and only few times as moderate. Uptake in the stomach wall and rectum was classified as mild in half of the cases and not significant in the other half (average SUVmax of 2.3). Uptake in left ventricle wall, adrenals, liver and spleen was mostly classified as not significant (average SUVmax of 1.68) and only few times as mild. Brain, parotids, lungs, bone, gluteal muscle and fat had not significant uptake. Nineteen avid foci of ^{68}Ga -RM2 uptake were detected in 11 patients. Uptake was identified in the prostate bed ($n=6$, average SUVmax 37.6), abdominopelvic and mediastinal lymphnodes ($n=8$, average SUVmax 21.3 and $n=2$ average SUVmax 27.1, respectively), skeleton ($n=2$ average SUVmax 21.4) and lungs ($n=1$). **Conclusion:** We presented data on patterns of physiological ^{68}Ga -RM2 uptake in normal tissues with the aim of creating an atlas to improve the interpretation accuracy of ^{68}Ga -RM2 PET scan. Our data also confirmed that ^{68}Ga -RM2 is a promising tracer for the assessment of GRPr expression in prostate cancer patients. Further evaluation in a larger cohort are needed to confirm these data.

EP-0575

^{18}F -PSMA-1007 PET/CT in staging of primary prostate cancer: correlation between SUVmax and both PSA level and Gleason score

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In newly diagnosed prostate cancer patients (PC) the assessment of tumor stage by PSA level and Gleason score (GS), has major implications for prognosis and treatment. The novel radiotracer ^{18}F -PSMA-1007 has demonstrated promising results for the diagnostic workup of prostate cancer. ^{18}F -PSMA-1007 is comparable to ^{68}Ga -PSMA-11, but has some advantages such as a longer half-life and non-urinary excretion[1]. **Aim:** To assess the intensity of ^{18}F -PSMA-1007 accumulation in tumor lesions in newly diagnosed PC patients in correlation to both PSA level and GS, according to the recently published Gleason grading system the grade group (GG)[2]. **Methods:** A retrospective analysis of 67 patients (mean age: 66.7 ± 8.0 years) referred for PET/CT (Siemens Biograph mCT 20) in primary staging of PC was performed. All with proven PC by transrectal ultrasound guided biopsy with GS (6-10) and PSA level (mean: 33 ± 58.1 ng/mL). PET images were acquired sixty minutes after injection of ^{18}F -PSMA-1007 (mean activity: 284 ± 18.3 MBq; range: 257-343 MBq). All the images were analyzed visually and semi-quantitatively by measuring SUVmax of the primary tumor and pathologic lesions suspicious for metastasis. A p -value < 0.05 was considered a statistically significant difference. **Results:** 100% of the patients demonstrated pathologic uptake in the primary tumor (mean SUVmax: 15.1 ± 15.3), 40.3% suspicious lymph node involvement (mean SUVmax: 10.7 ± 12.7) and 22.4% possible bone metastases (mean SUVmax: 7.8 ± 7.4). Patients with PSA > 10 ng/

mL exhibited significantly higher uptake in primary tumor than those with PSA levels ≤ 10 ng/mL (mean SUVmax: 20.4 versus 10.3; $p=0.0056$). The intensity of ^{18}F -PSMA-1007 uptake in the primary tumor and suspicious lymphatic involvement correlates with PSA levels ($r=0.5729$, $p<0.0001$ and $r=0.5846$, $p=0.014$, respectively). No correlations were found between GG and SUVmax or PSA level. **Conclusions:** In newly diagnosed prostate cancer patients the intensity of tracer accumulation of ^{18}F -PSMA-1007 in the primary tumor is significantly higher in patients with PSA levels > 10 ng/mL but failed to show correlation with the new Gleason grading system. [1] Giesel et al. Eur J Nucl Med Mol Imaging. 2017; 44(4): 678-688. [2] Epstein et al. Am J Surg Pathol 2016; 40: 244-252.

EP-0576

^{68}Ga PSMA-11-PET/CT changes external beam radiation therapy concept even in low PSA-recurrences up to 0,5ng/ml

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Introduction: Radiotherapy (RT) is an established part of the salvage treatment in patients (pts) with postprostatectomy PSA progression. Improved diagnostics by ^{68}Ga PSMA-11 PET/CT (PET) may lead to changes in treatment procedures (e.g. target volume, ADT). We analyzed the impact of PET on the RT concept in early-stage biochemical recurrence up to PSA 0.5 ng/ml. **Subjects & methods:** We retrospectively analyzed 76 pts with early-stage biochemical recurrence after prostatectomy in whom salvage RT was planned after PET. All pts had a PSA ≤ 0.5 ng/ml. A radiation oncologist determined the treatment concept, first based on the clinical and pathological situation without PET and second with consideration of the PET results. Changes in the treatment concept were defined as major, if a new target volume region (TVR) was elected. Minor changes were defined as target modifications inside a TVR. **Results:** Median PSA in the overall cohort was 0.245ng/ml. A change in the treatment concept occurred in 21 (28%) pts: major changes were noticed in 13(17%); minor changes in 8(11%). In 6 out of these 21 patients, the changes occurred due to detection of bone metastases on PET. Without PET, all (76) pts would have been given RT, 60 (79%) to the bed of the prostate and seminal vesicles alone, and 16(21%) also to the pelvic lymph nodes. Based on the PET, the indication for an extended dose-escalated RT to the pelvic lymph nodes was set in 17(22%) pats. **Conclusion:** ^{68}Ga PSMA-11 PET/CT changes treatment concept in up to 28% of the patients with low PSA value thereby enabling personalized treatment with external beam radiation therapy. Longer follow up and further prospective study is needed to assess the impact of PET on PSA progression rate and median progression free survival.

EP-0577

FDG PET/CT as a tool to provide the prognostic stratification and response assessment of metastatic castration-resistant prostate cancer (mCRPC) treated with radium-223 dichloride (Ra-223)

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Aim: Ra-223 is the only bone-directed treatment demonstrating an improvement in overall survival (OS) in mCRPC. Beyond its effect on OS, its clinical benefit has been mainly measured in terms of stabilisation of PSA, normalisation of the bone alkaline phosphatase (BAP) or reduction of number of lesions on bone scan. However, an effective and widely available method to predict and/or measure response to Ra-223 has not yet identified. Despite the well-known notion that FDG-PET/CT is not appropriate in the general population of prostate cancer patients, preliminary evidences suggest that it can be useful for the evaluation of the extent of metastatic disease, prognosis and assessment therapy response in patients with mCRPC. The aim of the present study is to evaluate the role of FDG-PET/CT as a tool to provide the prognostic stratification and response assessment of mCRPC treated with Ra-223. **Methods:** 20 mCRPC patients undergoing Ra-223 were enrolled. FDG-PET/CT was acquired at baseline and two months after the end of therapy. Similarly, BAP, PSA and blood cells counts were measured at baseline and at the end of therapy. Difference between final and initial BAP and PSA levels as well as blood cells counts were evaluated (Delta-BAP, Delta-PSA, Delta-Hb, Delta-WBC and Delta-Pt respectively). Maximum SUV of the hottest lesion (hSUVmax), mean SUV of all lesions (SUVmean) and metabolic tumour volume (MTV) of avid bone metastases were computed. **Results:** At baseline, hSUVmax, SUVmean and MTV were 9.78 ± 3.82 , 3.61 ± 0.66 and 362.58 ± 394.61 , respectively. MTV was inversely correlated with Delta-Pt ($R^2=0.29$, $p<0.05$), while hSUVmax and SUVmean were directly correlated with Delta-BAP ($R^2=0.44$, $p<0.01$ and $R^2=0.45$, $p<0.01$, respectively). By contrast, baseline FDG-PET-derived parameters were not significantly correlated with Delta-PSA value. In the five patients in which end-therapy FDG-PET/CT was available, hSUVmax and SUVmean were significantly reduced with respect to baseline (7.11 ± 3.3 vs 9.98 ± 3.82 , $p<0.05$ and 3.34 ± 0.5 vs 3.92 ± 0.6 , $p<0.05$, respectively). **Conclusion:** Higher FDG uptake at baseline seems to result in a lower effect on reduction of BAP after Ra-223 administration. The amount of non-differentiated disease might thus predict the low biochemical response to Ra-223 therapy. Additionally, baseline metabolic tumour burden predicts the degree of bone marrow toxicity. On the other hand, FDG-PET/CT-derived parameter might be able to capture the metabolic effect provided by Ra-223 administration in mCRPC patients. Based on the present data, FDG-PET/CT might represent a widely available method to improve patients' prognostic stratification and patients' selection and to assess response to Ra-223 therapy.

EP-0578

The positivity rates of 18F-fluciclovine and 18F-choline PET/CT in men with recurrent prostate cancer

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Introduction: Prostate cancer recurrence detection is increasing due to improvement in positron emission tomography/computed tomography (PET/CT) imaging utilizing new tracers such as ¹⁸F-choline and ¹⁸F-fluciclovine. In Europe choline PET/CT has changed the management of prostate cancer, while in the USA fluciclovine PET/CT has shown promising results. The objective of this study is to evaluate the positivity rates of choline and fluciclovine for detecting prostate cancer recurrence in patients with similar levels of prostate-specific antigen (PSA). **Subjects and Methods:** We retrospectively assessed 111 ¹⁸F-choline PET/CT scans and 147 ¹⁸F-fluciclovine PET/CT scans of patients with suspected recurrent prostate cancer after initial treatment, obtained from two different academic institutions, one from Europe and the other from the USA. Patients were grouped according to their PSA levels, as follows: G1 (PSA<0.5), G2 (PSA≥0.5-1), G3 (PSA≥1-2), G4 (PSA≥2-5), and G5 (PSA≥5). The positivity rates of both tracers were calculated for extraprostatic locations (overall and in bones only) in each group. Positivity rates for local recurrence were evaluated only for patients with prior prostatectomy. Evaluation of prostate cancer local recurrence in patients with preserved prostate was omitted, due to known high nonspecific tracer uptake and potential interpretation bias. A chi-square test was used to compare all positivity rates. **Results:** The overall extraprostatic positivity rates were 30% (G1,n=3/10), 27% (G2,n=3/11), 50% (G3,n=8/16), 56% (G4,n=19/34) and 80% (G5,n=32/40) for choline, and 39% (G1,n=14/36), 37% (G2,n=7/19), 60% (G3,n=9/15), 64% (G4,n=25/39) and 66% (G5,n=25/38), for fluciclovine. Positive bone lesions were found in 0% (G1,n=0/10), 0% (G2,n=0/11), 19% (G3,n=3/16), 24% (G4,n=8/34) and 50% (G5,n=20/40) of choline scans and in 11% (G1,n=4/36), 16% (G2,n=3/19), 33% (G3,n=5/15), 23% (G4,n=9/39) and 34% (G5,n=13/38) of fluciclovine scans. No significant difference in extraprostatic positivity rates was found between the two tracers ($p>0.05$). The local recurrence positivity rates among patient who underwent prostatectomy were 11% (G1,n=1/9), 0% (G2,n=0/9), 13% (G3,n=2/15), 25% (G4,n=4/16) and 11% (G5,n=2/19) for choline and 34% (G1,n=11/32), 22% (G2,n=4/18), 45% (G3,n=5/11), 53% (G4,n=10/19) and 50% (G5,n=6/12) for fluciclovine. Significant difference was found only in group G5, with higher positivity rates for fluciclovine scans ($p=0.014$). **Conclusion:** Both ¹⁸F-choline and ¹⁸F-fluciclovine PET/CT have high positivity rates for detecting extraprostatic lesions, with direct correlation of positivity rates and PSA levels. Overall, no significant difference between the two tracer positivity rates was found. However, population bias may have affected these data. Further inpatient analysis should be performed.

EP-0579

Comparison between 68Ga-PSMA PET/CT and mpMRI to detect local recurrence of prostate cancer and local lymph node restaging in patients with biochemical recurrence of prostate cancer

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Purpose: Purpose of this prospective study is to compare diagnostic modalities (68Ga-Labeled Prostate-specific Membrane Antigen Ligand Positron Emission Tomography/Computed Tomography and multi parametric Magnetic resonance imaging) for localisation of recurrent prostate cancer in prostate or prostate bed and local lymph node restaging. **Subjects & methods:** This study included 111 patients after initial radical treatment of prostate cancer with biochemical recurrence with PSA value 0,2–10,0 ng/ml, who underwent 68Ga-PSMA PET/CT. Study group underwent additional bone scintigraphy and mpMRI within 3 months before or 1 month after PET/CT. The PET/CT, MRI and scintigraphy results were compared based by patients, as well as based by site, using TNM classification: local recurrence, regional lymph node metastases and distant metastases. Sensitivity and specificity between all three methods were calculated. Histopathology and/or clinical and imaging follow-up data were taken as the reference standard. **Results:** From total 111 patients scanned with 68Ga-PSMA included were 24 patients, who met inclusion criteria. Sensitivity, specificity, positive predictive value, negative predictive value for evaluation of local recurrence in PET/CT and MRI - 62,5%, 92,9%, 89,80% 71% and 100%, 85,7%, 87%, 100%, respectively. Sensitivity, specificity, positive predictive value, negative predictive value for evaluation of regional lymph nodes in PET/CT and MRI - 100%, 100%, 100%, 100% and 62,5%, 92,9%, 89,80%, 71,24%. There was no statistical difference in sensitivity ($p=0,250$) and specificity ($p=1,0$) between study groups. **Conclusion:** There is a tendency of better diagnostic rates for local prostate cancer recurrence with MRI than PET/CT, whereas PET/CT shows higher diagnostic value for evaluation of regional lymph nodes, although our results did not prove any statistical difference between groups. This study should be continued to evaluate a clear diagnostic value of both methods in a case of biochemical recurrence of prostate cancer.

EP-0580

Comparison of Ga68-HBED-CC and F18-PSMA-1007 PET/CT in Staging Intermediate and High-risk Prostate Cancer

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Aim: Comparing the findings of F18-PSMA-1007 PET/CT and Ga68-HBED-CC PET/CT in same patients presenting with newly diagnosed intermediate and high-risk prostate cancer. **Patients & Methods:** Giving a written informed consent, six patients with Gleason score > 7 or Gleason score = 6 and PSA > 10 underwent F18-PSMA-1007 and Ga68-HBED-CC PET/CTs within two-weeks. Normal bio-distribution of the two tracers and scintigraphic lesions were compared. The radical prostatectomy pathological specimens were available for correlation in three patients. Specimens were divided into 24 segments (base/ mid-gland/ apex; left and right lobes and each lobe into central or peripheral ar-

eas), and location of the actual tumor sites were correlated with the scintigraphic abnormalities. **Results:** PSMA-avid lesions in the prostate were identified in all six patients. One patient had uptake also in both seminal vesicles and one patient had uptake in a pelvic lymph-node. In four of the six patients, the two tracers detected exactly the same lesion (including the above mentioned extra-prostatic lesions) and in two other there was partial agreement, with F18-PSMA-1007 detecting more lesions. Target to background ratios (T/B ratio) was higher with F18-PSMA-1007 (mean ratio 7.61 for the F18 tracer and 4.91 for the Ga68). F18-PSMA-1007 had almost no-urinary excretion as opposed to Ga68-HBED-CC. In one patient, who previously underwent TURP, the lack of increased uptake in the dilated area of the prostatic urethra, allowed better visualization of a central tumor that seemed equivocal on Ga68-HBED-CC. A good correlation was found between the scintigraphic abnormalities and histopathological findings. **Conclusion:** F18-labeled PSMA is a valuable tracer for staging prostate cancer, comparable to the routinely used Ga68 labeled tracer and at times superior, in view of its higher T/B ratio and no interference with physiologic urine uptake at the prostatic urethra.

EP-0581

Impact of ⁶⁸Ga-PSMA-PET/CT to drive targeted therapies in biochemical relapse prostate cancer

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Aim: Targeted curative therapies are increasingly proposed during the treatment of patients affected by prostate cancer in order to prolong survival without (biochemical) relapse, and even more to increase the overall survival. PSMA-PET/CT is recommended in the restaging of biochemical recurrence in patients affected by prostate cancer. Aim of this study was to establish the impact of PSMA-PET/CT in the management of patients during biochemical relapse of prostate cancer, in particular by calculating the PSMA-PET/CT driven therapy rate in a bi-centric study. **Subjects and Methods:** From December 2016 to March 2018, 297 males underwent ⁶⁸Ga-PSMA-PET/CT in one of the two centres that lead this study. For fifty-seven consecutive patients (mean age: 69.5 years old, range 44.5–81.4) undergoing ⁶⁸Ga-PSMA-PET/CT during biochemical relapse, the treatment established after ⁶⁸Ga-PSMA-PET/CT was collected and correlated with ⁶⁸Ga-PSMA-PET/CT result. The treatment was usually established in a tumour board including urologists, oncologists, radiation therapy physicians, radiologists and nuclear physicians. Other data such as Prostate cancer diagnosis date, the initial PSA, actual PSA, actual PSA doubling time, actual PSA velocity, Gleason Score, T staging, N staging, initial treatment and imaging data (including PSMA-PET/CT) were also collected. **Results:** Mean PSA value was 9.84 ng/ml, (range 0.05–108.68 ng/ml). ⁶⁸Ga-PSMA-PET/CT was positive in 44 cases (mean PSA value: 12.47 range 0.09–108.68 ng/ml) for a detection rate of 77.2%, ⁶⁸Ga-PSMA-PET/CT was negative in the remaining 13 patients (mean PSA value: 0.64 range 0.05–3.15 ng/ml, p-value

0.0687). In 32 patients relapse was localized in the prostate bed, in 26 cases metastatic lymph nodes were identified, in 11 men bone metastases were detected and in 2 scans lung metastases were described. Driven ^{68}Ga -PSMA-PET/CT therapies such as external beam radiation therapy (17), surgery (5), HIFU (5), ^{177}Lu -PSMA treatment (2), and brachytherapy (1) based on positive scan took place in 30 out of 57 patients (53%). **Conclusion:** ^{68}Ga -PSMA-PET/CT impacted significantly in the management of more than half of patients in biochemical relapse of prostate cancer and in more than 2/3 (30/44) of patients with positive scan, particularly to drive targeted therapy. ^{68}Ga -PSMA-PET/CT proved to be a game changer in this clinical setting, moreover, efforts should be done to demonstrate its impact at staging of prostate cancer as well as during the management of mCRPC patients.

EP-0582

Detection of non-prostatic pathologies on ^{68}Ga -PSMA-11 PET/CT: Gauging the 'specificity' of Prostate Specific Membrane Antigen

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Aims: Prostate specific membrane antigen (PSMA), as the name suggests, was initially proclaimed to be exclusively expressed in prostate tissue, more so in prostate malignancy. However, with wider availability and growing experience with ^{68}Ga -PSMA-11 imaging, several cases have been reported in literature documenting the 'non-prostatic specificity' of PSMA due to its expression on the neo-vasculature. The present study aimed to evaluate the in-vivo expression of PSMA on non-prostatic tissue on ^{68}Ga -PSMA-11 PET/CT. **Materials and Methods:** Clinical records of all the patients who underwent ^{68}Ga -PSMA-11 PET/CT imaging between January 2017 to January 2018, were retrospectively analyzed. All the cases showing atypical/ abnormal extra-prostatic ^{68}Ga -PSMA-11 uptake, not correlating with metastatic involvement and having documented histopathology confirmation were included. ^{68}Ga -PSMA avidity of these sites was assessed using standardized uptake value (SUV) and the sites were classified into neoplastic (benign/ malignant) and non-neoplastic based on the histopathologic features. **Results:** Out of a total of 334 male patients, who underwent ^{68}Ga -PSMA-11 PET/CT imaging during the study period, 69 had atypical PSMA avid sites, out of which histopathologic confirmation was available in 21 patients. Of these 21 patients, 17 had biopsy proved prostate adenocarcinoma while four underwent PET/CT due to elevated serum Prostate specific antigen. 5/21 patients were found to have ^{68}Ga -PSMA-11 uptake in a non-neoplastic entity (Inflammatory mediastinal lymph nodes, intracranial hemorrhage, cerebral infarct, stromal hyperplasia of breast and neurocysticercosis) with mean SUVmax of 5.9 (range:5.3-8.1). 16/21 patients had ^{68}Ga -PSMA-11 uptake in a non-prostatic neoplasm, 4/16 in benign (2-meningioma, paraganglioma, thymoma) with mean SUVmax of 14.5 (range:1.9-25) and 12/16 in malignant entities (Papillary urothelial carcinoma, adenocarcinoma of lung, rectum, stomach, papillary carcinoma thyroid, liposarcoma and breast invasive ductal carcinoma) with mean

SUVmax of 10.6 (range:2.3-25). Difference in SUVmax between neoplastic and non-neoplastic entities was not statistically significant on Mann-Whitney test (U value: 21). **Conclusion:** The present study reaffirms the non specificity of PSMA towards prostatic malignancy. This emphasizes on the need to cautiously interpret atypical/abnormal sites of PSMA uptake rather than instinctively marking them as metastatic prostatic carcinoma and histopathology should be used to solve the diagnostic quandary. This knowledge about non-prostatic ^{68}Ga -PSMA-11 avidity can significantly alter the patient management as is evident in the present study. Few of these cases have been published or accepted for publication. Finally, non-prostatic malignancies showing PSMA expression can be potential candidates for alternate novel theranostics.

EP-0583

Clinical implications of Ga-68-PSMA11-PET/CT scan in patients with very early biochemical relapse of prostate cancer following radical prostatectomy

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Aim: Patients with early biochemical relapse (eBCR) of prostate cancer may harbour potentially curable disease limited to the pelvis or a few treatable distant sites (oligometastases). Ga-68-HBED-CC-PSMA-11 (PSMA11) PET/CT is a recent imaging technique that has the potential to detect localised disease in the eBCR cohort with high sensitivity. The purpose of this study was to determine the sites of relapse identified by PSMA11-PET/CT imaging, and its impact on clinical decision making. **Materials and Methods:** 154 patients with BCR of prostate cancer were referred to our centre for PSMA11-PET/CT between November 2015 and August 2017. After excluding patients who had prostate-specific antigen (PSA) >0.5 ng/ml, had received recent (<12 months) androgen-deprivation therapy (ADT), or had undergone primary radiotherapy instead of radical prostatectomy, we identified 28 patients who underwent primary radical prostatectomy and experienced eBCR (PSA <0.5 ng/ml). Scans were scored for sites of disease and multi-disciplinary meeting (MDM) records were reviewed to access management decisions following PSMA11-PET/CT. **Results:** PSMA11-PET/CT was positive in 16 (57.1%) and negative in 12 (42.9%) cases. Mean PSA levels were similar for PET-positive (0.26 ± 0.1 ng/ml) and PET-negative (0.23 ± 0.15 ng/ml) patients ($p=0.57$). Management decision differed significantly for PET-positive versus PET-negative patients (Fisher's exact test; $p=0.004$). Specifically, 6 of 16 (37.5%) PET-positive patients received metastasis-directed therapy with surgical metastatectomy or ablative cyberknife radiotherapy ($p=0.02$). None of the PET-positive patients was subjected to active surveillance, compared with 7/12 (58.3%) PET-negative patients ($p=0.009$). In contrast, 4/16 (25%) PET-positive patients were started on palliative treatment compared with 1/12 (8.3%) PET-negative patient ($p=0.35$). Salvage radiotherapy (sXRT) was opted with similar frequency in both groups, i.e., 6/16 (37.5%) PET-positive patients versus 4/12 (33.3%) PET-negative versus patients ($p=1$). **Conclusion:** Ga-68-PSMA11-PET/CT had a sig-

nificant impact on decision-making by allowing metastasis-directed treatment in 6/28 (21.4%) patients with eBCR of prostate cancer, thus avoiding the side-effects of sXRT or ADT in these patients. It also assisted triage of patients into active surveillance or palliative treatment based on PSMA11-PET/CT results, whereas equivalent proportions of patients with positive or negative PSMA11-PET/CT imaging underwent sXRT.

EP-0584

Manifestation of coeliac ganglia on ^{68}Ga -PSMA-11 PET enhances the risk of a morphologic MR misinterpretation of them as metastatic lymph nodes on PET/MR imaging

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Objectives: Coeliac ganglia (CG) has been reported to cause pitfalls on ^{68}Ga -PSMA-ligand on PET/CT scans. The aim of this study was to investigate the morphologic features and ^{68}Ga -PSMA-ligand avidity of coeliac ganglia on hybrid PET/MR imaging.

Methods: ^{68}Ga -PSMA-11 whole body PET/MR examinations in 120 patients (mean age 64years; mean dose 169MBq), referred for primary staging or follow-up of prostate cancer, were retrospectively reviewed to investigate the radiotracer uptake (SUVmax) and morphologic features (size, shape and location on T1-weighted and T2-weighted MR images) of the coeliac sympathetic ganglia. The background ^{68}Ga -PSMA-11 activity was measured in gluteal muscles and descending aorta. Nodular (variable in number), nodular-longitudinal, nodular-linear, oval and longitudinal nodular, thick or with oval parts shapes of CG were regarded as mistakable with lymph nodes, whereas linear (regular, irregular, wavy, intermittent or with small nodules) and longitudinal shapes as non-mistakable. **Results:** On MR scans coeliac ganglia were visible in the case of 117 patients out of 120 (98%) on both sides and in the case of 1 patient only on the left side. In the case of 2 patients reliable identification of both CG was not possible neither on MR nor on PET scans, probably due to their extreme thinness. Mistakable with lymph nodes shape on both or at least one side presented 69% (83/120) of patients. The left CG were thicker (1.5-7.5, mean $4\pm 1.4\text{mm}$) than the right ones (0.5-7, mean $3\pm 1.3\text{mm}$). Mean SUVmax was 2.51 ± 1.17 (range 0.02-5.48) in the left CG and 2.23 ± 1.22 (range 0.02-5.91) in the right CG. Increased ^{68}Ga -PSMA-11 uptake, SUVmax above 2 on both or at least one side, was detected in 75% (90/120) of all patients. Both - erroneous shape and elevated ^{68}Ga -PSMA-ligand uptake - was observed in 55% (66/120) of all patients. The majority of CG: 48% (56/117) of the right and 38% (45/119) of the left CG, lied between coeliac trunk (CT) and superior mesenteric artery (SMA) not exceeding their levels. **Conclusions:** the nodular, oval and longitudinal (nodular, thick or with oval parts) shape of coeliac ganglia itself, especially of the thicker left CG, on MR scans may cause mistaking them for metastatic lymph

nodes. On whole body PET/MR imaging evident and sometimes high ^{68}Ga -PSMA-11 uptake in coeliac ganglia increases the risk of a misinterpretation of them as prostate cancer metastases. Coeliac ganglia on in-vivo PET/MR imaging are located lower than it has been presented in most anatomical atlases so far.

EP-0585

68Ga-PSMA PET/CT Interobserver Agreement: Preliminary Results of a Lesion Based and Subregional Comparison Study

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Purpose: 68Ga- prostate-specific membrane antigen (68Ga-PSMA) Positron emission tomography (PET) is an increasingly important imaging tool for detecting local recurrence and extra-prostatic disease in prostate cancer. The purpose of this study is to evaluate the interobserver agreement for 68Ga-PSMA PET/CT study interpretations. **Subjects and Methods:** 68Ga-PSMA PET/CT images of 50 patients with diagnosis of prostate cancer were included in the study (14 with primary diagnosis, 31 with biochemical recurrence and 5 with biochemical persistence after primary therapy). Images were reviewed by two high (>5 years with 18F-FDG PET/CT and >2 years with 68Ga-PSMA PET/CT), and one low (>5 years with 18F-FDG PET/CT but <2 years with 68Ga-PSMA PET/CT) experienced observers. Lesion detectibilities for local (T), nodal (N) and bone (B) involvement and the number of detected lesions for each lymph node regions were analyzed. Lymph nodes were separated into regions as pelvis minor (N-1), pelvis major (N-2), abdominal (N-3), and distant lymph nodes (N-4). Interobserver agreement was determined by Cohens κ and corresponding 95% confidence interval (CI). **Results:** Agreement among observers was substantial for positive versus negative scan results for almost all lymph nodes regions N-2 ($\kappa = 0.77$; $p < 0.001$), N-3 ($\kappa = 1.00$; $p < 0.001$), N-4 ($\kappa = 0.82$; $p < 0.001$) except N-1 ($\kappa = 0.52$; $p < 0.001$). Agreement was substantial to almost perfect for local lesions ($\kappa = 0.91$; $p < 0.001$) and bone involvement ($\kappa = 0.92$; $p < 0.001$). Also agreement among observers was substantial when analyzed the number of detected lymph nodes for separated regions N-1 ($\kappa = 0.78$; 95% CI, 0.62-0.88), N-2 ($\kappa = 0.94$; 95% CI, 0.91-0.97), N-3 ($\kappa = 1.00$; 95% CI, 1.00-1.00), N-4 ($\kappa = 0.97$; 95% CI, 0.96-0.98). **Conclusion:** In prostat cancer, the interpretation of 68Ga-PSMA PET/CT images for local and extra-prostatic lesion detection is consistent among observers with low and high levels of experience. In pelvis minor, evaluation should be done more algorithmically, since experienced and inexperienced observers have relatively lower agreement in the assessment of this region than the other regions.

EP-0586

Artificial Intelligence Based Method for Automated PET/CT Measurements of Prostate Gland Volume and Choline Uptake

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Purpose/Introduction: Artificial intelligence (AI) provides new opportunities for automated image analysis. Uptake of PET tracers in the prostate gland and the size of the gland may serve as guidance for management of patients with prostate cancer. We aimed to develop and validate an AI-based method for analysis of PET/CT studies of the prostate gland. **Subjects & Methods:** The AI-based method included a convolutional neural network trained by means of manually segmented PET/CT studies. The prostate gland and urinary bladder were segmented in the 150 PET/CT scans, by experienced nuclear medicine physicians. A network, taking both the PET and the CT scans as input, was used to delineate the prostate and the urinary bladder in the PET scans and a similar model was trained to delineate the prostate in the CT scans. Based on the resulting delineation in the PET scan the maximum standard uptake value (SUVmax) was calculated. Based on the prostate delineation in the CT scan the prostate gland volume was calculated. After training, the AI-based method was applied to a study group comprising 52 prostate cancer patients, who had undergone 18F-choline PET/CT prior to radical prostatectomy. Forty-five of these patients were operated within three months of the PET/CT study. The weight of the prostatectomy specimens after removal of the seminal vesicles were compared to the corresponding prostate gland volumes measured automatically in the CT studies. A nuclear medicine specialist recorded “manually” SUVmax in the prostate gland in all PET/CT studies for comparison with the corresponding automatically derived SUVmax scores. **Results:** The processing time with the AI-based method was less than one minute. The prostate weight was on average 50g (SD 19g) in the 45 patients with a prostatectomy less than 90 days after the PET/CT scan. The average volume of the prostate gland automatically measured from the CT studies was 63mL (SD 19mL). The correlation between prostate weight and the automated prostate volume measurements was 0.77. SUVmax was on average 7.5 (SD 3.1) and the manual and automated SUVmax measurements were the same in 49 of the 52 patients. **Discussion/Conclusion:** Our AI-based method for fast automated analysis of the prostate gland in PET/CT studies showed good agreement with manually obtained SUV measurements and pathology-derived weight of the prostatectomy specimens suggesting that this approach may become a promising adjunct to quantitative assessment of PET/CT studies in prostate cancer patients.

EP-0587

⁶⁸Ga-PSMA-11 PET/CT in assessment of prostate cancer patients - comparison with ¹⁸F-Choline PET/CT with regard to patient's management and therapy monitoring

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Aim: ⁶⁸Ga-PSMA-11 PET/CT is introduced as promising imaging in assessment of prostate cancer (PCa). ¹⁸F-fluoromethylcholine (¹⁸F-FCH) has been widely used in patients with recurrent PCa. This study compared the value of ⁶⁸Ga-PSMA-11 with ¹⁸F-FCH PET/CT in primary and recurrent Pca patients especially with regards to pattern of tracer uptake, patient's management and therapy monitoring. **Material & Methods:** Twenty-nine patients with PCa (mean age: 68.8±7.4) who underwent both imaging modalities within 30 days either in primary staging (n=11 Pts.) or recurrent disease (n=18 Pts.) were included in this study. Pathologic lesions were classified in 3 anatomical sections of local disease, lymph node metastases (LNM) and bone metastases (BM). Pathologic imaging findings have to be clarified histopathologically or by other imaging modalities and/or clinical follow-up. **Results:** Mean of PSA level was 32.2 ±23.8 ng/ml (range: 5.0 - 81.0 ng/ml) and 3.46±860 ng/ml (range: 0.21 to 3133.0 ng/ml) in staging and recurrent group, respectively. Overall 145 lesions (16 local, 69 LNM and 60 BM) were analyzed on both ⁶⁸Ga-PSMA-11 with ¹⁸F-FCH PET/CT. Significantly higher SUVmax was seen on ⁶⁸Ga-PSMA-11 comparing to ¹⁸F-FCH PET/CT in all 3 anatomical localizations (p<0.001). However, it has not led to change in patient's management in staging group. In recurrent group discordant findings were found between 2 imaging modalities in 3 groups of patients which led to change in patient's management: 1. Patients with recurrent disease and low PSA level of <0.5 ng/ml under anti-androgen therapy (ADT) (n=3 Pts.) in whom ¹⁸F-FCH PET/CT were negative; however, ⁶⁸Ga-PSMA PET/CT was able to detect local recurrence (n=1 Pts.) and LNM (n=2 Pts.). 2. Patients clinically defined as responders under ADT (n=7 Pts.) who underwent both imaging modalities for therapy monitoring in whom ⁶⁸Ga-PSMA PET/CT was clearly superior providing more reliable findings with significantly higher SUVmax (mean: 19.8±12.9, p=<0.01) comparing ¹⁸F-FCH PET/CT (mean SUVmax: 10.8±3.4) in both LNM and BM. ADT seems to affect the ¹⁸F-FCH uptake in this group of patients. 3. Hormone refractory patients with clinically evidence of progressive disease under ADT (n=4 Pts.) in whom ¹⁸F-FCH PET/CT was able to detect additional LNM (n=1 Pts.) and BM (n=3 Pts.) which were unremarkable on ⁶⁸Ga-PSMA PET/CT. **Conclusion:** ⁶⁸Ga-PSMA PET/CT showed superior results to ¹⁸F-FCH PET/CT with higher detection rate particularly in primary staging, therapy monitoring and recurrent disease in patients with low PSA. ¹⁸F-FCH PET/CT seems to be superior especially in assessment of BM in hormone refractory PCa patients with clinical evidence of disease progression under ADT. However, further studies are warranted.

EP-0588

Does fluorescence imaging provide sufficient surgical guidance or is preoperative imaging required? A blinded study in prostate cancer patients

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Introduction: Despite its increasing popularity, fluorescence guided surgery imaging is severely handicapped by tissue induced signal attenuation that limits the signal penetration (<1cm). The superficial nature of this modality, when using as primary imaging tool, could convert into an underestimation of the number of targets that have to be surgically removed. This theoretical shortcoming was the basis for the clinical introduction of dual-modality/ hybrid tracers. To for-the-first-time quantitatively document the detection limits of fluorescence imaging in clinical sentinel node (SN) trials, we performed a randomized and partially blinded comparison between pre-operative (nuclear medicine) and intraoperative (fluorescence based) findings. **Subjects & Methods:** 27 Patients scheduled for robot-assisted prostatectomy, receiving SN dissection and extended lymphadenectomy (ePLND), were randomized between a single injection of the hybrid tracer ICG-^{99m}Tc-nanocolloid (group 1) or two separate injections using ^{99m}Tc-nanocolloid and “free” ICG (group 2). Prior to surgery lymphoscintigraphy and SPECT/CT were used to non-invasively map the SN templates. During the nodal excision the surgeon was initially blinded for the preoperative imaging data and had to rely on fluorescence guidance alone. Subsequently the preoperative imaging data was presented and the SNs missed were removed. **Results:** The different SNB techniques did not yield a significant difference in the amount of harvested SNs (mean 8.4 versus 9.3, $p=0.782$) and ePLND LNs (mean 12.2 versus 13.8, $p=0.466$). In 14 of the 27 patients (52%), one or more radioactive SNs could not be resected under fluorescence guidance only; SPECT/CT findings were needed to isolate the anatomical location of SNs and dissect them. In 6 patients (20%; 18 SNs) remained in situ because the SPECT/CT images indicated that resection could lead to surgical complications. **Conclusion:** Fluorescence imaging alone does not provide reliable surgical guidance and demands the addition of preoperative imaging, in this case SPECT/CT, for accurate execution of the surgical procedure. With this study a clear warning is issued for the use of fluorescence as primary modality in surgical guidance.

EP-0589

Neutrophil/Lymphocyte and Platelet/Lymphocyte Rates Can Foresee Bone Metastasis in Prostate Cancer Patients?

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Introduction: Bone metastasis is common in advanced prostate cancer cases, pathologic bone fractures and bone pain caused by these metastases affect the quality of life of patients. It is noted that inflammatory markers such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and

neutrophil to monocyte ratio (NMR) may be prognostic biomarkers in solid tumors in recent years. Our aim is evaluate the relation between NLR, PLR, NMR and bone metastases detected in scintigraphy in cases with prostate cancer. **Methods:** Between March 2015 and January 2017, 85 patients with bone scintigraphy due to prostate cancer were included. The age of the patient, prostate-specific antigen (PSA) values, Gleason score, histopathologic features, presence of metastatic focus on bone scintigraphy and complete blood count were retrospectively studied. Bone scintigraphic images were obtained with a dual-headed gamma camera (Infinia II GP & Hawkeye 4) by obtaining whole body static images from the anterior and posterior projections. Neutrophil, lymphocyte, thrombocyte counts were measured with automatic blood counting analyzer (Dyn Ruby Cell, ABBOTT, USA). Patients were divided into two groups according to the median values of NLR, PLR and NMR. The relationship between clinicopathological features such as PSA, Gleason score, periprostic invasion, surgical margin positivity, seminal vesicle invasion, perineural invasion, bone scintigraphy with and without metastatic findings and median NLR, PLR and NMR were evaluated. Chi square test was used for statistical analysis ($p < 0.05$, significant). **Results:** The ages of 85 male patients who met the study criteria ranged from 52 to 86 years. The mean age of the patients was 68.5 ± 8.58 . Median NLR, PLR and NMR were 2.90, 125.69 and 8.38 respectively. When the relationship between NLR, PLR, NMR with bone scintigraphic findings and clinicopathologic features such as, PSA, Gleason score, extraprostatic invasion, seminal vesicle invasion, surgical border positivity and perineural invasion were analyzed, a statistically significant relationship was found between high NLR value and presence of scintigraphic bone metastasis ($p: 0.018$, table 1) and high Gleason score ($p: 0.034$). There was no significant statistical correlation between PLR and NMR and clinicopathologic features ($p > 0.05$). **Conclusion:** We present a significant relationship between high NLR and bone metastasis in patients with prostate cancer in our study. Although there are studies that suggest that NLR is an independent risk factor for prostate cancer prognosis, we think that its possible prognostic contribution can be determined by more extensive and detailed studies in this patient group.

EP-0590

Comparison of PET and DWI images in the detection of bone metastasis of prostate cancer in Ga-68 PSMA PET / MR

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Aim: In this retrospective study we aimed to compare PET and DWI images in the detection of bone metastases in prostate cancer patients who under-

went Ga-68 PSMA PET / MR. **Materials & Methods:** A retrospective analysis of 23 Ga-68- PSMA PET/MRI (1 h after injection) of prostate cancer patients was performed. MRI sequences involved T1W, STIR, and diffusion-weighted images (DWI-b:1000). Two readers separately (nuclear medicine and radiology physician) assessed both datasets regarding characterisation of bone lesions (negative, suspicious, positive). Both patient based and lesion based analysis were performed (maximum 10 lesion/patient). All bone lesions were also compared with CT, if present. **Results:** On patient-based analysis, we observed at least one abnormal lesion in 11 of 23 patients using both PET and DWI images. Among 64 lesions, that were detected using both imaging, 3/64 were negative and 61/64 were positive with PET; whereas DWI was negative in 12/64, suspicious in 2/64 and positive in 50/64 lesions. Among 12 lesions, that were PET positive and DWI negative; 10 of them had an additional CT scan, which confirmed sclerotic metastasis in 7 lesions and traumatic bone fractures in the rest of them. Re-evaluation of the DWI images of the remaining 2 lesions that were initially scored as PET positive and DWI negative were noticed to be positive on DWI images. Only one lesion was DWI positive and PET negative and additional CT image confirmed the presence of degenerative discopathy. Two bone lesions that were negative with PET and suspicious in DWI were confirmed to be false positive on CT. PET sensitivity, specificity, accuracy, PPV and NPV were 100%, 50%, 95%, 95% and 100%, respectively. Diffusion-weighted image sensitivity, specificity, accuracy, PPV and NPV were 84%, 50%, 81%, 94% and 25%, respectively. **Conclusion:** PSMA PET has higher sensitivity, accuracy and NPV in terms of bone metastasis detection compared to DWI.

EP-0591

Response assessment with ⁶⁸Ga-PSMA PET/CT in metastatic castrate resistant prostate cancer patients treated with Radium-223. Preliminary results

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Introduction: Response assessment in prostate cancer (PCa) patients treated with Radium-223 is challenging as PSA values can increase in responding patients and conventional imaging techniques (CIT) including bone scan and computed tomography are limited by the flare phenomena in bone lesions. Consequently there is a need for better response assessment tools. ⁶⁸Ga-PSMA is an oncotrophic PET-tracer which has shown promising results depicting PCa metastases. Moreover, it has recently been proposed as a response assessment tool for docetaxel. The aim of our study was to evaluate if ⁶⁸Ga-PSMA PET/CT can be used as a tool for response assessment in mCRPC treated with Radium-223. **Material and Methods:** This is a retrospective analysis of 11 progressive mCRPC patients treated in our institution with ²²³Ra-dichloride (55kBq/kg) between January 2016 and March 2018. Follow-up evaluation was performed at baseline, 3 cycles (interim) and end-of-treatment (EoT). Patients were classified as having progressive disease (PD), stable disease (SD), partial re-

sponse (PR) or complete response (CR) based on three different response tools: 1) clinical evaluation (CE) including pain score, performance status, blood test, tumor markers PSA and ALP, as done in routine clinical practice; 2) CIT following PCWG3 criteria (Scher et al JCO2016) and 3) ⁶⁸Ga-PSMA PET/CT using adapted PERCIST criteria (PR: decrease SUVmean≥30%; PD: new lesions or increase SUVmean≥30%; SD: SUVmean change<30%; CR: no lesion). Proportion of patients in each group and concordance of response between the three different response tools was measured taking CE as the standard reference. **Results:** All 11 patients received at least 3 cycles of Radium-223. 6/11 presented PD at interim-CE and stopped treatment, while 4/11 (36%) presented PR and 1/11 SD, continuing treatment. EoT-CE presented PD in 10/11 (90%). Interim-PET showed PD in 9/11 (73%) and PR in 2/11 (18%). EoT-PET: PD in 10/11 and 1 PR. Interim-CIT presented PD in 6/11 (55%) and SD in 5/11 with no changes at EoT. Concordance between CE and PET was found in 8/11 (73%) at interim and in 11/11 (100%) at EoT. Concordance between CE and CIT was found in 36% (4/11) at interim and 6/11 (55%) at EoT. Concordance between interim-PET and EoT-CE was found in 10/11 patients (91%). **Conclusion:** This study suggests that ⁶⁸Ga-PSMA PET/CT might be a promising tool for response assessment of mCRPC treated with Radium-223, better than CIT. Interim PET at 3 cycles seems to predict response at EoT. Future prospective studies are needed to confirm these encouraging preliminary findings.

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Bone scan activity concentration in prostate cancer bone metastases predicts response to Ra-223Cl₂-therapy: a SPECT/CT study

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Rationale: Assessing the prognostic significance of intensity of bone uptake in metastatic castration-resistant prostate cancer (mCRPC), which are to be treated with ²²³RaCl₂, is challenging. In fact, intense uptake or "superscan" on pretreatment bone scintigraphy was shown to be associated with poor survival after ²²³RaCl₂ therapy. On the other hand, high uptake of tumor lesions would be expected to be associated with high irradiation dose and thus favorable antitumoral effect. In this study, we applied a computational software analysis to bone scan SPECT/CT images to identify osteoblastic activity in bone metastases and normal bone and correlated findings to treatment response. **Methods:** 76 mCRPC patients, treated with ²²³RaCl₂ therapy, were retrospectively enrolled. Patients who were not able to complete 6 cycles of ²²³RaCl₂ therapy were excluded. Each patient underwent a whole-body bone SPECT/CT (^{99m}Tc-DPD) for baseline staging. This scan was analyzed with a segmentation analysis software, which identified bone volumes occupied by metastases (mVol) and the normal trabecular bone (bVol) to calculate mean activity concentration within these compartments.

A second SPECT/CT was carried out after completion of therapy: patients with newly evolved bone lesions were classified as having progressive disease (PD), clearly diminished uptake in known metastases was considered partial response (PR) with the remaining findings classified as stable disease (SD). **Results:** PR was achieved in 20/76 cases while SD or PD was observed in 35 and 21 cases, respectively. At baseline, mean counts in mVol of PD patients were significantly lower when compared to the other two groups (715 ± 190 , 1058 ± 255 and 975 ± 215 mean counts, for PD, SD, and PR, respectively, $p < 0.01$). The same pattern (lower mean counts in PD patients) was observed in bVol (275 ± 60 , 515 ± 188 and 975 ± 215 $p < 0.001$). **Conclusions:** High uptake of bone metastatic lesions and normal trabecular bone appears to be associated with therapeutic response in patients able to receive a complete course of $^{223}\text{RaCl}_2$. Further evaluation will elucidate whether this uptake/response relationship translates into favorable survival.

EP-0593

Uptake In Non-affected Bone Tissue Does Not Differ Between [^{18}F]-DCFPyL And [^{68}Ga]-HBED-CC PSMA PET/CT

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Purpose: [^{68}Ga]PSMA-HBED-CC and [^{18}F]DCFPyL have demonstrated high potential for the detection of recurrent prostate cancer. While ^{18}F -based tracers have several advantages with respect to availability and image resolution, sensitivity in the skeleton might be lower in comparison to ^{68}Ga -based tracers due to high bone affinity of [^{18}F]fluoride released from [^{18}F]DCFPyL. In turn, chemically unbound trivalent ^{68}Ga might also exhibit high binding affinities to bone structures and thereby influence bone signal. **Methods:** An analysis of average bone SUV was performed using a tool for automated bone tracer uptake-assessment (EBONI) in 17 patients who underwent PET/CT with both [^{68}Ga]PSMA-HBED-CC and [^{18}F]DCFPyL and did not have any skeletal lesions. Native bone SUVs, and SUVs relative to background uptake in gluteal muscles and liver were compared with paired T-test and Wilcoxon signed rank test. **Results:** Native SUVs in unaffected bone tissue and SUVs relative to liver uptake were lower in [^{18}F]DCFPyL (0.49) than in [^{68}Ga]PSMA-HBED-CC scans (0.52). SUVs relative to gluteal muscles did not differ between the two tracers. **Conclusion:** No increase of average bone signal intensity was observed for [^{18}F]DCFPyL -PET/CT in comparison to [^{68}Ga]PSMA-HBED-CC scans. This indicates that diagnostic assessment of the skeleton does not appear to be affected by non-specific accumulation of released [^{18}F]fluoride or trivalent ^{68}Ga .

EP-0594

^{18}F -DCFPyL PET/CT in Primary Staging of Prostate Cancer

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Purpose: Correct primary staging is mandatory for therapy selection and to determine prognosis in prostate cancer patients.

Commonly used cross-sectional imaging procedures including CT, MRI and Choline PET/CT and extended lymph node dissection (ePLND) have suboptimal diagnostic accuracy for primary staging. PSMA targeting radiopharmaceuticals have shown better diagnostic accuracy than commonly used imaging procedures. This study presents data of a retrospective cohort of patients that received PET/CT with ^{18}F -DCFPyL for staging of primary prostate cancer. **Material and Methods:** From November 2016 all consecutive patients that received ^{18}F -DCFPyL PET/CT for primary staging of prostate cancer were included in the study. Detection rates of metastases were calculated for different clinical parameters, including PSA, Gleason score, clinical T-stage and risk on having lymph node metastases according to MSKCC nomograms and ROACH formula. Subsequently ^{18}F -DCFPyL PET findings were compared to CT and extrapolated to ePLND. **Results:** One hundred thirty-three patients were analysed. In 69 patients suspicious lymph nodes were detected with ^{18}F -DCFPyL of which 59% and 29% showed no suspected lesions on CT, for locoregional and distant sites, respectively. In 43% of patients ^{18}F -DCFPyL PET/CT detected lesions suspicious for metastases outside the ePLND area. ^{18}F -DCFPyL PET/CT detection rates show great similarities in comparison to established prediction models of risk on lymph node metastases. **Conclusion:** This study shows that ^{18}F -DCFPyL PET/CT has clinical impact in primary staging of prostate cancer. Large prospective trials that compare ^{18}F -DCFPyL findings with histopathological findings after ePLND are needed in order to position ^{18}F -DCFPyL PET/CT in the staging algorithm for primary prostate cancer.

EP-0595

Comparison of Ga-68 PSMA PET/CT and Ga-68 PSMA PET/MRI with biparametric prostate MRI in terms of location and extension of primary prostate gland tumour

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Aim: Ga-68 PSMA PET/CT is an effective imaging tool for detection of lymph node and organ metastasis in prostate cancer patients. However, it has limited efficacy in the detection of presence and extension of primary prostate gland lesions and local recurrence, due to both poor anatomical resolution compared to PET/MRI and intense nearby bladder activity. We aim to compare Ga-68 PSMA PET/CT with PET/MRI including bi-parametric prostate MRI (bpMRI) in terms of detection of the site and extension of prostate gland tumours. **Material and Methods:** All patients had sequential Ga-68 PSMA PET/CT and PET/MRI involving bpMRI sequences of the prostatic bed including T1-weighted (T1W), T2-weighted (T2W) and focus diffusion weighted imaging (DWI) ($b=50$ -400-800 and $b=50$ -1400) and ADC mapping. PET/CT images were compared to PET/MRI involving bpMRI in

terms of localisation and extension of prostate lesions. All images were recorded on a prostate scheme and scored according to imaging agreement: Score-1=total agreement, score-2=mostly in agreement, score-3=poor agreement, score-4=disagreement.

Results: Among 28 prostate cancer patients included, no prostate lesion was detected in any of the imaging modalities in 6 patients (score-1). Comparing PET/CT and PET/MRI, among 22 patients with positive lesion, 16 were score-1, 4 were score-2 and 2 were score-3. In one of the score-3 patients, PET/CT underestimated the real extension of the primary tumour, which involved whole right lobe both in PET/MRI and bpMRI. In the other score-3 patient, urinary activity obscured the tumoral uptake on PET/CT, resulting in underestimation of the tumor involvement. Among score-2 patients, 2 had additional false-positive uptake on PET/CT, that was absent on PET/MRI or bpMRI, probably due to scatter artefact. In a score-2 patient, PET/CT overestimated the size of the prostate lesion compared to PET/MRI and bpMRI. In another score-2 patient, uptake on PET/CT was confirmed to be false-positive uptake of BPH nodules on PET/MRI. **Conclusion:** Due to better anatomical correlation, Ga-68 PSMA PET/MRI together with bpMRI, can more accurately delineate prostatic lesions compared to Ga-68 PSMA PET/CT.

EP-0596

¹¹C-choline Predicts Survival In Prostate Cancer Patients With PSA < 1 ng/mL

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Purpose: The main drawback of ¹¹C-choline PET/CT for restaging prostate cancer (PCa) patients with biochemical failure is the low positive detection rate for prostate specific antigen (PSA) < 1 ng/mL. This study was performed to assess whether ¹¹C-choline PET/CT predicts PCa survival for PSA < 1 ng/mL.

Methods: We retrospectively reviewed ¹¹C-choline PET/CT scans performed at the Department of Nuclear Medicine, IRCCS San Raffaele Scientific Institute, Milan, Italy on PCa consecutive patients treated with radical prostatectomy from December 1st, 2004 to July 31st, 2007 and with PSA < 1 ng/mL at time of PET/CT. Primary outcome variables were estimates of survival probabilities, as determined by Kaplan-Meier curves, and the association between covariates of interest and survival rates as identified by Cox-regression analysis. **Results:** Median follow-up after radical prostatectomy was 6.9 years (95% confidence interval, CI, 2.0-14.5 years). ¹¹C-choline PET/CT was positive in 20.5% of patients. Median PCa-specific survival was 13.4 years (95% CI, 9.9-16.8 years) in patients with positive ¹¹C-choline PET/CT and it was not achieved in patients with negative ¹¹C-choline PET/CT (Log-Rank, Chi-Square=15.0, P<0.001). 10-year survival probabilities for patients with positive ¹¹C-choline PET/CT and with neg-

ative ¹¹C-choline PET/CT were 86.0% (95% CI: 80.7%-91.3%) and 63.6% (95% CI: 54.5-72.7%) respectively. At multivariate analysis, only ¹¹C-choline PET/CT significantly predicted PCa-specific survival (hazard ratio=2.54, 95% CI, 1.05-6.13, P=0.038). Patients with pathological ¹¹C-choline uptake in the prostatic bed or in pelvic lymph nodes had longer PCa-specific survival in comparison to patients with pathological tracer uptake in the skeleton (Log-Rank: Chi-Square=27.4, P<0.001). Study limitation is the retrospective design. **Conclusion:** The role of ¹¹C-choline PET/CT for detection recurrent disease and PSA < 1 ng/mL is debated. Our data show that ¹¹C-choline PET/CT predicts survival in this low PSA range. As long as more sensitive radiotracers, such as ⁶⁸Ga-PSMA-11, do not become more widely available, these results might support a broader use of radiolabeled choline in restaging PCa for PSA < 1 ng/mL.

EP-0597

¹⁸F-Fluciclovine for the detection of patients with suspected biochemical recurrence of prostate cancer: results of a single center

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Purpose/Introduction: Early and accurate detection of the extent of local recurrence and of regional/distant metastases in biochemical recurrence (BCR) of prostate cancer can inform therapy decisions when tumours are small and most amenable to localized therapy. ¹⁸F-Fluciclovine is a synthetic amino acid positron emission tomography (PET) radiotracer that is EMA- and FDA-approved for use in the detection of BCR of prostate cancer based on its encouraging histologically-confirmed diagnostic performance. Here, we report the experience from our clinic in evaluating the utility of ¹⁸F-Fluciclovine PET/Computed Tomography (PET/CT) for the detection of lesions across a range of prostate-specific antigen (PSA) levels in patients with suspected BCR of prostate cancer. **Subjects and Methods:** Data were obtained at the Catharina Cancer Institute, Eindhoven, Netherlands. Scans were conducted and images were interpreted according to standardized procedures. The most recent PSA measurement before the ¹⁸F-Fluciclovine PET/CT took place was recorded as the baseline PSA level for each patient. Detection rates (the proportion of scans containing one or more area considered positive for cancer) were stratified by baseline PSA levels and were also determined for the subject as well as regional levels. **Results:** Between February 2017 and April 2018, 105 patients were scanned. Mean age was 72 years (range 59-87) and mean PSA level was 7.05 ng/mL (range 0.11-47 ng/mL). 7 patients (6.67%) had a baseline PSA between 0.1 and 0.2 ng/mL, 10 patients (9.52%) >0.2-0.5, 7 patients (6.67%) >0.5-1.0, 9 patients (8.57%) >1.0-2.0, 33 patients (31.43%) >2.0-5.0, and 39 patients (37.14%) had a PSA level >5.0 ng/mL. ¹⁸F-Fluciclovine PET/CT detected lesions in 76 patients (76.8%); lesions were detected in the prostate/prostate bed and in pelvic lymph nodes in 47 and 35 patients (47.5% and 35.4%), respectively. Metastatic

ic involvement outside the pelvis was detected in 21 patient scans (21,2%), while 17 scans (17,2%) showed lesions in skeletal sites. Generally, the detection rate increased with increasing baseline PSA, with detection rates of 28,6%, 70%, 28,6%, 44,4%, 81,8% and 92,3% among patients with baseline PSA levels in the range 0.1–0.2, >0.2–0.5, >0.5–1.0, >1.0–2.0, >2.0–5.0, and >5.0 ng/mL, respectively. **Discussion/Conclusion:** In line with previous studies, ^{18}F -Fluciclovine was able to sensitively detect BCR of prostate cancer, even at PSA levels ≤ 0.5 ng/mL. ^{18}F -Fluciclovine PET/CT shows utility for the detection of disease in the prostate/bed, as well as in extraprostatic tissue and bone.

EP-0598

68Ga-PSMA-11 PET/CT-derived Metabolic Parameters For Determination Of Whole-body Tumor Burden And Treatment Response In Prostate Cancer

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Purpose: We aimed at evaluating the role of 68Ga-PSMA-11 PET/CT-derived metabolic parameters for assessment of whole-body tumor burden and its capability to determine therapeutic response in patients with prostate cancer. **Methods:** A total of 142 patients with biochemical recurrence of prostate cancer underwent PET/CT with [68Ga]Ga-PSMA-HBED-CC (68Ga-PSMA-11). Quantitative assessment of all 641 68Ga-PSMA-11-positive lesions in the field-of-view was performed to calculate PSMA-derived parameters, including whole-body PSMA tumor volume (PSMA-TV) and whole-body total lesion PSMA (TL-PSMA), as well as the established SUVmax and SUVmean values. All PET-derived parameters were tested for correlation with serum PSA levels and for association with Gleason scores. In 23 patients who underwent 68Ga-PSMA-11 PET/CT before and after therapy with either external beam radiation, androgen deprivation, or docetaxel chemotherapy, SUVmax and TL-PSMA were compared to radiographic response assessment of CT images based on RECIST 1.1 criteria and to biochemical response determined by changes of serum-PSA levels. **Results:** PSMA-TV and TL-PSMA demonstrated a significant correlation with serum PSA-levels ($P < 0.0001$) and TL-PSMA was significantly different for different Gleason scores. The agreement rate between TL-PSMA derived from PET and biochemical response was 87% (95% confidence interval, 0.66–0.97) (Cohen's $\kappa = 0.78$; $p < 0.01$) and, thus, higher than for SUVmax, which was 74% (95% CI, 0.52–0.90) ($\kappa = 0.55$; $p < 0.01$). Furthermore, agreement to PSA was higher for TL-PSMA and SUVmax, than for CT-based response evaluation. Discordant findings between PET and CT were most likely due to limitations of CT and RECIST in rating small lymph nodes as metastases, as well as bone involvement, which was sometimes not detectable in CT. **Conclusion:** 68Ga-PSMA-11 PET/CT derived metabolic tumor parameters showed promising results for evaluation of treatment response. Especially TL-PSMA demonstrated higher agreement rates to biochemical response, compared to SUVmax. Larger, ideally prospective trials are needed to help to reveal the full potential of metabolic parameters derived from PET imaging with 68Ga-PSMA-11.

EP-0599

Localization And Restaging Of Carcinoma Prostate By 68Ga PSMA PET/CT In Patients With Biochemical Recurrence

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Introduction: Prostate cancer is the most common solid cancer in men. Its incidence increases with age and thus is a major health concern for the ageing population of the developing world. Following definitive treatment of prostate cancer by radical prostatectomy (RP) or radiotherapy, cancer recurrence is heralded by an increase in serum prostate-specific antigen (PSA) which is called biochemical recurrence. Depending on the patient population studied, 15–40% of patients experience rising serum PSA levels. Determining whether recurrence is local, regional (pelvic) or distant (outside the pelvis) is critical when considering appropriate further treatment options. Early localization of disease recurrence after definitive treatment of prostate cancer is vital to determine suitability for salvage treatment. **Aim:** To investigate the relationship between prostate specific antigen (PSA) level and detection of suspected cancer recurrence using 68 Ga-PSMA PET/CT in patients with biochemical recurrence after radical prostatectomy (RP) or radiotherapy. **Methods:** We prospectively analyzed retrospective data of men with carcinoma prostate post RP and post radiotherapy with biochemical recurrence from May 2014 to Jan 2018 by 68 Ga-PSMA PET/CT. We included men with suspected recurrent prostate cancer based on an elevated post treatment PSA level. The data collected analyzed the relationship of the pre-scan PSA level to the probability of a positive scan finding for recurrent prostate cancer. **Results:** Our cohort included 150 men, all had adenocarcinoma of prostate, 124/170 had a previous RP and 46/170 had prior radiotherapy. The median PSA of the RP group was 1.8 ng/mL and 5.6 ng/mL in the radiotherapy group. In the post RP cohort, the detection rate of 68 Ga-PSMA PET/CT was 39.3% for PSA 0.2 to <0.5 ng/mL, 45.3% for PSA 0.5 to <1 ng/mL, 72.0% for PSA 1 to <2 ng/mL and 89.5% for PSA ≥ 2 . Lymph node metastasis post RP was identified in 67% of men with suspected disease recurrence. In the post radiotherapy cohort the detection rate was 96.1 % for PSA 2 to 4 ng/mL, 99.2% for PSA 4 to 6 ng/mL and 100% for PSA ≥ 6 . Local recurrence after radiotherapy was present in 62 % of the cohort and 58 % had lymph node metastasis. **Conclusions:** 68Ga-PSMA PET/CT provides a novel imaging modality for the detection of prostate cancer recurrence and metastasis. Suspected PSMA avid metastatic lesions are common and are identified at low post treatment PSA levels, which if detected will help direct appropriate salvage treatment.

EP-0600

Utility of [^{11}C]-acetate PET/CT for prediction of prostate-cancer specific survival in patients with biochemical relapse after radiation therapy

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Purpose: [^{11}C]-acetate PET/CT is clinically used for localizing biochemical relapse of prostate cancer (PCa) after primary treatment and is a strong predictor of survival at relapse after prostatectomy. The long-term predictive value in patients treated with radiation therapy (RT) is not known. This study analyzed the prognostic value of [^{11}C]-acetate PET/CT and evaluated PET image metrics in relation to survival. **Methods:** All patients with documented PSA-relapse after previous RT alone or in combination with adjuvant therapy undergoing [^{11}C]-acetate PET/CT in one institution were retrospectively evaluated and clinical data were recorded. All previously reported findings of local recurrence, regional or distal lymph node metastases and bone metastases were counted. [^{11}C]-acetate PET/CT scans were evaluated regarding [^{11}C]-acetate uptake intensity (SUVmax) and tumor volume (TV). Total TV and total lesion activity (TLA; sum of SUVmax $\times$ TV) of all PET positive lesions in each patient were calculated. Survival analysis in the entire material by categorizing the patients into tertiles of PET image metrics was followed by Cox-proportional hazard ratios (HR) analysis. **Results:** Ninety-nine patients were included, and 37 PCa-specific deaths were registered. PET/CT identified at least one PET-positive lesion in 87% ($n=86$) of patients. PSA at time of PET was 10.98 ± 13.68 (mean $\pm$ SD). Five-year PCa-specific survival was 71% and 91% for a positive and negative PET, respectively ($p=0.09$). Univariate HR was significantly increased for Gleason score (1.74, $p<0.01$), PSA at time of scan (1.02, $p=0.02$), tertile of TTV (3.43, $p<0.01$), tertile of TLA (2.01, $p<0.01$), number of distal lymph node metastases (1.32, $p=0.002$) and number of bone metastases (1.13, $p=0.01$). In a multivariate model the strongest predictor was tertile of TTV (HR 9.24, $p<0.001$), followed by Gleason score and age. Five-year PCa-specific survival was 94, 80 and 31% for each TTV tertile ($p<0.001$). PSA at time of scan was not independently predictive of outcome and showed moderate but significant correlation ($p=0.51$, $p<0.001$) with all PET volumetrics. **Conclusion:** [^{11}C]-acetate PET/CT may predict survival in the setting of PSA relapse after RT. Total acetate-avid tumor volume was the strongest predictor of survival in this study.

EP-0601

68Ga-PSMA-11 PET/CT and salvage radiotherapy in patients with very low PSA after radical prostatectomy

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Purpose: To evaluate the role of 68Ga-PSMA-11 PET/CT (PSMA-PET) in salvage radiotherapy (SRT) in a cohort of patients with very low PSA after radical prostatectomy (RP). **Methods:** Enrolling criteria of our retrospective single-centre study (March 2016 - February 2018) were: a) prostate cancer (PC) treated with PR; b) PSA values comprised between 0.2 and 0.5 ng/mL at the time of PSMA-PET and c) eligibility for SRT. SRT treatment re-

sponse was defined as PSA ≤ 0.1 ng/mL. When available, the mean clinical follow-up time was 13 months (range 6-22). Student's t-test, Pearson's chi-squared test and logistic regression were employed to estimate factors associated with the post-SRT treatment response. **Results:** A total of 114 patients fulfilled these criteria (mean age 66 years) and 50/114 (43.9%) underwent SRT after performing PSMA-PET. Mean PSA value before PSMA-PET was 0.3 ng/mL (median 0.3). PSMA-PET resulted positive in 19/114 (16.7%) and among these 11/114 (9.6%) underwent SRT and subsequent clinical follow-up. 4/114 (3.5%) had a systemic spread of disease. The mean PSA values post-SRT were significantly different ($p=0.036$) between patients where SRT covered all PSMA-positive lesions 6/36 (16.7%) and patients where SRT did not cover all PSMA-positive lesions in 5/36 (13.9%). Among PSMA-negative scans, 25/114 (21.9%) underwent SRT and clinical follow-up. Treatment response was reached in 19/25 (76.0%) of which 4 on ADT. A slightly significant difference between PSA post-SRT and histological N stage was found in patients which performed PLND both in positive and negative PSMA-PET scans ($p=0.08$). On logistic regression none clinical parameters significantly correlated with treatment response. In patients eligible for SRT with a negative PSMA-PET, avoiding SRT increase the risk of an increased PSA (odds ratio 2.118; 95%CI=1.499-2.991). **Conclusions:** 68Ga-PSMA-11 PET/CT may play a role in patients with very low PSA after RP addressing patients with a negative scan to a SRT whereas patients with PSMA-positive scan should consider a SRT covering all detected lesions and/or other metastases-directed therapies if feasible.

EP-0602

Complementary role of diffusion weighted imaging and PSMA-PET in PET/MRI of recurrent prostate cancer

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Introduction: PSMA-PET has demonstrated markedly superior performance compared to morphologic imaging for the localization of tumor lesions in biochemical recurrent prostate cancer. However, as is known from histologic studies, 20% of primary prostate cancers cells and a substantial number of metastases do not overexpress PSMA and therefore may be undetectable by PSMA-PET. Diffusion-weighted MRI (DWI) is an evolving method, which has shown good sensitivity in the detection of lymph node metastases of prostate cancer. However, the positive predictive value of the method has been shown to be limited. With the introduction of combined PET/MRI systems, PSMA-PET and DWI can be performed simultaneously together with standard MRI sequences for morphological assessment. We hypothesized that adding DWI to a PSMA-PET/MRI protocol, would result in the detection of additional PSMA-negative lymph node metastases, thereby improving overall performance of PET/MRI. **Methods:** 43 patients with biochemical recurrence of prostate cancer (median PSA level 3.9 ng/ml),

without prior systemic treatment underwent PSMA-PET/MRI, including DWI of the abdomen and pelvis. PSMA-PET and DWI images were evaluated side by side for positive lymph nodes. Lesions were categorized as positive in PSMA, DWI or both. Assessment of lesion growth in morphologic imaging was used as the reference standard. DWI positive but PSMA negative lymph node lesions that showed an increase in size were categorized as PSMA-negative metastases. **Results:** Overall PSMA-PET detected 23 lymph nodes lesions in 15 patients (range 0–3 per patient). DWI detected 25 lymph nodes lesions in 15 patients (0–3 per patient). 17 lymph nodes were positive in DWI as well as in PSMA (positive percent agreement 74%). 6 lymph node lesions were only positive in PSMA and 8 lymph node lesions were only positive in DWI but negative in PSMA. 4 of the 8 DWI-positive but PSMA-negative lymph nodes showed growth (50%). Overall DWI identified 4 additional lymph node metastases (+17%). All 4 were found in 2 patients without lesion detection in PSMA-PET. **Conclusion:** Adding DWI to a PSMA-PET/MRI-protocol significantly increases PET/MRI performance by identifying additional PSMA-negative metastases.

EP-0603

Prostate Cancer PET imaging: variability in healthy tissue uptake and quality control of [⁶⁸Ga]Prostate Specific Membrane Antigen (PSMA), [¹⁸F]fluoromethylcholine (FCH) and [¹⁸F]dihydrotestosterone (FDHT).

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Introduction: PET imaging is increasingly used in prostate cancer diagnostics as it enables sensitive lesion detection and molecular characterisation of cancer lesions *in vivo*. For accurate PET interpretation and cancer staging, understanding of healthy tissue uptake is important, as the uptake of suspected tumours is compared to background activity (surrounding healthy tissue or a reference organ). Hence, high variability in healthy tissue uptake could impair reliable PET reading, both between patients and within patients at different time points during treatment. The aim of this study was to quantify the variability of [⁶⁸Ga]Prostate Specific Membrane Antigen ([⁶⁸Ga]PSMA), [¹⁸F]fluoromethylcholine ([¹⁸F]FCH) and [¹⁸F]dihydrotestosterone ([¹⁸F]FDHT) uptake in healthy tissues, in order to evaluate their appropriateness as reference region. Additionally, reference ranges for standardized uptake values (SUV) will be provided, which are applicable as image-derived Quality Control (QC) for future PET acquisitions. **Materials and Methods:** N=201 PET scans from multiple hospitals were analysed, including n=87 [⁶⁸Ga]PSMA; n=87 [¹⁸F]FCH and n=27 [¹⁸F]FDHT PET/CT scans. Tracer uptake in the aortic blood pool, lung, liver, bone marrow and muscle was assessed, using several SUV metrics (i.e. *SUVmax*, *SUVpeak*, *SUVmean*). Variability in uptake was analysed using Coefficients of Variations (COV %). For image-derived QC purposes, SUV reference ranges (mean ± 1.96*SD) were provided for all healthy

tissues, for each radiotracer. **Results:** For [⁶⁸Ga]PSMA, lowest variability was observed for blood pool SUVpeak (COV 19.0%; reference range 0.8 - 1.7). All other tissues displayed considerable variability (range COV 27.6 - 32.0%). For [¹⁸F]FCH, liver SUVpeak was most stable (COV 16.8%; reference range 7.3 - 14.4). Reliable uptake was also observed in the blood pool and bone marrow (COV 19.1 - 19.5%). For [¹⁸F]FDHT, stable uptake was observed in the liver, blood pool, and bone marrow (COV 14.0 - 18.3%; reference range liver SUVpeak 3.3 - 5.8). Acquisition efficiency rates (i.e. total image-detected Bq / injected dose at start scan) were stable for all tracers (COV 6.2 - 10.7%). **Conclusion:** Only blood pool provide a reliable reference region for [⁶⁸Ga]PSMA PET scans. For [¹⁸F]FCH and [¹⁸F]FDHT PET, either liver, blood pool or bone marrow could be used as reference regions. Reference ranges for healthy tissue uptake and scanner efficiency per tracer are proposed as image-derived QC measures.

EP-0604

Evaluation of Prostate Cancer Bone Lesions With a PSMA Agent (18F DCFPyL) Compared to 18F NaF

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Introduction: PSMA radiotracers are finding prostate cancer imaging utility in all disease phases. A next generation PSMA agent, 18F DCFPyL, is being evaluated. In prostate cancer, 18F NaF PET/CT shows increased sensitivity for bone metastasis compared to standard bone scintigraphy. In this study, a comparison between 18F DCFPyL and 18F NaF for prostate cancer bone metastasis detection was performed. **Methods:** Patients with known metastatic prostate disease underwent separate whole-body imaging with DCFPyL and NaF. Tumor uptake was compared between the two scans for the number and location of skeletal metastases. **Results:** Twenty patients (ages 50–83 years) with average serum PSA 12 ng/mL (range 0.01–57.3 ng/mL) were enrolled in the study. Definitive therapy for prostate cancer at initial diagnosis was performed in 75% (n=15/20) with 33% (n=5/15) undergoing radiation therapy and 67% (n=10/15) undergoing prostatectomy. On average, patients were imaged 6 years after initial prostate cancer diagnosis (range 1 month–17 years). 138 bone metastases were detected by either tracer. DCFPyL detected 64% (n=89/138) of total bone lesions compared to 98% (n=135/138) detected by NaF. For both tracers, lesions were predominantly seen in the pelvis (37%, n=51/138) and spine (28%, n=39/138). NaF detected more bone lesions than DCFPyL in 35% (n=7/20) of patients and detected equal lesions in 30% (n=6/20). DCFPyL detected 3 more bone lesions than NaF in 1 patient. Superscan appearance was seen in 2 patients (11%) by

both agents. There were 30% ($n=6/20$) of patients without bone lesion uptake on either scan (PSA range 0.02–13.06 ng/mL). Soft tissue metastases were observed with DCFPyL in 3 patients with negative skeletal findings with either tracer. DCFPyL detected mixed bone and soft tissue metastases in 55% ($n=11/20$) of patients. Bone metastasis without soft tissue disease was seen in 3 patients. Bone biopsy verified prostate cancer metastasis in 4 lesions with concordant NaF/DCFPyL uptake but was negative in 1 lesion with concordant NaF/DCFPyL uptake. Further metastasis biopsy results are pending. **Conclusion:** NaF detected more bone lesions than DCFPyL in this group. Decreased bone lesion visualization on DCFPyL compared to NaF could suggest identification of viable tumor versus continued bone remodeling from metastasis reported with NaF. This information could impact therapeutic strategies that rely on accurate disease mapping. PSMA overexpression was also detected in non-osseous tumors by DCF. **Acknowledgements:** This research was supported by the NCI Contract No. HHSN261200800001E.

EP-0605

Correlation of Ga-68 PSMA PET/CT Findings with Gleason Grades and Serum PSA Values for the Primary Staging of Patients with Prostate Adenocarcinoma

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Aim: Prostate Specific Membrane Antigen (PSMA) is a transmembrane protein located mainly in the prostate tissue. PSMA expression is present in almost all primary and metastatic lesions of the adenocarcinomas of the prostate gland. With Ga-68 PSMA PET/CT scan, prostate cancer lesions can be detected with high diagnostic accuracy. PSMA expression is known to increase in aggressive disease. In our study, the correlation of SUV max values of primary prostatic lesion with serum PSA levels and Gleason grade and importance of SUV max value in predictability of extra prostatic disease were investigated in the patients whom Ga-68 PSMA PET/CT were done for primary staging. **Method:** 37 patients newly diagnosed with prostate adenocarcinoma by fine needle aspiration biopsy and referred to our clinic for Ga-68 PSMA PET/CT imaging for disease staging are included in our study. Their mean age was 65.6 (ranged 44–84). Gleason grades were 1 in 3 patients, 2 in 10 patients, 3 in 4 patients, 4 in 8 patients and 5 in 12 patients. Serum PSA values, Gleason Grades and SUV max value of primary lesions were noted. **Results:** When statistical analysis were done, we found out that there was a statistically significant correlation between SUV max value of primary lesion and Gleason Grade ($p=0.005$) and also between SUV max value of primary lesion and serum PSA values ($p<0.001$). In all cases, uptake of the primary tumor was detectable from nearby normal prostate tissue. Gleason grade groups were found to be statistically significantly correlated with detection of lymphatic metastasis ($p=0.04$), on the other hand it was found that there was no correlation between Gleason grade and detection of bone metastasis. Also there was no statistically significant correlation between serum PSA levels and detection of lymphatic and bone metastasis. In addition, a statistically significant correlation was found between SUV max

values of the primary prostatic tumor and detection of metastasis. With an optimal SUV max cut off value of 8.97, extraprostatic involvement can be predicted with 81.25% sensitivity and 66.67% specificity. **Conclusion:** Ga-68 PSMA PET/CT is a diagnostic imaging tool useful in detecting prostate cancer lesions. PSMA expression, which is indicated by SUVmax, is highly related with serum PSA values and Gleason scores, so that high expression may show more aggressive disease in primary staging.

EP-0606

Comparison of multiple time-point acquisition in PSMA PET/CT to assess pelvic biochemical failure

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Purpose: The aim of the study was to evaluate the diagnostic value of the prostate-specific membrane antigen (PSMA) ligand 68Ga-PSMA-11 (HBEDD-CC) PET/CT in patients with biochemical failure prostate cancer and evaluate the value of early and late imaging of the pelvis. **Methods:** Patients were prospectively evaluated to assess biochemical failure after prostatectomy due to prostate cancer, in a total of 143 patients. Standard whole-body PSMA PET/CT images were acquired at 60 minutes post injection (p.i.) injection. Additionally were acquired an early static imaging of the pelvis starting 3 minutes after injection and a late static imaging of the abdominopelvic region 180 minutes after injection. From 143 patients, 16 had one missed acquisition (early or late) for different reasons, being in total 127. Assessment of suspicious lesions was based on visual analysis and measured the maximum standardized uptake (SUVmax) of pathologic lesion located in the pelvic region on all 3 PET images dataset (3, 60 and 180m p.i.). **Results:** Overall 29 (22.8%) patients were considered positive for local recurrence (LR). On early PET acquisition 23/29 (79.3%) were considered positive for LR, with statistical significant better diagnostic confidence compared to the other sequences ($p<0.05$). On standard 60min PET acquisition 22/29 (75.8%) were considered positive for LR and on late acquisition 20/29 (68.9%) were considered positive for LR. There was no statistical significance between early and late acquisition compared to the standard 60min. There was significantly better signal to background in early acquisition (SUVmax lesion / SUVmax bladder) compared to standard 60min and late acquisitions ($p<0.05$). **Conclusion:** Performance of early imaging in 68Ga-PSMA PET/CT in addition to whole-body scans 60 min p.i. increases the diagnostic confidence of local recurrence and despite no statistical difference can add detection rate of local recurrence in prostate cancer patients with biochemical recurrence.

EP-0607

Validation Of Diagnostic Accuracy Of Standardized Uptake Value (SUV) In Quantitative Skeletal SPECT/CT For Newly Diagnosed Patients With Bone Metastasis From Prostate Cancer

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Purpose: We previously reported the utility of standardized uptake value (SUV) for the evaluation of active bone metastases using the quantitative skeletal single photon emission computed tomography/computed tomography (SPECT/CT) for patients with bone metastasis from prostate cancer (Kuji I. et al. European Journal of Hybrid Imaging. 2017;1(1):2.). The present study aimed to compare the diagnostic accuracy of SUV of skeletal quantitative SPECT/CT with that of bone scan index (BSI), artificial neural network (ANN), prostate-specific antigen (PSA), and alkaline phosphatase (ALP) in patients with newly diagnosed prostate cancer. **Subjects & Methods:** Subjects comprised 92 consecutive patients with newly diagnosed prostate cancer who underwent bone scan with a dedicated quantitative SPECT/CT scanner (Symbia Intevo, Siemens Healthcare K.K., Japan) 3 h after administration of Tc-99m-methylenebisphosphonic acid (740 MBq) for staging. The maximum and peak SUV (SUVmax, SUVpeak) were obtained for each patient using skeletal quantitative SPECT/CT based on the conjugate gradient reconstruction with tissue zoning and attenuation and scatter corrections applied (CGZAS, xSPECT bone). BSI and ANN values were obtained for each patient using automated analysis software (BONENAVI, Fujifilm RI Pharma and EXINI Diagnosis) based on data generated from the whole-body scan. **Results:** Among 92 patients, 19 patients were positive for bone metastases (pBM group) and 73 patients were negative for bone metastases (nBM group). There were significant differences between pBM and nBM groups with respect to SUVmax (pBM, 47.6 ± 34.3 vs. nBM, 16.1 ± 5.1 , $p < 0.001$), SUVpeak (pBM, 40.1 ± 31.5 vs. nBM, 13.5 ± 4.4 , $p < 0.001$), BSI (pBM, 1.67 ± 2.29 vs. nBM, 0.12 ± 0.46 , $p < 0.001$), ANN (pBM, 0.81 ± 0.28 vs. nBM, 0.26 ± 0.30 , $p < 0.001$), PSA (pBM, 687.3 ± 1666.5 ng/mL vs. nBM, 20.6 ± 50.1 ng/mL, $p < 0.001$), and ALP (pBM, 697 ± 1089 U/L vs. nBM, 238 ± 69.4 U/L, $p = 0.003$). According to receiver operating characteristic (ROC) curve analyses on the patient basis, SUVmax and SUVpeak showed comparable area under curve (AUC) to BSI and ANN (Table 1). Each threshold value at the highest sum of square of sensitivity and square of specificity was determined from the ROC curve analyses, and each positive predictive value (PPV) and negative predictive value (NPV) was obtained at the threshold (Table 1). **Conclusion:** On quantitative skeletal SPECT/CT, SUVmax and SUVpeak demonstrated comparable diagnostic accuracy to that of BSI and ANN, indicating that SUV measurement using bone SPECT/CT may be a useful and feasible imaging biomarker for diagnosis of bone metastases at initial staging of patients with prostate cancer.

EP-0608

Evaluating the impact of ^{18}F -Choline PET/CT on prostate cancer management: Our retrospective study.

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Purpose: To evaluate the role of the ^{18}F -Choline PET/CT in prostate cancer management and the therapy changes guided by PET/CT results. **Subjects & Methods:** A retrospective evalua-

tion was performed on ^{18}F -Choline PET/CT scans of patients with prostate cancer. Staging, planning radiotherapy scans and biochemical recurrence were selected in patients with at least 9 months follow up. There was a total of 279 studies, 25(9%) for staging, 32(11.5%) for planning radiotherapy, 209 (74.9%) for biochemical recurrence and 13(4.6%) follow-up. All scans were obtained using a hybrid PET/CT scanner. The PET/CT acquisition protocol consisted of a dual-phase procedure after the administration of an intravenous injection of 296–370 MBq of ^{18}F -Choline. **Results:** Of the 279 studies performed, 212 (76%) were considered positive and 67 (24%) negative. On multivariate analysis PSA level and Gleason were independent predictors ($P < 0.001$ and $P = 0.008$). In positive studies the involvement was local in 57 (20.4%), 28 included local and regional lymph nodes (10%), 13 local and distant (4.6%), 20 regional lymph nodes (7.2%), 32 (11.5%) only distant, 36 only regional lymph nodes and in 26 (9.4%) the involvement was at all levels (local, lymph nodes and distant). Changes in therapy after ^{18}F -choline PET/CT were implemented in 171 of the 279 studies (61.3 %). A major clinical impact was observed in 139 studies and a minor clinical impact in 32 (28.7 %). In 55 of the 279 studies (19.7%) the ^{18}F -choline PET/CT findings modified the classification of metastasis (M). In 7 of the 55 studies the M status reduced (discarding distant involvement), and in 48 (69.3%) unknown distant disease was detected. **Conclusion:** ^{18}F -choline PET/CT is an useful technique for staging, detection of biochemical recurrence and RT planning in patients with PC as well as localization of distant disease not detected with conventional imaging studies. Evidence of this is increasingly greater, and greater mention of its use should be included in the current guidelines for the management of PC.

EP-0609

Comparison of Ga-68 PSMA PET/CT and Bone Scintigraphy Findings in the Primary Staging of Prostate Carcinoma

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Aim: Prostate cancer is the second most common cancer in the world and is ranked fifth on the list of cancer related deaths. Lymphatic and skeletal metastases are most frequently observed in prostate cancer and skeletal metastasis particularly affects the prognosis of the disease. According to international guidelines, bone scintigraphy (BS) is recommended in primary staging of moderate to high risk patients, for restaging when PSA relapse is seen after operation or radiotherapy, or when the patient is symptomatic independently from the clinical stage. However, due to low specificity, additional imaging methods are needed for differential diagnosis when there is a finding on BS. By demonstrating the PSMA expression of prostate cancer cells, it is known that bone metastases can be detected with Ga-68 PSMA PET/CT examination with high diagnostic accuracy. In our study, we aimed to compare the findings of patients with prostate cancer who underwent BS and Ga-68 PSMA PET/CT imaging at the time of primary staging. **Method:** 33 patients who were diagnosed with prostate adenocarcinoma and who underwent concurrent BS and Ga-68 PSMA PET/CT for preop-

erative staging were included in our study. The findings of BS and Ga-68 PSMA PET/CT were analysed comparatively. **Results:** Scintigraphic findings were normal in 6 out of 33 patients (18%), findings were evaluated as metastases in 2 patients (6%), in 25 patients (76%) there were suspicious findings in terms of metastasis. In 8 out of 33 patients (6 patients with no evidence of metastases on BS and 2 patients with metastatic findings on BS), concurrent PET/CT results were similar to scintigraphic findings. On the other hand, in 20 out of 25 patients with suspicious scintigraphic findings, bone metastasis was excluded as there were no skeletal PSMA expression on PET/CT and the findings on BS were accepted secondary to benign (degenerative or traumatic) processes. In the other 5 patients, pathological PSMA expression accepted as metastatic processes was seen in PET/CT scan and bone metastasis was confirmed. **Conclusion:** When concurrent BS and PET/CT findings were evaluated, in 76% of the patients who had suspicious scintigraphic findings, Ga-68 PSMA PET/CT was superior in distinguishing benign and metastatic lesions, providing an important clinical contribution in terms of clinical staging and patient management.

EP-0610

Comparison of ^{68}Ga -PSMA and ^{64}Cu -PSMA in Patients with Recurrent Prostate Cancer

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Purpose/Introduction: The aim of this study is to compare these tracers in Patients with recurrent prostate cancer with low level of PSA. There are many data published about clinical application of ^{68}Ga -PSMA in recurrent Prostate Cancer¹ and few data about ^{64}Cu -PSMA²; however ^{68}Ga has a limit considering the positron range of 4 mm that do not permit to detect lesion lower than 6 mm. Particularly in the early phase, this limit could represent a problem to analyze small lesions. Copper-64 has a positron range of 1 mm instead, that permits to identify small lesions. For this reason, to investigate the role of these different tracers in recurrent Prostate Cancer with low level of PSA could be interesting. **Subjects & Methods:** 24 Patients, with previous surgery and histological diagnosis of Prostate cancer, were selected. All patients had a level of PSA between 0.2 and 1. All patients are subjected to a previous PET-CT scan with ^{68}Ga -PSMA with a limit of 30 days before. A PET-CT scan with ^{64}Cu -PSMA is performed in the same patients. After this PET analysis, all patients did radiotherapy on the prostatic bed and the variation result of PSA after 4 weeks became the Gold Standard of the two PET scan. Sensibility and Specificity of two tracers were calculated and statistical analysis were done. **Results:** The results showed a sensibility and specificity of 50 % for ^{68}Ga -PSMA on the prostatic bed and of 65 % - 70% for ^{64}Cu -PSMA. **Conclusion:** In

order to better evaluate the specificity of two tracers, the number of patients negative in PET-CT should be increased. Footnotes: ¹ M. Eiber; T. Maurer; M. Souvatzoglou; A. J. Beer; A. Ruffani; B. Haller; F. Graner; H. Kübler; U. Habernhorn; M. Eisenhut; H. Wester; J. E. Gschwend; M. Schwaiger. *Evaluation of Hybrid ^{68}Ga -PSMA Ligand PET/CT in 248 Patients with Biochemical Recurrence After Radical Prostatectomy*. J Nucl Med 2015; 56:668-674. ² F. Cantello, V. Gangemi, G.L. Cascini, F. Calabria, M. Moschini, M. Ferro, G. Musi, S. Buttice, A. Salonia, A. Briganti, R. Damiano. *Diagnostic Accuracy of ^{64}Cu Prostate-specific Membrane Antigen Positron Emission Tomography/Computed Tomography for Primary Lymph Node Staging of Intermediate-to High-risk Prostate Cancer: Our Preliminary Experience*. Urology, 2017; 106:139-145.

EP-0611

Role of ^{18}F -Fluorocholine PET/CT metabolic parameters in patients treated with ^{223}Ra -therapy.

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Introduction: The targeted alpha-therapy with Radium-223 (^{223}Ra) is indicated for treatment of patients with castration-resistant prostate cancer (CRPC), symptomatic bone metastases and without visceral metastases. Bone scan is usually performed to evaluate skeletal involvement in this set of patients; ^{18}F -Fluorocholine (^{18}F -FCH) PET/CT permits also to evaluate extra-skeletal disease and provides parameters expressing tumour burden and metabolic activity of lesions. In the present study, we have reported our experience and correlated bone scan and ^{18}F -FCH PET/CT imaging data with overall survival (OS). **Subjects & Methods:** We retrospectively evaluated 21 patients with bone metastases from CRPC who underwent ^{223}Ra -therapy at Our Institution from May 2015 to November 2017. All patients were ECOG 0-1. ^{223}Ra -dichloride was administered at the therapeutic activity of 55 KBq/Kg every 4 weeks for 6 times in all patients. Bone and ^{18}F -FCH PET/CT scans were acquired at baseline and after two months from the completion of ^{223}Ra -therapy. Bone scan images were classified using ALSYMPCA criteria (i.e. Score 1: 1-5 bone lesions; Score 2: 6-20 bone lesions; Score 3: > 20 bone lesions; Score 4: superscan). Linear regression was used to assess correlation of bone scan scores and ^{18}F -FCH PET-derived metabolic tumour volume (MTV, using a cut-off value of 4 in SUVmax), at baseline and after therapy, with OS. **Results:** Mean age of patients was 69.11 years (range 55-80). 12 patients (57.1%) experienced pain relief. No skeletal-related events occurred. Mean OS was 19.61 months (median 20.57, range 7.3-32). Bone scan scores did not correlate with OS. Mean MTV of bone lesions before and after ^{223}Ra -therapy was 209.45 cm³ and 551.14 cm³, respectively. Average difference between pre-therapy and post-therapy MTV of bone lesions calculated in percentage was 391.5% (ranging -100% to 2538%). Linear regression between MTV of bone lesions at baseline and OS showed a negative significant correlation ($R^2=0.23$; $P=0.033$); also linear regression considering MTV of bone lesions after the end of treatment and OS showed a negative significant correlation ($R^2=0.22$; $P=0.031$). Difference between baseline and post-therapy MTV (ΔMTV)

of bone lesions did not correlate with OS. **Conclusion:** Our results confirm literature and real-life data about effectiveness of ^{223}Ra -therapy in patients affected by bone metastases from CRPC. In our experience, we found notable OS data in patients undergoing ^{223}Ra -therapy; additionally, MTV of bone lesions on ^{18}F -FCH PET/CT images at baseline and after ^{223}Ra -therapy inversely correlated with OS and can be proposed not only to assess tumour burden, but also for prognostic evaluations.

EP-0612

^{68}Ga -PSMA-11 PET/CT in prostate cancer local recurrences: impact of early images and parametric analysis

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Aim: ^{68}Ga -PSMA PET/CT performed 60 minutes post tracer injection (p.i.) can underestimate the detection of PC local recurrence due to physiologic tracer accumulation in the urinary bladder. The aim of this retrospective analysis is to evaluate the complementary role of early dynamic and parametric PET imaging in patients with local recurrence of PC. **Methods:** 16 patients with biochemical relapse of PC attributed to local recurrence were enrolled in the study. All patients underwent dynamic PET/CT scanning of the pelvis and lower abdomen for 60 minutes following the intravenous administration of ^{68}Ga -PSMA-11, as well as whole-body PET/CT after the end of the dynamic acquisition. Data analysis was based on visual analysis of the static and dynamic PET/CT scans, semi-quantitative evaluation based on SUV calculations, quantitative analysis based on two-tissue compartment model and parametric imaging based on Patlak analysis. Parametric images of the slope and the intercept were evaluated visually and quantitatively. **Results:** Visual analysis of the static ^{68}Ga -PSMA PET/CT scans (60 minutes p.i.) revealed that 12/16 patients were PET/CT-positive. Respectively, visual analysis of the early dynamic images showed that all these 12 lesions could be detected in earlier frames of the dynamic PET acquisition at a median time of 4.5 minutes p.i. (range= 1.5 - 11.5 minutes). Moreover, early dynamic PET imaging could detect local recurrence in 1/4 static PET/CT-negative patients; this lesion was masked in the late/static images from bladder activity. Tracer accumulation in the urinary bladder began at a median time of 10 minutes (range= 6.0 - 17.5 minutes). According to parametric analysis, all PC lesions visible on late static ^{68}Ga -PSMA PET/CT images were also positive both on the slope and the intercept patlak images. The local recurrence, which was positive in the early dynamic PET images but negative in the late static PET images, could be delineated on the intercept images. **Conclusions:** Early dynamic ^{68}Ga -PSMA PET/CT scan of the pelvis approximately 5 minutes p.i. performed in addition to the conventional PET/CT acquired at 60 minutes p.i.

is a practical approach to increase the detection rate of PC local recurrence. Patlak analysis may provide additional information in detection of PC local recurrence by means of ^{68}Ga -PSMA PET/CT. Nevertheless, the need for dynamic scanning during the whole time range of 60 minutes may be impractical in everyday clinical practice. A short data acquisition protocol may be a good compromise.

EP-0613

^{18}F FMCH intratumor heterogeneity analysis by advanced texture analysis in patients with prostate cancer recurrence

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Background: The role of ^{18}F FMCH in patients with biochemical recurrence for prostate cancer (PCa) is well established. An alternative to visual image analysis, which represent the current standard for PET/CT assessment, is the evaluation using textural features with the scope of a more objective and quantitative evaluation. In this work we evaluated the feasibility of radiomics analysis of ^{18}F FMCH PET/CT in patients with recurrent PCa after primary radical therapy. **Methods:** Within a prospective trial, we evaluated a series of 82 patients (mean age 72 ± 7 years, median age 71 years, range 56-83) with recurrent PCa (mean PSA at the time of ^{18}F FMCH PET/CT 10.39 ng/ml). Histology data and current treatment were recorded in all patients. Whole-body PET/CT (GE Discovery ST) was acquired about 45 mins after ^{18}F FMCH (4 MBq/kg of body weight) administration. Based on ^{18}F FMCH PET/CT results patients were classified in on Oligometastatic (< 3 lesions) or Multimetastatic (> 3 lesions) disease. A total of 339 lesions were found and classified according to TNM in skeleton (n=180), distant Ln (n=78), regional Ln (n=55), prostatic lodge (n=12), other (n=34). Radiomics texture features were extracted using the LIFEx package from semiautomatically segmented PET and CT images. Statistical analysis was performed with JMP Statistical Discovery™. The Spearman correlation coefficient two-sided Wilcoxon rank-sum test or Kruskal-Wallis test were used and corrected for multiple testing using the Bonferroni-Holm method (significance level $\alpha = 0.05$). **Results:** Radiomic analysis allowed to discriminate between patients with oligometastatic and multimetastatic recurrence as well as among PCa subtypes (Gleason score) thus characterizing a signature of a more aggressive PCa. In addition, texture parameters showed ability in distinguishing among site of recurrence being different in bone lesions recurrence, distant Ln recurrence and local Ln recurrence. Hormone-therapy impact on textural features was assessed to identify texture features characterizing lesions independently from ongoing therapy. **Conclusions:** Our

preliminary results after these first series of patients showed that texture analysis of [^{18}F]FMCH PET/CT is able to characterize the heterogeneity of lesions in patients with recurrent PCa, more efficiently than the semi-quantitative indexes. Radiomic analysis proved its ability in investigating lesions heterogeneity, providing imaging biomarker to be add to the current available to better characterize disease PCa burden and biological aggressiveness, thus guiding patients' treatment decision making. *This work has been funded by Bando AIRC 2017 IG 20819*

EP-0614

Role of PSMA-PET/CT in staging Prostate Cancer

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To assess the diagnostic value of [^{68}Ga]-PSMA PET-CT (PSMA-PET) in primary staging of patients with prostate cancer (PCa) and to assess PSMA-PET impact on patient management in the context of a Pca Unit. We retrospectively analysed 90 PET/CT exams with ^{68}Ga -PSMA performed in our institution between April 2016 and March 2018, for staging biopsy-proven prostate adenocarcinoma. PET results were verified with postoperative histopathology (6 pts with PSMA uptake in lymph nodes), multiparametric MR (25 pts), biopsy (5 pts) or other diagnostics like Bone Scan (10 pts), ceCT and follow-up. Results were available for 78 patients. Synthesis of [^{68}Ga]-PSMA-HBED-CC was performed using an automated module (Scintomics GRP). ^{68}Ga was obtained from a IGG100 $^{68}\text{Ge}/^{68}\text{Ga}$ generator (Eckert & Ziegler). Mean yield of labelling was 65.53% and radiochemical purity 99.90%. Whole body PET/CT was acquired, from vertex to femur medium thigh, 60 min after i.v. tracer injection (150 MBq) on a hybrid scanner Discovery IQ (GE Healthcare). At the moment of the PET scan mean PSA value was 14.6 ng/mL (range 2.3–124 ng/mL), Gleason Score (GS) 7 in 35 pts and 8–10 in 23 pts. Moreover, PSMA PET was performed in 20 pts with GS 6 disease evaluated for active surveillance or wait&see. In 7/78 patients PET was performed during androgen deprivation therapy (ADT). PSMA-PET revealed at least one distant finding (bone, lung or lymph node metastases) in 17/78 patients (22%) with PSA range 3.5–124 ng/mL, 3 pts with GS 6. In 41/78 patients PET showed PSMA uptake corresponding to the primary (mean PSA 13.5 ng/mL, range 2.7–61.8). Oligometastatic disease (<3 lesions) was assessed in 6/17 pts with distant lesions driving to localized treatment. In 4/7 patients during ADT PSMA-PET revealed distant metastases (bone, lung and abdominal and thoracic lymph nodes) and intraprostatic lesion in 3/7. Fifty-eight PET scans were performed in pts with intermediate/high-risk Pca with positive rate of 81% and distant disease detection rate of 28% (16 pts). Number of distant lesions at PSMA-PET increased with Gleason Score and current ADT. In GS disease 3+4 PSMA-PET didn't reveal any nodal or bony lesions. In our cohort, ^{68}Ga -PSMA PET/CT showed to identify patients with intermediate- to high-risk PCa and metastatic disease allowing lesion driving treatment. Moreover, PSMA-PET allows to positively influence treatment management

of pts candidate to surveillance (GS 6) identifying underestimated metastatic lesions and to change the planned treatment with more enlarged surgery (lymph node dissection) and/or lesion targeting therapies.

EP-0615

Clinical Contribution of Dual-Phase Ga-68 PSMA PET/CT Examination in Patients with Prostate Cancer

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Aim: Dual phase examination is widely used in F-18 FDG PET/CT studies as it is well known that the FDG uptake of tumor cells increases with time. In current literature, there is a limited number of studies investigating the effect of dual phase examination of Ga-68 PSMA PET/CT. Some in vitro studies have shown that PSMA uptake of prostate cancer cells increases with time so that clinical use of dual phase examination may contribute to differential diagnosis of benign and malignant lesions. The aim of our study was to investigate the clinical contribution of the dual-phase Ga-68 PSMA PET/CT examination in the staging of prostate cancer patients. **Method:** Twenty-seven patients diagnosed with prostate adenocarcinoma who underwent Ga-68 PSMA PET/CT scan for preoperative staging were included in our study. Late pelvic images were taken at 2nd hour in order to re-evaluate the PSMA negative suspicious millimetric pelvic lymph nodes seen in routine images taken at 1st hour. Also the alteration of PSMA expression of the primary tumor was analysed. **Results:** Three of the patients were diagnosed as Gleason grade (GG) 1, 7 patients were GG 2, 4 patients were GG 3, 5 patients were GG 4, 8 patients were GG 5. Simultaneous serum PSA levels ranged from 0.7 to 168.1 ng/mL. In 10 of 27 (37%) patients, PSMA positive pelvic lymph nodes were observed in routine early images. No additional PSMA positive lesion was detected in late images, but the lymph nodes were more visually distinguishable. The SUVmax values of the primary tumour decreased in 11 patients (early SUVmax ranged 6.3–29.5, late SUVmax ranged 3.1–26.6), increased in 9 patients (early SUVmax ranged 3.7–26.9, late SUVmax ranged 6.6–33.3) and no difference was seen in 7 patients. Although there was no statistically significant correlation between serum PSA values, Gleason grades and the change in the SUVmax values observed in late images, there was a correlation close to statistically significant level between PSA levels and detection of increase in SUV max value in late images ($p=0.06$). **Conclusion:** Although our study did not reveal significant contribution of dual-phase images in 27 prostate cancer patients, it can be said that in the presence of suspicious lesions, late images may contribute clinically and more effective results can be obtained when the serum PSA level is higher. It is concluded that different results could be obtained by prospective studies with high number of patients.

EP-0616

Retrospective evaluation of ^{68}Ga -PSMA-11 and ^{11}C -Choline in two different cohorts of prostate cancer patients, with PSA values between 0.2–1.00 ng/mL after radical prostatectomy.

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Aim: The aim of this study was to assess the performance of ⁶⁸Ga-PSMA-11 PET/CT and ¹¹C-Choline PET/CT in two different cohorts of prostate cancer (PCa) patients with serum PSA level range 0.2–1.00 ng/mL after radical prostatectomy (RP). **Methods:** All PCa patients referred to our center from February 2016 to March 2018 were evaluated and two different cohort of patients were retrospectively analysed according the following inclusion criteria: a) RP as primary therapy; b) PSA between 0.2 ng/mL and 1.00 ng/mL. One hundred twelve underwent ¹¹C-Choline PET/CT (mean PSA: 0.55 ng/mL, median PSA: 0.5 ng/mL) and were defined as Group A. One hundred and seventy-one patients underwent ⁶⁸Ga-PSMA-11 PET/CT (mean PSA: 0.51 ng/mL, median PSA: 0.49 ng/mL) and were defined as Group B. All images were qualitatively evaluated by at least 2 nuclear medicine physicians. The performance of both PET/CT scan was evaluated as detection rate in a per-patients analysis. **Results:** In Group A ¹¹C-Choline resulted positive in 38/112 (33.93%) of cases and negative in 74/112 (66.07%) of cases. In Group B ⁶⁸Ga-PSMA-11 imaging was positive in 85/171 (49.71%) of cases and negative in 86/171 (50.29%) of cases. **Conclusion:** Our single-center, retrospective analysis is consistent with the available data in current literature, as we observed in two different cohorts of patients that ⁶⁸Ga-PSMA-11 PET/CT is more sensitive to detect PCa lesions than ¹¹C-Choline PET/CT, especially in recurrent PCa patients with low PSA levels.

EP-0617

Vertebral Fracture Analysis and the use of ¹⁸F-NaF PET/CT in Diagnosing non-traumatic Vertebral Fracture in Men with Metastatic Prostate Cancer

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Aim: Androgen deprivation therapy (ADT) is frequently used as a treatment for advanced prostate cancer. Despite therapeutic benefits, ADT is associated with bone loss and increased fracture rates. The presence of non-traumatic vertebral fracture (VF) defines a patient who has clinical osteoporosis. Vertebral Fracture Analysis (VFA) can be conducted as an adjunct to Dual energy X-ray Absorptiometry (DXA) in order to identify VFs. ¹⁸F-NaF positron emission tomography/computed tomography (PET/CT) performed in these patients defines the extent of skeletal metastatic disease, but may also serve as a reference for evaluation of VF. The objective of this study is to determine the frequency of VF in patients with known metastatic prostate cancer by VFA with ¹⁸F NaF-PET/CT serving as a reference method. **Method:** So far, 101 men with metastatic prostate

cancer underwent VFA in addition to DXA of the spine, hip, distal third part of radius bone. The threshold for identifying a VF was set as a 25% reduction of vertebral height as compared to the neighboring vertebra or a similar reduction of the anterior or posterior edge. The frequency of VF as detected by VFA was analyzed with ¹⁸F NaF-PET/CT serving as a reference.

Results: A total of 29 patients had VFs defined by VFA. In 13 patients ¹⁸F NaF-PET/CT verified VFs of which 4 also had osteoporosis as determined by DXA, whereas 16 had no detectable VF of which 5 had osteoporosis. Among the 72 without VF there were 9 with osteoporosis. There were no cases of missed VFs as determined by VFA. The negative predictive value and sensitivity were thus both 100%, and specificity and positive predictive value were 82% and 45%, respectively. **Conclusion:** VFA in DXA tends to overestimate the rate of vertebral fractures in men with prostate cancer compared to evaluation of VF by ¹⁸F NaF-PET/CT. VFA can be omitted when performing subsequent DXA if a proper evaluation of VF by SPECT/CT is already available.

EP-0618

Detection of rib lesions in Prostate Cancer patients with biochemical recurrence after radical treatment

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Purpose/Introduction: The aim of this study was to assess the performance of ⁶⁸Ga-PSMA-11 PET/CT for identifying oligometastatic patients (defined as having greater than or equal to 5 lesions), with particular regard for patients with rib involvement. **Subject & Methods:** In our retrospective, single-center study patients were included with the following criteria: histopathological diagnosis of PCa, previous radical treatment (either prostatectomy or external beam radical radiotherapy) and ⁶⁸Ga-PSMA-11 PET/CT during Biochemical Recurrence (BCR). We reviewed all the reports of the patients who underwent a ⁶⁸Ga-PSMA-11 PET/CT between March 2016 and February 2018 matching all the inclusion criteria. **Results:** Overall we included 808 ⁶⁸Ga-PSMA-11 PET/CT scans and we found 93/808 scans with reported rib findings at ⁶⁸Ga-PSMA PET/CT (occurrence 11.5%). Out of 93 positive scans, 18 scans (in 18 patients) were PSMA positive at a single rib (occurrence 2.2%); 7 scans (in 7 patients) showed increased ⁶⁸Ga-PSMA-11 uptake in a single rib and in another site (prostate bed 3/7, pelvic lymph nodes 5/7); 10 scans (9 patients) were PSMA positive but could be classified as oligometastatic patients (less than 5 bone lesions); 34 scans (in 30 patients) showed advanced disease (greater than 4 lesions). In 18 cases PET/CT scans showed suspect but inconclusive findings (low PSMA uptake); 6 scans (6 patients) were reported as rib fracture or small high density areas only seen at CT. **Discussion/Conclusion:** In our study ⁶⁸Ga-PSMA-11 PET/CT was found positive at one or more ribs in a relevant number of cases (11.5%), with a significant number of scans (2.2 %) reported as positive for rib single lesions due to PCa recurrence. On the basis of ⁶⁸Ga-PSMA-11 PET/CT 4.2 % of patients could be classified as oligometastatic with bone lesion, with clear importance for further treatment.

EP-0619**The Value of MRI Including High-Resolution Sequences for Spinal and Pelvic Bones for the Detection of PSMA-Negative Bone Metastases in Patients with Biochemical Recurrence of Prostate Carcinoma undergoing PSMA PET/MRI**

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Introduction: PSMA PET is a promising imaging modality in prostate cancer with detection rates surpassing conventional imaging. Even with PSA values below 0.5 ng/ml tumour localisation is achieved in about 50% of patients with biochemical recurrence. However, PSMA-negative tumour manifestations have been described and histopathologic studies confirm the absence of relevant PSMA expression on the cell membrane in some primary tumours as well as some metastases. MRI is highly effective in the detection of osseous lesions. Therefore the addition of dedicated MR sequences for bone assessment in spinal and pelvic areas (the most likely locations of bone metastases) promises an improved overall performance of PSMA PET/MRI. We quantified the detection rates of suspicious bone lesions in PSMA PET and MRI, where further evaluation or follow-up is warranted. **Subjects and Methods:** 30 patients with biochemical recurrence of prostate cancer after local and without systemic therapy (mean PSA level 2.0 ng/ml) underwent whole-body ^{68}Ga -PSMA-11 PET/MRI (T1w, T2w and CET1w images) with additional high resolution native T1 TSE and STIR of the lower spine (sagittal) and the pelvis (coronal). Additional MR imaging was performed in 15 to 20 minutes. PSMA PET and MRI were evaluated independently for osseous metastases and found lesions subsequently compared. Regarding PET, all lesions with uptake in bone surpassing the background signal were regarded as suspicious. Regarding MRI, all T1-negative lesions were evaluated. In order to be rated as possible metastases, lesions had to be T1-hypointense, STIR-hyperintense, contrast-enhancing and not attributable to benign origin. **Results:** Two lesions in one patient were equally suspicious in PSMA PET and MRI. One lesion in another patient was positive in PET but classified as osteochondrosis in MRI. This patient had two additional suspicious lesions on MRI that were negative in PET. 11 more lesions in 6 patients (1 to 3 per patient) were suspicious in MRI and negative in PET. MRI furthermore detected 15 lesions with unclear dignity and 60 non-suspicious lesions. **Conclusion:** Whole-body MRI with dedicated MR imaging of the lower spine and pelvis revealed a relevant number of suspicious lesions, invisible in PSMA PET, necessitating further evaluation or follow-up.

EP-0620**Role of Tumor Textural Heterogeneity in ^{68}Ga -PSMA PET-CT for Therapy Response Assessment and Prognosis in Prostate Cancer Patients undergoing ^{177}Lu -PSMA Therapy**

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Objective: PSMA therapy has proven to be quite effective in hormone refractory prostate cancer patients and has shown a low toxicity profile. However, it is vital to identify non-responders for better outcome. Analysis of textural heterogeneity parameters has been associated with determination of innately aggressive and therapy resistant cell lines thus emphasizing their importance in therapy planning and response prediction. The purpose of this study was to investigate the role of tumor heterogeneity in pre and post therapy ^{68}Ga -PSMA scans for early response prediction and estimation of over-all survival in patients with ^{177}Lu -PSMA therapy. **Materials and Methods:** Retrospective analysis of 50 patients undergoing ^{177}Lu -PSMA therapy (3 therapies) was performed. Pre-therapy, mid-therapy and post-therapy ^{68}Ga -PSMA PET scans were used for analysis. Interview Fusion (MEDISO Medical Imaging) was used for entire analysis. 3D volumes (VOIs) for 3 lesions each in bones and lymph nodes were manually delineated in static PET images. In addition to conventional parameters, 5 PET based textural heterogeneity parameters were determined. Results obtained were then compared with clinical parameters including pre and post therapy PSA, alkaline phosphate, bone alkaline phosphate levels and ECOG criteria. ROC and Kaplan-Meier analyses were used for response assessment, time to progression and survival. **Results:** In bone lesions entropy, homogeneity and intensity variation (AUC 0.725, 0.679, 0.716 respectively) showed statistically significant ability to predict response prediction. Entropy showed a statistically significant capability to evaluate disease progression and to predict survival. Any of the conventional PET parameter did not show any statistical significance. In pre-therapy analysis the lesions with higher textural heterogeneity showed better response to treatment, however after 3 therapies patients having lesions with persistently high textural heterogeneity showed poor prognosis and survival. **Conclusions:** Tumor heterogeneity analysis proved to be superior to the investigated conventional parameters, as an important predictive factor in patients with prostate cancer. Furthermore, it also provides prognostic information. Therefore, its application can be an important milestone towards personalized treatment of prostate cancer.

EP-0621 **$^{99\text{m}}\text{Tc}$ -PSMA-SPECT/CT in Patients with Prostate Cancer**

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Introduction: The prostate-specific membrane antigen (PSMA) is a transmembrane protein, that is highly expressed on the surface of prostate cancer cells. In the last few years a great number of PSMA specific ligands have been developed, that can be successfully used to detect primary prostate cancer as well as finding recurrences and metastases according to the data collected so far. The goal of our work was to examine the clinical application of a $^{99\text{m}}$ -technetium labelled radiopharmaceutical as part of the routine diagnostics of prostate cancer. **Subjects and Methods:** We examined 26 male patients with histologically verified prostate adenocarcinoma, and the progression or recurrence of the illness was suspected. We performed whole body SPECT/CTs and multiparametric 3T MRIs of the prostate

and the pelvic regions within two weeks. In two cases MRI could not be performed (claustrophobia, pacemaker). We used the ^{99m}Tc -mas3-y-nal-k(Sub-KuE) radiopharmaceutical for the SPECT scans. The images were visually evaluated independently from each other. The results were compared against the bone scintigraphy images made during the follow up of our patients as well. **Results:** In 24 patients 32 PSMA positive lesions were found. Nine of them were localized outside, 23 were within the MRI's field of view. From these 23 lesions 14 were in accordance with the PSMA-SPECT/CT scans and in 5 cases the MRI images showed no abnormalities. In case of 4 patients the MRI image raised suspicion of a metastasis but there was no associated pathological tracer uptake on the SPECT image. In case of 4 patients none of the examinations have found any signs of a prostate related malignancy. Six patients had PSMA positive bone metastases, 2 of them had a matching PSMA/SPECT and bone scintigraphy result and in 2 cases the PSMA examination showed a metastasis in spite of the negative bone scintigraphy. **Conclusion:** The ^{99m}Tc -mas3-y-nal-k(Sub-KuE) radiopharmaceutical is a well usable and promising diagnostic tool in the examination of prostate cancer. It's capable of visualizing bone metastases specifically and it can be used to detect local recurrences and visceral metastases as well.

EP-0622

^{68}Ga -PSMA uptake in lung nodules of prostate cancer patients evaluated by PET/CT at biochemical relapse

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The clinical value of ^{68}Ga -PSMA PET/CT in the diagnostic work-up of patients with prostate cancer at biochemical recurrence has been clearly described. On the other hand, the finding of increased ^{68}Ga -PSMA uptake in non-prostate malignancies as primary lung cancer has not been plainly recognized. As a result, the metastatic prostatic involvement of lung parenchyma can lead to differential diagnostics with a second tumor. The aim of this study was to evaluate the finding of lung cancer when performing a ^{68}Ga -PSMA PET/CT in the evaluation of patients with prostate cancer at biochemical recurrence. We analyzed a sample of 644 patients with prostate cancer at biochemical relapse evaluated with ^{68}Ga -PSMA PET/CT between August 2015 and March 2018. Of this group we selected patients with pulmonary nodules with ^{68}Ga -PSMA uptake. Pulmonary PET/CT findings were compared with histopathology when available. We found 20 patients (3.1%) with different degrees of ^{68}Ga -PSMA uptake in one or more pulmonary nodules (apart from lesions in prostate, bones or lymph-nodes). Median age 69 (range 57-78) years. Primitive lung cancer was confirmed in 3 of these patients and treated accordingly. Five patients were histologically confirmed as lung metastatic disease for prostate cancer. One patient underwent biopsy and the result did not reveal malignancy. One patient died soon after the PET/CT with no further evaluation. Pathology confirmation was not available for the remaining pa-

tients and they were considered and treated as metastatic prostate cancer. ^{68}Ga -PSMA PET/CT is a useful tool in the diagnostic of patients with prostate cancer at biochemical recurrence. It must be kept in mind that some lung lesions with ^{68}Ga -PSMA uptake may correspond to primary lung cancer which would imply a different clinical management and treatment.

EP-0623

Dual-phase ^{11}C -Choline PET/MR and multiparametric MR for the study of prostate cancer and nodal disease

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Aims and Objectives: Determinate the usefulness of dual-phase ^{11}C -Choline PET/MR and his correlation with multiparametric MR (mp-MR) images for differentiate malignancy or benignancy in prostate lesions and lymph nodes for prostate cancer(PC) patients.

Materials and Methods: 24 patients diagnosed by biopsy with PC underwent dual-phase PET/MR consisting on initial whole body PET (3min/bed) starting 5 minutes after injection of 2.035 MBq/kg of C11-Choline followed by 30 min-delayed PET scan (6min/bed) on pelvic region. For WB PET, simultaneously MRAC (for correction attenuation), T1LAVA, T2 SSFSE and DWI sequences were acquired. Next, mp-MR prostate study was performed to obtain T2W, T1W, DWI, DCE images. PET data were reconstructed using 3D OSEM with 2 iterations and 20 subsets with scatter and attenuation correction. In all patients, mp-MR images and PET/MR images were use to identify one dominant focal malignant lesion (24 lesions located at peripheral zone), and benignant hyperplastic areas (24 areas located at central zone), that were correlated with previous histology results. Fifty-one lymph nodes that evidenced DWI restriction and tracer uptake (moderated or elevated) located in iliacs regions (37), retroperitoneum (7) and inginals regions (7) were evaluated. SUVmax in prostate and lymph nodes on initial and delayed images were measured. Also, lymph nodes size were measured in their short axis. **Results:** The average SUVmax for dominant malignant regions increased in 13% between initial and delayed scans (initial SUVmax 6.95, delayed SUV 7.92). For benign regions, the average SUVmax between initial and delayed scans showed a little decrease, around 2%(for 5.8 to 5.72). About lymph nodes, the average size was 6.2mm, and all of them demonstrated DWI restriction. The average SUVmax for the lymph nodes showed a minimum decrease of activity on delayed images, from 4.17 to 4.12 (2%). **Conclusions:** On dual-phase PET/MR and mp-MR in the prostate malignancy areas demonstrated increase of tracer uptake, whereas benign regions showed decrease. Although the fifty-one lymph nodes demonstrated DWI restriction and low decrease of tracer uptake in mp-MR images, so that they do not have a good correlation between DWI and metabolic images to detected metastatic nodes.

EP-0624

Choline metabolism and proliferation of cancer cells - value of F-18 choline PET/CT

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Aim: To assess the significance of incidental F-18 choline uptake in prostate cancer patients in regions not characteristic for metastatic spread of the disease. **Subjects and Methods:** Two hundred and twenty-one prostate cancer patients were scanned with F-18 choline PET/CT. Mean age of our patient population was 70 years, and mean PSA value was 10.8 ng/ml. Mean administered activity was 200 MBq of F-18 choline (IASOCholine, IASON GmbH). Additional findings uncharacteristic for metastatic spread of prostate cancer were reported and prospectively analyzed based on histopathological, clinical or radiological follow-up. The mean follow-up period was 23 months (range 9 to 44 months). **Results:** One hundred and fifty-four patients had a positive finding on the F-18 choline PET/CT characteristic for prostate cancer metastases (70%). Regional lymph node metastases were found in 110 patients (49%), and bone metastases were found in 71 patient (32%). A second malignancy was discovered in 15 patients due to F-18 choline uptake. Histopathology of focal intense FCH uptake in the thyroid reported two papillary thyroid carcinoma and one follicular thyroid carcinoma. Mesothelioma was found in one patient, reporting a SUVmax value of 4, and in another, a hepatocellular carcinoma was detected. One patient had a previously unknown chronic lymphocytic leukemia. Several patients had an increased uptake in suprarenal adenomas and in one a suprarenal gland carcinoma was detected. Focal uptake of FCH was found in lung nodules in multiple patients, and further invasive procedures reported primary lung cancer in five patients. Histopathology indicated three squamous cell carcinomas, one adenocarcinoma, and one bronchioalveolar carcinoma. Metastases of other malignancies were found in three patients (renal and colon cancer). Other nonspecific F-18-choline uptake included low metabolism in lymph nodes of the mediastinum, axillary and inguinal regions, reported in 84 patients (38%), with a mean SUVmax value of 4.7, 3.7 and 4.1, respectively. Ultrasound and biopsy in the follow-up period reported granulomatous inflammation in these patients. **Conclusion:** Functional imaging with F-18 choline PET/CT provides additional information on various cancer cells metabolism and activity. It has an important impact on therapeutic strategy, providing physicians with clinical certainty for the appropriate and individual patient management.

EP-0625

The Correlation of Ga-68 PSMA PET/CT Findings with Serum PSA Values and Gleason Grades For Patients with Recurrent Prostate Cancer

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Aim: Recurrence of prostate carcinoma after radical prostatectomy or other curative therapies is a common clinical problem especially in intermediate and high risk disease. Detecting the location and the extend of disease as early as possible is important for treatment planning and the clinical outcome. Traditional methods like CT, MRI and bone scan can be used for restaging but are known to show low sensitivity and specificity especially at low PSA values. In our study, we aimed to investigate the correlation between serum PSA values and Gleason grades

and detectability of local-lymphatic, bone and visceral metastases on Ga-68 PSMA PET/CT and also the cut-off PSA values for PSMA PET positivity in both operated and non-operated patient groups. **Method:** A total of 43 patients with prostate adenocarcinoma who were directed to our clinic for Ga-68 PSMA PET/CT scan were included in our study. 20 patients were diagnosed with biochemical recurrence after radical prostatectomy (Group 1) and 23 were non-operated patients diagnosed with biochemical failure after other treatment modalities (Group 2). **Findings:** The mean age of the 43 patients was 68.5 ± 8 (range 53–83). Gleason grades were 1 in 1 patient (2.3%), 2 in 5 patients (11.6%), 3 in 10 patients (23.3%), 4 in 7 patients (16.3%) and 5 in 20 patients (46.5%). In Group 1, 9 out of 20 patients were PET positive (45%) and in group 2, 21 out of 23 patients were PET positive (91%). PSA values ranged between 0.25–34.6 ng / ml in Group 1 and 1.0–3475 ng / ml in Group 2. Statistically significant correlation were detected between serum PSA values and PET positivity in both groups ($p < 0.001$). Optimal cut-off PSA value for PET positivity was 0.7 ng/ml in Group 1 and 2.1 ng/ml in Group 2. In addition, statistically significant correlation was observed between serum PSA levels and detection of lymph and bone metastases in Group 1. In Group 2, there was significant correlation between serum PSA levels and detection of lymphatic and visceral metastases. No correlation was detected between PET positivity and gleason grades. **Conclusion:** In patients with biochemical recurrence, optimal cut-off values for Ga-68 PSMA PET/CT positivity were found for operated and non-operated patient groups separately. In both groups, disease was detected with high diagnostic accuracy even at low PSA values and we concluded that Ga-68 PSMA PET/CT has a very important role in patient management with recurrent prostate cancer.

EP-0626

Impact of positive ^{11}C -Choline PET/CT in the therapeutic management of prostate cancer biochemical relapse

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Aim: ^{11}C -Choline PET/CT has shown good results in re-staging prostate cancer (PCa) with raised serum levels of prostate specific antigen (PSA). Our aim was to evaluate the impact of positive ^{11}C -Choline PET/CT results in the therapeutic management of PCa patients with biochemical relapse (BR) after curative intention treatment. **Material and Methods:** One hundred and twelve consecutive patients (mean age: 69.5 ± 7 years) with BR of PCa and positive ^{11}C -Choline PET/CT were retrospectively evaluated. The mean serum PSA levels at study were 8.1 ± 15.9 ng/ml, range 0.36–135 ng/ml. Initial treatment was radical prostatectomy (RP) with or without adjuvant treatment in 43 patients (38.4%), external beam radiotherapy (EBRT) with or without adjuvant treatment in 57 (50.9%), prostatic brachytherapy (PB) in 11 (9.8%) and hormone therapy (HT) in 1 (0.9%). PET/CT was acquired 20 minutes after intravenous administration of 555–740

MBq of ^{11}C -Choline. Minimum follow-up time was 18 months. **Results:** In 80 out of 112 patients (71.4%) ^{11}C -Choline PET/CT showed local recurrence of PCa: 50 in prostate, 14 in prostate bed, 11 in regional lymph nodes (LN), and 5 in combinations of them. In 17 patients (15.2%) ^{11}C -Choline PET/CT showed distant recurrence: 8 in bone, 6 in distant LN, 2 in bone plus distant LN, and 1 in a soft-tissue mass. Finally, in the other 15 patients (13.4%) local plus distant recurrence was observed. Additionally, in 5 patients (4.5%) a second malignancy was detected in lungs and colon. The planned therapeutic management was changed as per the positive ^{11}C -Choline PET/CT result in 74 out of 112 patients (66.1%). In these 74 patients, ^{11}C -Choline PET/CT showed local recurrence in 50, distant recurrence in 11 and local plus distant recurrence in 13. Patients were treated as follows: 22 (19.6%) with HT, combined with other treatments in 17 (15.2%); 17 (15.2%) with PB; 13 (11.6%) with EBRT; 1 (0.9%) with RP; and 4 (3.6%) with chemotherapy. The planned therapeutic management was not modified in 37 out of 112 patients (33%). No data was available from one patient (0.9%). **Conclusions:** Positive ^{11}C -Choline PET/CT had an important impact in the therapeutic management of patients with PCa and BR, leading a change in the planned approach in two thirds of patients (66.1%). In addition, in 4.5% of the patients, ^{11}C -choline PET/CT allowed the detection of a second malignancy.

EP-0627

Incremental Value Of Ga-68 PSMA PET/CT Imaging On Prostate Cancer Management

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Purpose/Introduction: Prostate cancer (PCa) is the most common cancer in men and the second leading cause of cancer death in the Western World. Biochemical recurrence (BCR) is seen 30-40% of PCa patients following curative intent primary therapy. It is thought to be due to incomplete local response or initially occult nodal and distant metastases which were undetected by conventional imaging modalities (CIM). Ga-68 Prostate Specific Antigen (PSMA) is the new promising agent for primary staging and recurrence site localization after BCR. Accurate staging is very important for therapy planning. Our aim in this study to investigate the impact of additional Ga-68 PSMA PET/CT findings to CIM on accurate staging and recurrence site localization. **Subjects & Methods:** Ga-68 PSMA PET/CT was performed 125 intermediate/ high-risk patients (Gleason grade equal or more than 7 or PSA more than 20 ng/mL) who were referred for primary staging and 65 patients with BCR for localization of recurrence sites. Ga-68 PSMA PET/CT findings were compared with CIM findings and importance of these additional findings on patients' management were investigated. **Results:** In primary staging group, Ga-68 PSMA PET/CT detected extraprostatic infiltration in 15 patients (6 seminal vesicle infiltration, 5 rectal and 4 bladder wall invasion), pelvic metastatic lymph nodes in 26 (20%) patients, extrapelvic metastatic lymph nodes

in 12 (9.6%) patients, bone metastasis in 8 (6.4%) patients and lung metastasis in 4 (3.2%) patients which were not detected by CIM before. Additional Ga-68 PSMA findings changed patients' treatment plans in 34 (27%) patients. In BCR group, Ga-68 PSMA PET/CT detected recurrence site in 55 (84%) patients and in 25 (39%) patients recurrence sites were not detected by CIM and initial therapy planning (planned surgery type or radiotherapy field) was changed in these patients. **Discussion/Conclusion:** PCa is a biologically heterogeneous disease with a high prevalence of it is indolent disease and patient-specific treatment design, noninvasive evaluation of tumor prognostic variables, including tumor location, aggressiveness and extent has a great clinical importance. Ga-68 PSMA PET/CT has been found to meet all these clinical needs. It is found superior to CIMs for the evaluation tumor extent and evaluation of aggressiveness of the disease and improved the detection of metastatic disease especially metastasis in normal size lymph nodes and distant metastasis. These additional findings increased the accuracy of preoperative staging and allowed to choose the adequate treatment strategy which is expected to improve patients' outcome.

EP-0628

^{18}F -Fluciclovine for staging of patients with primary prostate cancer and the correlation with PSA values: Results from a single center

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Purpose/Introduction: Early and accurate detection of the extent of primary prostate cancer (PPC) can change therapy course when tumors are small and most likely to respond to localized therapy. ^{18}F -Fluciclovine is a synthetic amino acid positron emission tomography (PET) radiotracer that is EMA- and FDA-approved for use in the detection of biochemical recurrence (BCR) of prostate cancer based on its encouraging histologically-confirmed diagnostic performance. Here, we report the experience from our clinic in evaluating the utility of ^{18}F -Fluciclovine PET/computed tomography (PET/CT) for the detection of lesions in 30 patients with PPC. **Subjects & Methods:** Data were obtained at the Catharina Cancer Institute, Eindhoven, Netherlands. Scans were conducted and images were interpreted according to standardized procedures. The most recent prostate-specific antigen (PSA) measurement before the ^{18}F -Fluciclovine PET/CT took place was recorded as the baseline PSA level for each patient. Detection rates (the proportion of scans containing one or more area considered positive for cancer) were stratified by baseline PSA levels and were also determined for the subject as well as regional levels. **Results:** Between April 2017 and April 2018, 30 patients were scanned. Mean age was 69 years (range: 57 - 83). All scans have found to be image positive on patient level. The median PSA was 21,50 ng/mL (range: 0,64 - 97). 2 patients (6,7%) had a baseline PSA <5.0 ng/mL, 12 patients (40,0%) between 5.0 and 20.0 ng/mL, 10 patients (33,3%) >20.0-50.0 ng/mL and 6 patients (20,0%) >50.0-100.0 ng/mL. ^{18}F -Fluciclovine

detected lesions in 30 patients (100%); lesions were detected in the prostate/prostate bed and in pelvic lymph nodes in 29 and 9 patients (96.67% and 30%), respectively. Metastatic involvement outside the pelvis was detected in 7 patient scans (23.33%), while 3 scans (10%) showed lesions in skeletal sites. In case of PPC there is no correlation between detection rate and baseline PSA levels. In all cases PPC was detected with ^{18}F -Fluciclovine, noted that there were only 2 cases of low PSA levels (<5.0 ng/mL) included in this study. **Discussion/Conclusion:** Previous studies with ^{18}F -Fluciclovine were able to sensitively detect BCR of prostate cancer, even at PSA levels ≤ 0.5 ng/mL. In this study, no correlation has been found between detection rate and baseline PSA levels. ^{18}F -Fluciclovine PET/CT in PPC shows excellent utility for the detection of disease in the prostate/bed, as well as in extraprostatic tissue with highest detection rates in the pelvic area.

EP-0629

The image quality and clinical interpretation of pre versus post Lasix Ga68-PSMA scan

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Background: Ga68-prostate specific membrane antigen (PSMA) is introduced as a PET ligand to image patients with prostate cancer. Normal Ga68-PSMA bio-distribution include brain, liver and urinary system which is the main excretion route. In order to decrease the background uptake of the urinary system and thus increase the diagnostic accuracy, different clinics use a furosemide to clear the activity from both ureter and bladder. However, this is not a standard patient preparation for most hospital. Therefore, the aim was to evaluate image quality and clinical interpretation in pre and post diuretic administration. **Materials & Methods:** Twenty five patients have been injected with Ga-68 PSMA according to their weight i.e. 0.06 mCi/Kg. A whole body PET/CT with 2-3 time/bed was performed 45-60 min post injection. Then 40 mg furosemide was given slowly over 1-2 minutes and 15 min later, the patient voided and 2 images over the pelvis and abdomen were acquired with the same previous parameters. Both sets of images were processed with OSEM and corrected for attenuation using CT. The CNR and COV was calculated for lesions located in the pelvis and all continuous variables were expressed as mean $\pm$ SD. Images were assessed on a 3-point scale by two experienced NM physicians to evaluate lesion detectability and delineation that have an impact on clinical interpretation (1 no difference, 2 slight difference, 3 obvious difference). The Wilcoxon signed rank test and McNemar test was used to evaluate the significance and the agreement was tested using Cohen's Kappa coefficient. **Results:** 6/25 (24%) of the patients were found to have no abnormality after the clearance of ureteric activity in post Lasix images. The amount of noise in post Lasix images was significantly decreased in the lesions and in the background by 35.2% (range, 8%-62.3%), p value <0.0001 and by 52.6% (range, 24.4%-91.2%), p value <0.05 respectively. The CNR was significantly improved by 49.6 $\pm$ 24.5, p value = 0.02. Average score for observer one and two was 2.4

± 0.71 and 2.53 $\pm$ 0.52 respectively with substantial agreement ($k=0.76$). Both observers agreed that lymph nodes and prostate lesions were better delineated due to the clearance of ureteric activity. Besides, local recurrence and rectal extension were more obvious. **Conclusion:** The ability to identify true increased uptake near prostate region was enhanced in post Lasix scan. Therefore, we are in favor of using both pre and post Lasix scan to increase the diagnostic accuracy of 68-Ga PSMA scan.

EP-0630

The impact of Ga-68 PSMA PET/CT scan on decision-making strategy in biochemical recurrence after primary treatment for prostate cancer

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Aim: Ga-68 PSMA PET/CT visualises prostate cancer residual disease or recurrence at lower PSA levels compared to conventional imaging. We evaluate the impact of Ga-68 PSMA PET/CT on decision-making strategy of patients with relapsing prostate cancer presenting biochemical recurrence after radical prostatectomy and salvage radiotherapy. **Material & Methods:** Fifty patients underwent Ga-68 PSMA PET/CT due to biochemical recurrence retrospectively analyzed. Twenty three of 50 patients were addressed to Ga-68 PSMA PET/CT for a biochemical recurrence after radical prostatectomy. Twenty seven of 50 patients were addressed to Ga-68 PSMA PET/CT for a biochemical recurrence after a salvage radiotherapy. The prostate specific antigen level ranged between 0.1 and 1.71 ng/ml (median value: 0.62 ng/ml). We studied the impact on the decision-making process of additional data obtained from Ga-68 PSMA PET/CT. **Results:** Forty-one out of 50 evaluated patients showed positive findings at Ga-68 PSMA-11 PET/CT (82%). Of them, seven were positive in the prostatic bed, twelve in the pelvic nodes, fifteen in nodes outside the pelvis and eleven at bone level. Ten patients presented two different sites of relapse (20%). Ga-68 PSMA PET/CT data changed the therapeutic approach in 36 patients (72%). **Conclusions:** Ga-68 PSMA PET/CT can be a useful tool in the restaging of post-radical prostatectomy and salvage radiotherapy presenting biochemical recurrence of prostate cancer patients and it could change the decision-making process in up of 72 % of these patients. Prospective, larger series are needed to establish the role of Ga-68 PSMA PET/CT in the therapeutic approach of prostate cancer patients.

EP-0631

The use of F18 Choline PETCT in the evaluation of patients with biochemical recurrence of prostate cancer: The Maidstone experience

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Introduction: Choline PETCT is an imaging technique used to detect disease recurrence in patients with biochemical failure following radical treatment of prostate cancer. Serum PSA is used as a biochemical marker for monitoring recurrence in patients who have previously been treated for localised prostate

cancer. Previous studies have suggested choline PETCT detection rate is influenced by the PSA level. Our aim was to evaluate the relationship between the detection rate of Choline PETCT and PSA at the time of request and initial tumour histology (Gleason score). **Methods:** This is a retrospective analysis of all patients receiving a choline PETCT at our centre between November 2016 and April 2018. Scans which were for initial staging of prostate cancer were excluded. Data collected included patient demographics, previous treatment of prostate cancer, PSA at the time of request, Gleason score and the PETCT study results. **Results:** Between November 2016 and April 2018, 60 choline PETCT studies were performed, of which 46 were for re-staging in biochemical recurrence and 14 were for initial staging of prostate cancer. Within the biochemical recurrence group; 11 patients had radical prostatectomy, 10 had radiotherapy, 20 had a combination of radical prostatectomy and radiotherapy, and 6 had brachytherapy. Thirty-four (72%) choline PETCT studies identified at least one site of recurrence. Within this group, 65% demonstrated nodal recurrence, 32% demonstrated recurrence in the prostate/prostate fossa and 15% demonstrated skeletal lesions. The average PSA for positive scans was 4.8ng/mL (0.9–11.5, median 4.0) and for negative studies it was 2.3ng/mL (0.3–5, median 1.6). The detection rate with a PSA >2.0ng/mL was 81%, while in patients with a PSA <2.0ng/mL was 41% ($p=0.003$). The detection rate did not vary significantly with Gleason score; patients with a Gleason score of 7 had a PETCT detection rate of 72%, compared to Gleason score >7 had a detection rate of 88% ($p=0.2$). **Conclusion:** The majority of choline PETCT studies performed at our centre (72%) were successful at detecting sites of recurrence in patients with biochemical failure. Previous studies have suggested a higher detection rate is achieved in a trigger PSA >2.0ng/mL, our data supports this and has shown that the likelihood of a choline PETCT detecting recurrence does significantly increase with higher serum PSA. Choline PETCT is a useful tool in the setting of biochemical failure to enhance patients' selection for salvage treatment.

EP-46

e-Poster Area

Clinical -> Diagnostic study -> Adult study ->
Oncology study -> Organ-based oncology -> Thyroid,
malignant I

EP-0632

BRAF Mutation Analysis for Initial Risk Stratification in High Risk Papillary Thyroid Carcinoma

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Aim: Evaluation of BRAF analysis in high risk papillary thyroid carcinoma (PTC): is BRAF mutation associated with initial metastases and radioiodine-refractory disease? **Methods:** We retrospectively analysed the data of patients with high risk PTC

(T3/T4 and/or N1/M1) who underwent postoperative ¹²⁴I-PET/CT-dosimetry and [¹⁸F]FDG-PET/CT for staging and radioiodine treatment planning. PTC was confirmed by a pathology reference laboratory. Primary tumor tissues were screened for BRAF-mutation by next generation sequencing (BRAF-mutation: BRAF+, wildtype: WT). For iodine positive metastases, the lesion dose per GBq (LDpA) and blood dose (BD) during therapy were estimated by ¹²⁴I-dosimetry. We compared the rate of radioiodine positive versus radioiodine-refractory metastases as well as patient and tumor characteristics between BRAF+ and WT PTC applying nonparametric tests for independent samples. A tumor was defined as radioiodine-refractory if at least 1 iodine negative metastasis was identified or if in poorly radioiodine accumulating metastases a target dose greater than 80 Gy could be only achieved if BD exceeded 2 Gy. **Results:** 80 patients with high risk PTC were included in the study. Initial metastases were detected in 24/53 BRAF+ and in 16/27 WT PTC ($p=0.34$). Whereas 75% of metastases were iodine positive in WT PTC, the rate of radioiodine-refractory tumors was significantly higher in BRAF+ PTC (16/24, 67%) than in WT PTC (4/16, 25%), $p<0.05$. The LDpA of iodine positive metastases was lower in BRAF+ PTC (7.5 Gy/GBq in median, range 2–56) than in WT PTC (19 Gy/GBq, range 4–180), $p=0.16$. Further risk factors for metastases (age, gender, TNM stage, extrathyroidal extension, multifocal tumor) were well-balanced between the groups. **Conclusions:** In our cohort of patients with high risk PTC, the rate of metastases was not higher in BRAF+ tumors than in WT PTC. BRAF+ tumors were highly associated with radioiodine-refractory metastases and showed less iodine accumulating metastases than WT tumors. BRAF mutation analysis helps to identify patients that are at risk to have initial radioiodine-refractory metastases, but cannot replace [¹⁸F]FDG-PET/CT and radioiodine diagnostics for individual therapy management.

EP-0633

⁶⁸Ga-DOTA-RGD₂ PET/CT in differentiated thyroid carcinoma patients, with thyroglobulin elevation and negative ¹³¹I scintigraphy (TENIS) - paving the way for a novel molecular targeted therapy

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Purpose: To assess the tracer uptake pattern on ⁶⁸Ga-DOTA-RGD₂ PET/CT in differentiated thyroid carcinoma (DTC) patients with Thyroglobulin elevation and negative ¹³¹I scintigraphy (TENIS) syndrome for determining suitable candidates for a peptide-based radionuclide therapy. **Subjects & Methods:** 19 patients (mean age: 51.2±10.7 years) of DTC diagnosed with TENIS syndrome [rising stimulated serum thyroglobulin (S.Tg >2 ng/mL) with negative anti-Tg antibodies and negative ¹³¹I whole body scintigraphy] were enrolled in this pilot study after voluntary, written and informed consent. These patients underwent ⁶⁸Ga-DOTA-RGD₂ PET/CT, on which semi-quantitative measurement of tracer uptake was done using SUVmax values. Histopathologic correlation was performed wherever feasible. Correlation of S.Tg at the time of study, with number of trac-

er avid sites and SUVmax was performed. **Results:** The median S.Tg at the time of study was 230.5 ng/mL (range:33-1278). 16/19 patients had a minimum of one tracer avid lesion on ^{68}Ga -DOTA-RGD₂ PET/CT with 11 patients having two or more tracer avid lesion sites (maximum 5). Mean SUVmax of the lesions was 6.1 ± 2.3 with the least avidity on cervical lymph nodes (SUVmax 2.4) and maximum avidity on a skeletal lesion at right femur (SUVmax 10.5). Tracer avid thyroid remnant tissue was observed in 10/16 (mean SUVmax 5.0), lymph nodes in 12/16 (mean SUVmax 5.2), skeletal in 8/16 (mean SUVmax 6.6) and lung nodules in 8/16 (mean SUVmax 3.7) patients. Histopathologic analysis of the accessible lesions was done in 11/16 patients which was consistent with metastatic thyroid carcinoma. S.Tg at the time of study had a statistically significant positive correlation with the number of tracer avid sites ($r=0.7$, $P=0.002$). S.Tg had a positive correlation with SUVmax which was not statistically significant ($r=0.2$, $P=0.45$). Age at diagnosis of TENIS syndrome had a negative correlation with the number of tracer avid sites which was not statistically significant ($r=-0.16$, $P=0.5$). Three patients (mean S.Tg 37.6 ng/mL) who did not show any uptake on ^{68}Ga -DOTA-RGD₂ PET/CT did not have any structural abnormalities on CT. They were kept on follow-up with serial Tg values and ultrasound neck. **Conclusion:** This is the first study exploring the evaluation of DTC patients with TENIS syndrome using ^{68}Ga -DOTA-RGD₂ PET/CT. Since patients of TENIS syndrome have limited effective treatment options, the need of the hour is to develop a novel molecular targeted therapy with minimal adverse effects and maximal benefit. The patient group with RGD avid, surgically inaccessible lesions may be potential candidate for radioligand therapy using ^{177}Lu -labelled RGD peptide.

EP-0634

Correlation of ^{131}I SPECT-CT and ^{68}Ga PSMA PET-CT in differentiated thyroid cancer patients

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Introduction: Currently there are histopathological studies that show overexpression of the prostate-specific membrane antigen (PSMA) in neo-vascularity of different neoplasms such as thyroid cancer, which normally has a favorable prognosis, however, during the course of the disease they lose the ability to concentrate the radioiodine. The use of radiotracers such as PSMA could offer a teragnostic option in patients with elevated thyroglobulin with low or absent ^{131}I uptake. **Subjects and Methods:** We analyzed 5 female patients with a median age of 58 years, with papillary thyroid cancer who underwent ^{68}Ga HBED-CC PSMA PET / CT and ^{131}I SPECT / CT, 2 patients post- ablative dose, and 3 patients post treatment (^{131}I dose range 2.7MBq-5.5MBq) performed in 2-week interval. The data were analyzed through a qualitative analysis of the ^{131}I uptake SPECT / CT and the semiquantitative quantification (SUVmax) of each lesions, as well as correlation with thyroglobulin levels and cumulative dose of ^{131}I . **Results:** 9 lesions were observed (3 thyroid bed, 3 visceral metastases, 3 lymph nodes). 2 patients post radioiodine ablative dose showed no ^{68}Ga -PSMA uptake, but an intense ^{131}I uptake in the thyroid bed. In patients with a

cumulative dose of ^{131}I with an average of 12.74 MBq (range 4.05 MBq-16.21 MBq) ^{131}I moderate or poor uptake was observed with and intense ^{68}Ga -HBED-CC PSMA uptake, in these patients the average levels of thyroglobulin were 471.66 ng/ml (range 219-2,889) and average TSH 60.5 (range 30-100). **Conclusions:** These preliminary results suggest that the use of PSMA ligands could offer a teragnostic alternative in patients with metastatic disease due to papillary thyroid cancer with mild or no ^{131}I uptake.

EP-0635

Pre-ablation rhTSH-stimulated F-18 FDG PET/CT changes patient management in intermediate to high-risk thyroid cancer even in the presence of low thyroglobulin levels

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Purpose: To evaluate the clinical impact of pre-ablation rhTSH-stimulated FDG PET/CT in addition to posttherapeutic whole body radioiodine (RAI) scanning in patients with intermediate to high risk differentiated thyroid carcinoma (DTC) without clinical evidence of metastasis. **Subjects and Methods:** A retrospective single center study including 73 patients (44 female, mean age 43.2 ± 16.2 years, 62 % papillary, 31 % follicular, 7 % poorly differentiated) who underwent initially ablative intended RAI treatment using rhTSH after thyroidectomy $\pm$ lymph node (LN) dissection between 01/13 and 10/16. All patients underwent F-18 FDG PET/CT (4 MBq/kg body weight, low dose CT) after rhTSH preparation before administering RAI with a mean activity of $3,661 \pm 673$ MBq ^{131}I . Posttreatment whole body scan (WBS) was obtained 9 days afterwards in planar technique and in case of equivocal or abnormal findings using SPECT/CT. Stimulated thyroglobulin (TG) levels were measured on day 3 following rhTSH injection. **Results:** 31 patients (42%) showed FDG avid lesions of whom 14 exhibited more lesions in FDG PET/CT imaging than detected in WBS. All abnormal lesion detected were in agreement in 13 showed identical PET and WBS results. Four patients had more lesions in WBS than PET imaging. The mean stimulated TG level was 75.6 ± 205.9 ng/ml with a range 0.1 to 1,145.0 ng/ml. One patient presented with a TG level > 100 ng/ml but a negative FDG-scan exhibiting RAI-positive lung metastases. Three patients with histologically proven LN metastases presented with stimulated TG-levels < 2.0 ng/ml. The initial treatment plan was changed from follow-up to therapy (surgery, systemic therapy using tyrosin-kinase inhibition) in 8 patients (11%) only on the basis of PET/CT imaging, only. **Conclusion:** The study suggests a clinical benefit of pre-ablation rhTSH-stimulated FDG PET/CT imaging in about 20% of patients with intermediate to high risk DTC, even in the presence of low rhTSH-stimulated TG levels due to early detection of RAI-refractory or negative lesions.

EP-0636

Determining thyrotropin receptor and thyroglobulin gene transcripts in peripheral blood of thyroid carcinoma patients and healthy individuals

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Introduction: Thyroid carcinoma (TC) comprises a spectrum of different tumors with wide range of biological behavior and prognosis. The techniques based on the latest trends in molecular biology may have application in diagnosis of metastatic TC. The aim of this study was to apply and analyze mRNA expression of thyrotropin receptor gene (*TSHR-mRNA*) and thyroglobulin gene (*Tg-mRNA*) in peripheral blood of healthy individuals and patients with differentiated TC. Then to correlate between the total received ¹³¹I therapy dose and expression levels of two evaluated genes. **Material and Methods:** In the study were included 57 subjects, consisting from 40 patients with TC and 17 healthy volunteers as a control group. Total RNA was isolated from peripheral blood and used for two-step reverse transcriptase-PCR. Real time PCR was performed with appropriate primers. Relative quantification using 2^{-ΔΔCt} method was applied. **Results:** TC patients with metastatic disease or loco-regional relapse expressed *TSHR* by a 8.57-fold higher level than healthy control individuals. TC patients with biochemical relapse expressed *TSHR* by a 14.17-fold higher level than healthy controls, while expression of *Tg* was 6.6 -fold higher in TC patients with metastatic disease and loco-regional relapse than healthy controls and 8.34 -fold higher level compared with TC patients with excellent response to treatment. **Conclusion:** Our preliminary study showed that *TSHR* gene expression might have more useful application as a biomarker compared to detection of *Tg* gene expression. Positive non-significant correlation between ΔCt values for both target genes and total received dose of ¹³¹I therapy with Spearman Rank was found. **Key words:** Thyroid carcinoma, TSH receptor gene expression, thyroglobulin gene expression

EP-0637

The clinic role of FDG-PET/CT and Ga68-DOTATATE PET/CT in differentiated thyroid cancer patients with negative iodine-131 whole body scan and elevated serum thyroglobulin level

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Introduction/Purpose: In differentiated thyroid carcinoma (DTC) patients with negative whole body scan (WBS) and elevated serum thyroglobulin (Tg), tumor focus localisation and treatment remains a challenge because of loss of iodine avidity. PET imaging with 18F-FDG and 68Ga-DOTATATE are recently being used to localise disease and management of treatment in these patients. The aim of the study was to evaluate the clinic value of PET imaging using 18F-FDG and 68Ga-DOTATATE in DTC patients with negative WBS and elevated serum Tg. **Methods:** In

this retrospectively study, 43 DTC patients (20 women and 23 men; mean age=51.34 years, range=15-84 years) with negative WBS and elevated serum Tg levels, attending thyroid outpatient department for follow-up, underwent initial complete thyroidectomy followed by radioiodine treatment were enrolled. All patients had underwent PET imaging with 18F-FDG and 68Ga-DOTATATE. There were papillary thyroid carcinoma (n=34), follicular thyroid carcinoma (n=6), poorly differentiated carcinoma (n=2), and simultane papillary and follicular thyroid carcinoma (n=1). The 18F-FDG and 68Ga-DOTATATE PET/CT findings were classified as positive or negative on visual interpretation. **Results:** PET/CT imaging both 18F-FDG and 68Ga-DOTATATE were in 14/43 patients positive and completely negative in 18/43 patients. 18F-FDG PET/CT demonstrated disease in 22/43 (51.1%) patients and 68Ga-DOTATATE PET-CT in 17/43 (39%) patients. Five patients with positive both 18F-FDG and 68Ga-DOTATATE were treated with 177Lu-DOTATATE. In 8/43 patients, 18F-FDG PET/CT was positive while 68Ga-DOTATATE PET/CT was negative. However, in 3/43 patients, 18F-FDG PET/CT was negative while 68Ga-DOTATATE PET/CT was positive. Of these 3 patients, one was classified as false positive because single lesion in the brain was proved meningioma by histopathologic confirmation. In one patient, 68Ga-DOTATATE PET/CT was demonstrated additional brain lesion compared with 18F-FDG. Positive PET/CT with 18F-FDG and/or 68Ga-DOTATATE in 25/43 patients is found high elevated Tg level compared with negative PET/CT in 18/43 patients. **Conclusions:** PET/CT imaging with 18F-FDG is superior to 68Ga-DOTATATE for detection of recurrent/residual in our series. The combination of 18F-FDG and 68Ga-DOTATATE PET/CT imaging provided an accurate disease restaging. Although 68Ga-DOTATATE PET/CT not sufficient to recommend it as a routine imaging modality, it plays complementary role to other imaging techniques including 18F-FDG PET/CT. 68Ga-DOTATATE PET/CT can also help in selection of potential candidates for peptide receptor radionuclide therapy. Positive PET/CT with 18F-FDG and/or 68Ga-DOTATATE is more likely to occur in patients with highly elevated thyroglobulin concentrations.

EP-0638

68Ga-DOTATATE PET/CT imaging in medullary thyroid carcinoma patients with raised serum calcitonin

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Introduction/Purpose: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumour (NET) that expresses somatostatin receptors and secretes calcitonin. Surgery is the primary curative modality but is achieved only when the diagnosis is timely so there is a high rate of persistent and recurrent disease indicated by a rise in the serum calcitonin levels. Successful management of recurrent disease requires accurate localisation with anatomic and functional imaging. The introduction of 68Ga-DOTATATE PET/CT imaging has significantly improved the detection of NET and has been reported as a valuable adjunct in MTC localisation. The aim of the study was to present 68Ga-DOTATATE PET/CT finding in MTC patients with raised serum calcitonin. **Methods:** In this retrospectively study, 17 pa-

tients (10 women and 7 men; range=28–68 years) with raised serum calcitonin were referred for 68Ga-DOTATATE PET/CT scan for localisation of persisting recurrent MTC. Thyroidectomy had been performed in all patients with the exception of two patients. Of the 17 patients, 12 had undergone several imaging modalities including USG or CT or MRI or 18F-FDG PET/CT. The 68Ga-DOTATATE findings were classified as positive or negative on visual interpretation. The 68Ga-DOTATATE-avid lesions were also recorded per patients as well as per region: thyroid bed/local recurrence, cervical lymph nodes (LN), supraclavicular LN, mediastinal LN, lungs and bones. **Results:** 68Ga-DOTATATE PET/CT imaging detected at least one site of malignant disease in 16 of 17 patients. There was only one case with negative 68Ga-DOTATATE and cervical LN was showed on USG. Excisional biopsy of the LN proved negative disease by histopathologic confirmation. In the region-based evaluation, 68Ga-DOTATATE was positive in 33 metastatic MTC region. The cervical region was the most frequent region, followed by the mediastinum, bone, lung, supraclavicular and thyroid bed. Six patients with metastatic MTC in multiple region were treated with 177Lu-DOTATATE. One patient with cervical LN positive underwent surgery and histopathology was confirmed metastatic MTC. **Conclusions:** 68Ga-DOTATATE PET/CT can be a useful imaging tool for localising metastatic spread of MTC and can also identify patients suitable for consideration of peptide receptor radionuclide therapy in inoperable patients.

EP-0639

3T Magnetic resonance spectroscopy as a powerful diagnostic modality for assessment of thyroid nodules

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Purpose: Magnetic resonance spectroscopy (MRS) is a powerful tool for structural studies of chemical compounds and biomolecules and also documented promising findings as a potential imaging technology in thyroid oncology. This prospective study was to ascertain the clinical significance of 3Tesla MRS in the evaluation of patients with thyroid nodules (TNs) as an ancillary diagnostic technique for thyroid carcinoma. **Materials and Methods:** Magnetic resonance spectroscopy at 3T at echo-times (TEs) 136 and 270 ms was carried out on 15 patients with total number of 32 TNs, which all were surgically resected. Choline (Cho) to Creatine (Cr) ratio was assessed at 136 and 270 TEs on each nodule and a receiver operating characteristic (ROC) curve was used to determine optimal cut-off point. The findings were compared with histopathology of thyroid specimens. **Results:** There were 23 benign and 9 malignant lesions (7 papillary and 2 follicular thyroid carcinomas). The mean values of Chol/cr at 136 and 270 TEs was 2.28 ± 3.65 and 1.52 ± 1.67 respectively and the difference between benign and malignant nodules was only significant at 136 TEs. The study revealed that Cho to Cr ratio cut-off point of 2.5 best correlates with histopathology results (sensitivity = 75%; specificity = 100%; PPV = 100%; NPV = 92%). **Conclusion:** This preliminary study showed that 3T mag-

netic resonance spectroscopy might be a specific modality for the evaluation of thyroid nodules in differentiation of benign from malignant thyroid tissue. However, a larger series would give much greater confidence that this state-of-the-art technology will worth pursuing in clinical practice.

EP-0640

Clinical Value of a Preablation Scan in Patients with Differentiated Thyroid Carcinoma

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Introduction: The standard treatment in patients with differentiated thyroid carcinoma (DTC) consists of thyroidectomy and subsequent I-131 ablation. A preablation scan is a diagnostic I-131 scan before starting ablation, potentially altering later clinical management. However, in the current guidelines, there is no consensus regarding the use of a preablation scan nor regarding treatment adjustments based on an increased preablation I-131 uptake. Therefore, the objective of this study was to evaluate the value of a preablation scan in the treatment of differentiated thyroid carcinoma. **Subjects & Methods:** We included 262 consecutive DTC patients diagnosed from January 2005 until July 2015 at the University Medical Center Groningen. We collected data on patient characteristics, preablation scan outcomes, and treatment. The primary endpoint was the percentage of patients with an uptake > 5%. In addition, we performed binary logistic regression to study risk factors for an uptake > 5%. We studied altered clinical management and clinical complaints. Finally, we studied the association between uptake and ablation success. **Results:** The uptake at the preablation scan was > 5% in 52 of 262 patients (19.8%). Risk factors for an uptake > 5% were a two-step surgical procedure (OR 2.7, 95% CI 1.5–5.0), and surgery in non-tertiary hospital (OR 4.1, 95% CI 1.9–8.9). In 32 of 52 patients (61.5%) with an uptake > 5% the clinical management was changed by decreasing I-131 dosage (n = 7), performing additional surgery (n = 5) and prescribing anti-inflammatory drugs (to avoid radiation thyroiditis and neck edema) (n = 24). In patients with an uptake > 5%, 15 out of 52 patients (28.8%) reported clinical complaints after I-131 ablation. An increased uptake at the preablation scan was not associated with a worse ablation success (OR 1.0, 95% CI 0.9–1.1). **Conclusion:** Based on the current findings we conclude that the preablation scan proves to be of value for clinical management and treatment changes in the setting of a tertiary academic endocrine clinic. One out of five DTC patients had an uptake > 5%. The preablation scan results led to alterations of treatment including decreased I-131 dosages, additional performed surgeries and additional prescription of anti-inflammatory drugs.

EP-0641

Pilot Study On Somatostatin Receptor Imaging In Iodine Refractory Differentiated Thyroid Carcinoma: Local Experience From Singapore

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Introduction: Ga-68 DOTATATE positron emission tomography / computed tomography (Ga-68 DOTATATE PET/CT) and its therapeutic analogue Lu-177 DOTATATE have been reported to be a promising theranostic option for the treatment of non-iodine concentrating metastatic differentiated thyroid carcinoma with SSTR-imaging positivity of up to 63%. The objective of our study is to determine feasibility of this novel imaging and treatment technique in our local population (Singapore). **Subject and Methods:** In this pilot prospective study, we recruited a total of 7 patients with non-radioiodine avid differentiated thyroid cancer with elevated serum thyroglobulin levels and evidence of structural disease for SSTR-imaging with Ga-68 DOTATATE PET/CT. Imaging was performed with acquisition performed 1 hour after tracer administration. Non-contrast CT was performed for the purposes of attenuation correction and anatomical localization. **Results:** Of the 7 patients, only 2 patients had lesions that demonstrated tracer-avidity. In 1 patient, only 1 lesion showed mild tracer-avidity (SUVmax 3.1) whilst the others demonstrated no tracer-avidity. In the other SSTR-imaging positive patient, SSTR positivity was heterogeneous. The majority of lesions showed Grade III uptake (equal to liver) with SUVmax values ranging from 9.8 to 12.7 whilst 1 lesion showed Grade IV uptake (above the liver) with an SUVmax value of 16.3. The rest of the lesions demonstrated Grade II uptake with SUVmax values ranging from 3.2 to 6.8. 5 of the 7 patients demonstrated no tracer-avid lesion. **Discussion / Conclusion:** In contrast to the published data, our local experience suggests that SSTR-positivity is observed in a comparatively low proportion of patients. Moreover, in the SSTR-imaging positive group of patients, it would appear that only a fraction of them would exhibit dota-peptide tracer avidity sufficient to consider treatment with Lu-177 DOTATATE peptide receptor radionuclide therapy.

EP-0642

Neck lymph node metastases in patients with differentiated thyroid carcinoma (DTC) in long-term follow-up: a diagnostic 131I-SPECT/CT study

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Aim: Neck lymph node metastasis identification in DTC patients in long-term follow-up is mandatory for the most precocious and appropriate treatment since a worse prognosis may be related to their involvement, in particular cervical lymph nodes. In a retrospective study we further investigated 131I-SPECT/CT usefulness in neck lymph node metastasis detection comparatively to planar whole body scan (WBS). **Methods:** We selected 213 DTC patients already submitted to total thyroidectomy and radioiodine therapy and in long-term follow-up, all of them with ascertained radioiodine-avid foci only in the neck at 131I-SPECT/CT with diagnostic dose (185 MBq) using a hybrid dual head gammacamera for total 239 exams. First, in all patients WBS was also performed (5 cm/min). **Results:** SPECT/CT evidenced 454 neck radioiodine-avid foci in the 213 patients while WBS 322 in 160/213, all of these foci also identified at SPECT/CT. Of positive foci at WBS, 259 were classified as residues and 63 were

unclear; SPECT/CT confirmed 250 residues while 8 were characterized as lymph node metastases and 1 as physiologic uptake. Among unclear foci, SPECT/CT characterized 20 lymph node metastases, 24 residues and 19 physiologic uptakes. Moreover, SPECT/CT identified 133 occult foci at WBS classifying these as 74 lymph node metastases and 59 residues. Globally, SPECT/CT identified and characterized 102 neck lymph node metastases in 54 patients, representing single foci in 26 cases, while WBS evidenced 28 foci, some of which unclear or wrongly classified as residues. At thyroidectomy, 24/54 patients were classified as at high risk (H), 10/54 at low risk (L) and 20/54 at very low risk (VL); 20/54 patients were T1aN0M0. Twelve/20 VL patients with neck metastases, 7 of whom with lymph nodes near submandibular glands, had Tg undetectable or <2.5 ng/ml and were T1aN0M0. Globally, SPECT/CT had an incremental value than WBS in 43.7% of patients and a more correct classification changing therapeutic approach in 27.6 % of cases; moreover, SPECT/CT contributed to avoid unnecessary treatments in 7% of patients with single foci of physiologic uptake unclear at WBS. **Conclusions:** 131I-SPECT/CT proved to play an important role in DTC long-term follow-up in detecting and characterizing neck lymph node metastases giving more information than WBS of which SPECT/CT improved the interpretation also of unclear foci and reduced false positive results. 131I-SPECT/CT high performance in DTC patients with only neck lymph node metastases is particularly significant in cases with WBS inconclusive, at very low risk, T1aNoMo and with undetectable or very low Tg levels.

EP-0643

Influence on patient management after introduction of an interdisciplinary endocrine tumor board

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Purpose/Introduction: Thyroid surgery is among the most common surgical procedures in Germany with about 110.000 operations per year. Indications for surgery are defined in national and international guidelines. In Germany, the proportion for benign versus malignant indications is still high with an estimated ratio of 15-20 : 1 being much lower in other European countries or the U.S.A. Our goal was to evaluate the percentage of malignant histopathologic findings after establishing an interdisciplinary endocrine tumor board at the University Hospital Cologne. **Subjects & Methods:** Retrospective analysis of the endocrine tumor board recommendations in the years 2015 and 2016 and correlation with histopathologic findings of those patients who had undergone thyroid surgery because of suspicion of malignancy. **Results:** In 2015 and 2016, a total of 376 different patient cases were discussed in the endocrine tumor board. In 173 of these patients thyroid surgery was recommended because of suspicion for malignancy. 111 of 173 patients consented in the recommendation and underwent thyroid surgery. In 28 out of these 111 patients a thyroid carcinoma was verified by histopathological examination (25.2%). Thus, the ratio of benign to malignant histologic findings was 1:3. **Conclusions:** Since an endocrine tumor board with interdisciplinary review of

cases was introduced the recommendations for thyroid surgery resulted in a higher rate of malignant in comparison to benign histopathologic findings than commonly reported for Germany.

EP-0644

Clinical Association Of C-x-c Chemokine Receptor 4 Expression In Papillary Thyroid Cancer And Response Of I-131 Treatment

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Background: Papillary thyroid cancer (PTC) has an excellent prognosis, even though recurrent and mortality rates increase in patients with radionuclide refractory. CXCR4 expression representing tumor aggressiveness in PTC, would be able to predict radioiodine treatment response in these patients. **Materials and Methods:** Collected data of PTC patients treated by total/near-total thyroidectomy and radioiodine treatment in King Chulalongkorn Memorial Hospital (KCMH) from January 2007 to January 2013 were retrospectively reviewed and classified as non-radioiodine- refractory (non-RAIR) or radioiodine-refractory (RAIR) treatment response. The tissue specimens were performed CXCR4 immunostaining and analyzed by automated digital imaging analysis for intensity and extension. CXCR4 immunostaining score was calculated. **Results:** This is the first study to demonstrate clinical association of CXCR4 expression and I-131 treatment response. CXCR4 immunostaining scores of seventy-four specimens were 2.03 (0.52) (mean (SD)) significantly higher than of normal thyroid tissue 1.4 times ($P = 0.0001$). We demonstrated that CXCR4 immunostaining scores has a tendency of higher scores in RAIR treatment response group (2.13(0.47) than non-RAIR treatment response group (1.95 (0.54)) ($P = 0.149$). Odds ratio of CXCR4 immunostaining score for predicting RAIR treatment was 1.99 ($P = 0.150$). Moreover, we found that there is tendency of the correlation of CXCR4 immunostaining score and tumor size ($R = 0.298$, $P = 0.01$). However, we is not be able to demonstrate significant association of CXCR4 immunostaining score among other clinicopathologic factors such as cervical lymph node metastases. **Conclusion:** This study is not able to demonstrate clinical association of CXCR4 expression in primary tumor of PTC among both groups of I-131 treatment response. However, our data support the notion that CXCR4 are significantly expressed in PTC cells in primary tumour over normal thyroid tissues regardless of treatment response of I-131. Therefore, imaging or treatment with CXCR4 ligands may be promising for patients with refractory thyroid cancer.

EP-0645

Is ^{18}F -FDG SUV value predictive factor for malignancy in incidentals thyroid nodes?

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Purpose/Introduction: To analyze the predictive value of Standard Uptake Value (SUV) for malignancy in thyroid nodes found incidentally in PET-CT with ^{18}F -FDG (performed for non-thyroidal cause) comparing to the cytological study. **Subjects and Methods:** Between 2012 and 2017 a total of 91 patients were evaluated with ^{18}F -FDG PET-CT study, performed to evaluate nonthyroidal disease. After thyroid node was found, all of them underwent ultrasound guided fine needle aspiration (FNA). The cytological results were based on the Bethesda classification system and/or subsequent thyroidectomy/lobectomy. SUVmax with ROI, SUVmax and SUVpeak with VOI was calculated according to routine clinical fashion. We performed statistical analysis using a 2-tailed t test and significance was set at $P < 0.05$. **Results:** 36 men and 55 women were analyzed. The mean of age was 66.86 (age range 32-87). 85 of them showed hypermetabolic focal uptake (in 6 cases it was identified normometabolic thyroid node in low-dose CT study). Cytological study detected 25 malignant nodes (Bethesda 6), 10 suspicious for malignancy (Bethesda 5), 16 suspicious for a follicular neoplasm (Bethesda 4) and 7 atypia/follicular lesion of undetermined significance (Bethesda 3). 27/91 were labeled as benign (Bethesda 2) and in 6 of 91 were categorized as nondiagnostic (Bethesda 1). 43 patients underwent thyroidectomy/lobectomy, showing metastases histology in 10 of them, 1 lymphoma, 20 papillary carcinoma and 3 medullary carcinoma (40% of the nodes with hypermetabolic focal uptake). The other 9 nodes were labeled as nonmalignant. In our results 3/6 patients with normal ^{18}F -FDG normal uptake were malignant findings. We studied the SUVmax with ROI, SUVmax and SUVpeak with VOI. In our patients the mean of SUVmax with ROI was 9.55 for benign lesions and 11.33 for malignant lesions; the mean of SUVmax with VOI was 11.3 for benign lesions and 13.37 for malignant lesions and the mean of SUVpeak with ROI was 6.48 for benign lesions and 7.43 for malignant lesions. None of them showed statistical differences between the two groups ($P > 0.05$). **Discussion/ Conclusion:** The incidental finding of a hypermetabolic thyroid node in ^{18}F -FDG PET-CT was associated with malignant lesion in the 40% of our patients. It's mandatory to perform a ultrasound guided FNA as first diagnostic approach, and depending of the results, undergo surgery. It's important the remark the absence of prognostic utility of SUV-value for malignancy. The analysis of VOI, ROI, SUVmax or SUVpeak do not modify this value.

EP-0646

Impact of 131I SPECT/CT Imaging on the Management of Differentiated Thyroid Carcinoma

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Introduction: Metastases screening and treatment follow-up of patients with differentiated thyroid carcinoma (DTC) are usually performed with 131I-iodide whole body scan (WBS) with or without additional SPECT/CT images. Although SPECT/CT images aid in the interpretation of the WBS findings, their impact on patient management is not fully demonstrated in the literature. The purpose of this study was to evaluate possible changes

in patient staging and management determined by additional SPECT/CT images performed after WBS before radioiodine therapy (RIT) in patients with DTC. **Subjects & Methods:** Two hundred and two patients with DTC who performed SPECT/CT images additionally to pre-RIT WBS were retrospectively selected, 170 women and 32 men, mean age 46.5 years, 189 with papillary DTC and 13 follicular DTC, 151 of them performing staging WBS and 51 follow-up WBS. The images were taken 48 or 72h after oral administration of 5 mCi of ¹³¹I-iodide. Two nuclear physicians blindly evaluated possible changes in staging and therapeutic management as determined by SPECT/CT images associated with pre-RIT WBS, compared to WBS alone. **Results:** Patient management was changed in 20.8% (42/202) of the cases after additional SPECT/CT images, most of them because of a modification of the administered activity of ¹³¹I for RIT, which was reduced for 66.7% (28/42) patients and increased for 30.9% (13/42) patients. The differentiation between benign cervical structures and affected lymph nodes was the main determinant factor for changing ¹³¹I activity for RIT. One (1/42) patient was submitted to surgery (bone resection) because of SPECT/CT findings. Disease staging was changed in 26.2% (53/202) of the cases, 35.8% (19/53) of them being upstaged and 64.2% (34/53) downstaged. The mean [standard deviation] ¹³¹I activity for RIT was reduced from 124.3 [92.7] to 112.3 [62.2] after additional SPECT/CT images ($p = 0.0126$). **Conclusion:** Additional SPECT/CT images performed after pre-RIT WBS change management in one-fifth and disease staging in one-fourth of patients with DTC, and result in a global decrease of ¹³¹I activity used for RIT.

EP-0647

Impact of Anthropomorphic / Demographic Factors and Renal Function on the Pharmacodynamics of rhTSH: a Prospective Study in Differentiated Thyroid Carcinoma Patients

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Aim: In patients with differentiated thyroid carcinoma (DTC) radioiodine therapy or diagnostic radioiodine whole body scan might be performed after exogenous stimulation with recombinant human thyrotropin (rhTSH). Standard procedures with two applications with a 24 hour interval are recommended. However, this approach results in a wide range of TSH peak blood levels another 24 hours after the second dose. Previous studies identified various factors influencing the TSH peak, among them body surface area (BSA), age, renal function, sex and height. However, little is known about the impact of these factors on the subsequent metabolism of rhTSH and the resulting integral of TSH stimulation over the entire course of radioiodine treatment / imaging. Here, we further characterize the interaction of the named and additional factors on TSH peak, TSH half-life and TSH integral. **Materials & Methods:** 267 data sets of DTC patients were prospectively investigated. The patients underwent a total of five TSH blood tests every 12 hours starting 24 hours after the second rhTSH injection. Additionally, as independent variables serum creatinine, age, sex, weight, height, BSA, BMI,

lean and fat body mass, total body water (TBW) and total bone mass were collected. In univariate and multivariate analyses the correlations of these factors with TSH peak, TSH half-life and TSH integral-over-time were estimated. R^2 changes of significant factors indicated their relevance on the residual variance. **Results:** For TSH peak, multivariate analyses indicated BSA, age and creatinine as significant variables of highest impact followed by sex and TBW (cumulative R^2 change 0.44). Regarding TSH half-life, age, BMI and weight were the most relevant factors (cumulative R^2 change 0.18) while all other factors were not significant by multivariate means. The TSH integral-over-time was significantly influenced by age, creatinine, BSA and height (cumulative R^2 change 0.48). **Conclusion:** With respect to TSH peak we could prospectively demonstrate that the already known factors BSA, age, creatinine and sex were of significance. While the contribution of all tested independent variables to the variance of TSH half-life was only minor the TSH integral-over-time as combination of TSH peak and TSH half-life thus representing the total TSH stimulation was mainly correlated to age, creatinine, BSA and height. Given these four factors one might speculate on individualizing rhTSH application in future either by applying less in older patients with low BSA and diseased kidneys or vice versa applying higher doses in young patients with higher BSA and unimpaired renal function.

EP-0648

Clinical Role of FDG PET/CT in Differentiated Thyroid Cancer Patients with Elevated Tumor Markers

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Purpose: We aimed to evaluate the clinical benefit of FDG PET/CT for detecting metastasis/recurrence in differentiated thyroid cancer (DTC) patients who had elevated thyroglobulin (Tg) or anti-thyroglobulin antibody (aTg) levels on routine follow-ups after total thyroidectomy and radioactive iodine ablation. We also aimed to investigate the role of FDG PET/CT for focus detection without radioactive I-131 whole body scanning scintigraphy (WBS) in those patients. **Subjects and Methods:** PET/CT findings, Tg/aTg values, WBS images, treatments and clinical follow-up of 65 DTC patients who underwent PET/CT due to elevated Tg/aTg levels at Akdeniz University Medical Faculty Hospital in 2017 were examined retrospectively. **Results:** Among 65 patients; 54 had elevated Tg levels, 9 had elevated aTg levels and 2 had elevated Tg and aTg levels. PET/CT was found to be positive in 28 (50%) of 56 patients who had elevated Tg levels and in 7 of 11 patients (63.6%) who had elevated aTg levels. 17 of 65 patients had WBS for metastasis/recurrence detection and 16 patients' WBS images were negative. PET/CT was positive in 6 of these 16 patients (37.5%). PET/CT findings were positive in 2 of 4 patients with elevated aTg levels and negative WBS (50%) and in 4 patients (33.3%) of 12 patients with elevated Tg levels and negative WBS. In patients' clinical follow-up, 18 patients received recurrent radioactive I-131 (RAI) treatment. 14 of 18 patients had

positive findings on the whole body scanning scintigraphy performed after RAI. Among 14 patients, 9 had positive findings on PET/CT images, 5 had negative PET/CT images. 6 of 35 patients who were positive for PET/CT showed regression after RAI, 7 patients were followed up with sorafenib/zoledronate/radiotherapy/surgery (other treatments), and no additional treatment was given in 6 patients. 5 patients had progression after RAI/other treatments, and 11 patients left clinical follow-up voluntarily. Among 48 patients who underwent PET/CT but didn't underwent WBS before that, 28 had positive findings on PET/CT images. 6 of these patients showed regression after RAI, 7 patients showed regression with other treatments, 3 patients had no additional treatment, 4 patients had progression after RAI/other treatments, 8 patients left clinical follow-up voluntarily. **Conclusion:** PET/CT may be more useful than WBS for detecting recurrence/metastasis in DTC patients who had elevated Tg/aTg levels. The advantages of PET/CT over WBS are; the recurrences/metastasis that don't accumulate iodine can be detected, PET/CT provides better anatomical correlation, the possible stunning effect after WBS isn't seen and radiation exposure is less.

EP-0649

Prognostic value of nodal uptake on pretreatment F-18 FDG PET/CT in N1b papillary thyroid carcinoma patients

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Purpose: It is unclear that the metabolic characteristics of metastatic lymph node (LN) on preoperative 18F-FDG positron emission tomography/computed tomography (FDG PET/CT) in papillary thyroid carcinoma (PTC) patients associated with the prognosis. Aim of the study was to investigate predictive factors of response to initial therapy and recurrence using pretreatment FDG PET/CT in PTC with lateral neck node metastasis (N1b).

Methods: Among PTC patients who underwent pretreatment FDG PET/CT, total thyroidectomy and radioactive iodine ablation between January 2007 and July 2014, 96 (F: M= 72 : 24, median age 44.5 years) patients revealed pathologic N1b. Response to initial therapy was classified as acceptable response group (excellent, indeterminate) and incomplete response group (biochemical incomplete, structural incomplete). Clinicopathologic factors and metabolic parameters on preoperative FDG PET/CT were reviewed, and their relationships were analyzed to predict response of initial therapy and recurrence. **Results:** Fifteen patients (15.6%) among 96 N1b patients revealed incomplete response group. Multivariate analysis showed SUVmax of N1b LN ($p = 0.018$), preablation stimulated thyroglobulin ($p = 0.006$) and total LN ratio ($p = 0.012$) were related to incomplete response to initial therapy. Nine (9.4%) patients revealed recurrence during the median follow-up period of 50 months. Kaplan-Meier analysis revealed SUVmax of N1b LN (cutoff value 2.3, $p = 0.025$) was prognostic factor of recurrence, and total LN ratio ($p = 0.037$) and lateral LN ratio ($p = 0.037$) were also significant predictors of recurrence. None of the patients with recurrence had SUVmax of N1b LN less than 2.3. **Conclusions:** High SUVmax of N1b LN on preoperative FDG PET/CT might predict incomplete response to initial therapy and recurrence in PTC patients with N1b.

EP-0650

Quality of life and psychological impact of ^{131}I radioprotection measures in thyroid cancer patients

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Background & Aims: The aim of our study is to identify how is affected the quality of life in differentiated thyroid cancer population and to investigate changing in anxiety pre and post RIT (radioiodine therapy) using dedicated and special designed questionnaires. **Methods:** A cross-sectional study of 135 differentiated thyroid cancer patients was conducted for the quality of life assessment. Patients who met the inclusion criteria were invited to complete the quality of life questionnaire -thyroid version (QOL-TV). The questionnaire comprises four sections with the consequent items (physical well-being, psychological well-being, social concerns and spiritual well-being). For the impact of ^{131}I radioprotection measures we selected 54 differentiated thyroid cancer patients. Patients who met the inclusion criteria were invited to complete the radioprotection questionnaire pre and post RIT. The questionnaire comprises two sections (pre and post radioiodine treatment) with specific questions regarding aspects of radioprotection measures and the impact on the overall well-being. For uniform distribution of variable we used Pearson correlation and for monotonic relationship between variables, Spearman correlation. **Results:** We found that tiredness is the most important factor influencing the physical well-being; initial diagnosis and surgery had a big impact on psychological well-being, thyroid cancer has a big impact on patient's families and religious activities may help the patients to restore the spiritual well-being. The pre-treatment questionnaire reported a strong confidence of the patients in the medical team, good and accurate information reading the treatment, >50 % with different levels of anxiety pre-treatment. The post treatment questionnaire revealed no fear of isolation, a lot of useful information and most of the patients will undergone another treatment, if it will be necessary and will recommend it to others. **Conclusion:** The quality of life in thyroid cancer patients is influenced by many factors and we are responsible for identifying which of the problems are having the big impact on our patients. The milestone in having a good and compliant patient remains a very good communication between medical team and the patient. We are able to influence and change things and have less anxious patients if we dedicate enough time in giving them the adequate information in the adequate way so it will be correctly received and applied.

EP-0651

Assessment of risk criteria in patients with metastatic versus non-metastatic Follicular Thyroid cancer

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Objectives: to explore risk factors in patients with metastatic versus non-metastatic follicular cancer thyroid. **Methods:** This retrospective study was conducted on 38 histo-pathologically

proved FTC patients who were referred to nuclear medicine department NCI, Cairo University between July 2000 & December 2010, for RAI-131 therapy. They included 28 females & 10 males; their age ranged from 18 to 75 years. Clinico-pathological parameters, details of RAI-131 therapy & its outcome as well as serial follow up serum TG levels and I-131 WBS were extracted from their medical records. **Results:** Based on the extent of disease, the patients were classified into two groups: (1) Non-metastatic group: 19 patients. (2) Distant metastatic group: 19 patients; 12 were metastatic to bone, 1 to lung & 6 to both bone & lung. The non-metastatic patients were generally younger with a median age of 40 years compared to 54.5 years for those with distant metastases ($P < 0.001$). The sex ratio was similar in both groups with male: female ratio of 1: 2.8. Variations in histo-pathological features in both groups with respect to tumour size, grade of tumour invasion, multifocality & presence or absence of vascular invasion as well as extra-thyroidal extension were assessed. Apart from the multi-focality that shows no significant difference between non-metastatic & distant metastatic group ($P=1$), there was a statistically significant difference in all other pathological variables among the two groups. Incidence of metastases was more frequent in patient with widely invasive tumors than with minimally invasive (p value= 0.019). According to tumor size (using 4 cm as a cut off value), 68.4 % of patient with distant metastases had primary tumour size >4 cm (p value =0.003). Vascular invasion was a predominant criteria among all FTC patients develop distant metastases (P value = 0.001). **Conclusion:** Apart from the multi-focality, all other clinico-pathological risk criteria appear to directly influence the metastatic potentiality of Follicular thyroid cancer.

EP-0652

Predictive factors of cervical lymph node metastases of differentiated thyroid carcinoma

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Purpose: The aim of our study was to identify predictive factors for cervical lymph node metastases (CLNM) in children and adolescents with differentiated thyroid carcinoma (DTC) and their impact on survival. **Methods:** We conducted a retrospective study including 314 patients who were followed up in our Nuclear Medicine department for DTC with a median follow-up time of 7.8 ± 3.4 years. We investigated patients' demographic characteristics, clinicopathological features of DTCs, and persistence or recurrence of the disease. **Results:** The female/male ratio was 5.54 (266/48) with a median age at diagnosis of 41.1 ± 15 years. Total thyroidectomy was performed in all patients, followed by cervical lymph node dissection in 84.4% of cases ($n=265$). CLNM was confirmed in 60.9% of patients ($n=154$) located in the central compartment (CC), lateral compartment

(LC) and both of it respectively in 32.5% ($n=50$), 22.7% ($n=35$) and 44.8% ($n=69$) of cases. Distant metastasis was present at diagnosis in 7.32% of patients ($n=23$). Persistence and recurrence of disease were respectively seen in 24.8% ($n=78$) and 3.2% ($n= 10$) of patients. On multivariate analysis, cervical extension ($p=0.05$), classic papillary variant of DTC ($p=0.01$) and the presence of CLNM in the LC ($p < 0.001$) were significantly associated with CLNM in CC. Only the presence of CLNM in the CC was significantly associated with CLNM in the LC ($p < 0.001$) on multivariate analysis. Age, presence of distant metastasis at diagnosis and vascular invasion were not correlated with the presence of CLNM. The Cox univariate analysis showed in our study population that the presence of CLNM in the CC ($p=0.01$, HR=2.37, CI= [1.44-3.89]) as well as in the LC ($p=0.03$, HR=2.07, CI= [1.28-3.36]) increased the risk of persistence and recurrence of DTC. **Conclusion:** We confirmed that in our study population, features like the histological type and tumour extension had a prognostic effect in CLNM. We also found that in CLNM, both LC and CC metastases had an effect on the progression free survival. Therefore, an accurate pre- and intra-operative evaluation of CC and LC to detect suspicious lymph nodes in addition to prophylactic central neck dissection in patients with advanced primary tumors may be considered to improve the prognosis.

EP-0653

¹⁸F-DG-PET/CT in the diagnostic algorithm of the progression of differentiated thyroid cancer

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Purpose: In Russia, relatively recently, since 2011 new nuclear medicine centers have started to open. Hence scientific research in the field of ¹⁸FDG-PET/CT visualization of thyroid cancer in Russia is unique. Therefore, the purpose of this study was to compare the diagnostic efficacy of ¹⁸FDG-PET/CT and ¹³¹I-WBS in detecting and assessing the spread of DTC progression in the monitoring of combined treatment. **Methods and Materials:** 82 patients were included between January 2011 and March 2017. The work is based on the results of 120 ¹⁸FDG-PET/CT and 120 ¹³¹I-WBS studies. ¹⁸FDG-PET/CT examinations were performed on a positron emission tomograph combined with a 16-slice computer tomograph, Biograph 40 and 64, Siemens. **Results:** ¹⁸FDG-PET/CT has a high sensitivity in detecting tumor progression (89%) and significantly superior to ¹³¹I-WBS, $p < 0.001$. The predictive value of the negative result of ¹⁸FDG-PET/CT in 62% also significantly exceeds that of ¹³¹I-WBS in 34%. Therefore, in the negative ¹⁸FDG-PET/CT, the presence of progression can be more confidently rejected than in the negative ¹³¹I-WBS result. The predictive value of the positive result of ¹⁸FDG-PET/CT and ¹³¹I-WBS was similar - 92% and 95%, respectively. Therefore, according to the positive results of ¹⁸FDG-PET/CT and ¹³¹I-WBS, it is possible to assert with the same certainty the presence of progression. During follow-up the following types of tumor recurrence were identified: in 32 cases (34%) - isolated locoregional recurrence, in 34(36%) - isolated distant metastasis, in the remaining 29(30,5%) - a combination of lo-

coregional recurrence with distant metastases. The sensitivity of 18FDG-PET/CT in detecting all types of recurrence was quite high and there was no statistically significant difference, $p > 0.05$. For ^{131}I -WBS isolated distant metastasis is best reveals then other types of recurrence ($p < 0.05$). 18FDG-PET/CT was superior to ^{131}I -WBS in the diagnosis of all three types of recurrence, $p < 0.05$.

Conclusion: More metastatic foci of both local and distant metastasis were detected by PET/CT than by ^{131}I -WBS; the tactics of treatment and follow-up changed in 49% of cases. With similar specificity, PET/CT is superior in sensitivity and accuracy to ^{131}I -WBS in terms of the spreading of DTC progression. The inclusion of PET/CT in the diagnostic examinations complex of DTC patients during combined treatment allows to detect or exclude the presence of metastatic foci in 87% of patients. Structural and metabolic information of PET/CT and ^{131}I -CBT have an important complementary importance, combined application of these diagnostic methods allows to significantly improve the diagnostic efficiency.

EP-47

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Thyroid, malignant II

EP-0654

Incidence, recurrence and survival of tall cell papillary thyroid carcinoma in a study group.

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Introduction: Thyroid cancer is the most frequent endocrinological tumor, with papillary carcinoma being the most prevalent subtype, and the tall cell variant one of the most aggressive. The main of this study was to evaluate the incidence, recurrence and survival of this histological variant in a study group. **Methods:** A total of 820 patients with differentiated thyroid carcinoma (DTC) from the Department of Nuclear Medicine and Endocrinology of the Santiago de Compostela University Hospital were retrospectively reviewed. Of the total number of patients, 57 cases (6.9%) of tall cell variant carcinoma were selected. All patients underwent total thyroidectomy and treatment with radioiodine. The TNM staging was determined in all cases. **Results:** The mean age at diagnosis was 49.7 years, 19 men and 38 women. According to the TNM classification, 60.2% presented a stage I; 9.4% a stage II; 16.4% a stage III and 14% a stage IV. From all patients, 33.3% had PAAF prior to the diagnosis resulting in Bethesda I or inconclusive. 42.1% had postoperative complications (hypercalcemia, vocal cord paralysis, seromas and perforation of the pleura) and 40.3% had lymph node involvement. 17.5% (10 cases) presented disease recurrence, of which 3 patients died in a follow-up at least 12 months later due to thyroid cause. **Conclusions:** The tall cell variant carcinoma presented in 6.9% in our study group, being more frequent in women,

presenting a high rate of post-surgical complications and recurrence of disease. Death presented in 5.2% of the study group.

EP-0655

Malignancy rate in thyroid incidentalomas detected by ^{18}F -FDG PET/CT

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Aim: Thyroid incidentalomas detected by ^{18}F -fluorodeoxyglucose positron-emission-tomography/tomography-scan (^{18}F -FDG PET/CT), have attracted attention due to the increased risk of malignancy associated to high glycolytic metabolic nodules. With this retrospective work, we aimed to compare the maximum standardized uptake values (SUV_{max}) of benign and malign thyroid incidentalomas discovered on ^{18}F -FDG PET/CT, detected by both imaging modalities, PET and the CT. **Materials and Methods:** The reports of 25842 ^{18}F -FDG PET/CT scans, performed between January 2010 and December 2017, were reviewed. All cases with focal thyroid incidentalomas (FTI) were selected and, for each thyroid lesion, SUV_{max} was recorded. After reviewing the clinical data of those selected patients, incidentalomas were then classified as benign or malign, based on histological diagnosis, fine needle aspiration cytology (FNAC), ultrasound (US) imaging or scintigraphy imaging. All relevant data was recorded, including demographic variables and thyroid stimulating hormone (TSH). Statistical analysis was performed using SPSS version 25.0. **Results:** FTI were reported in 96 patients (61 women, 35 men; age: 62.7 ± 14.2 years, 12–85). Seventy-seven (80.2%) were categorized as benign and nineteen (19.8%) as malign incidentalomas. The median SUV_{max} of benign incidentalomas was 4.1 (interquartile amplitude=3.2;1.1–11.2) and of malign incidentalomas 6.8 (interquartile amplitude=6.7;2.8–25.5). For a significance level of 5%, the observed difference is statistically significant (U Mann-Whitney, $p < 0.001$). The area under the ROC curve for SUV_{max} was 0.785 (95% confidence interval (CI) 0.677–0.894, $p < 0.0001$). A 4.4 cut-off point of SUV_{max} was calculated with 84% sensitivity and 60% specificity for predicting malignancy. The cut-off point for maximal (100%) sensitivity was 2.75, which had a specificity of 29%; whereas the cut-off point for maximum specificity (100%) was 11.25, which had a 26% sensitivity. We collected TSH levels of 88 patients: 71 with benign incidentalomas (10 subnormal, 52 normal and 9 high hormone levels) and 17 with malign incidentalomas (0 subnormal, 15 normal and 2 high hormone levels). No statistical difference is TSH was found between the two groups. **Conclusion:** In our population, the presence of malignancy was confirmed in about 20% of the FTI. Malignant lesions had higher SUV_{max} than patients with benign findings.

EP-0656

The assessment of relation between clinic-pathologic findings and ratios of neutrophil-to-lymphocyte and platelet-to-lymphocyte in papillary thyroid carcinoma

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Introduction: Inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been recently introduced as a potential biomarker for tumor prognosis in solid tumors. Our aim is to assess the relationship between clinicopathological features and NLR and PLR in papillary thyroid carcinoma patients. **Methods:** Total 201 papillary thyroid carcinoma patients were divided into separate groups according to preoperative median NLR value of 1,92 (group-1 <1,92 and group-2 ≥1,92) and median PLR value of 123,9. NLR was calculated by dividing absolute neutrophil count by the absolute lymphocyte count; similarly, the PLR was calculated by dividing the absolute platelet count by the absolute lymphocyte count. The relationship between NLR and PLR and clinicopathological features including age, tumor size, extra-thyroidal extension, thyroid capsule invasion, surgical margin positivity, multifocality, bilaterality, serum thyroglobulin (Tg) and anti-thyroglobulin antibody (anti-Tg) levels of the patients were analyzed. **Results:** The mean NLR and PLR were 2.11 ± 0.94 , 129.69 ± 42.81 , respectively. Larger tumor size (group 1: 2.24 ± 1.14 cm; group 2: 2.79 ± 1.49 cm, $p: 0.002$), and higher positivity of extra-thyroidal spread (group 1: 3 patients, group 2: 11 patients, $p: 0.028$) were found to be statistically related with the higher values of NLR in patients in group 2. No significant relationship was found between NLR and age (<45 years, ≥45 years), presence of thyroid capsule invasion, surgical margin positivity, multifocality, bilaterality, lymph node metastasis, Tg and anti-Tg values at the 6th month. Also no significant association was observed between the clinicopathological features and PLR. **Conclusions:** High NLR was found to be related with tumor size and extra-thyroidal extension, whereas no other relationship was detected between the other clinicopathological features assessed. NLR may have the potential to be used as a prognostic biomarker for risk stratification of papillary thyroid carcinoma patients.

EP-0657

The role of Thyroglobulin doubling time in the follow up of differentiated thyroid cancer and its relationship with demographic and histopathologic risk factors and with 18F FDG PET/CT parameters

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Purpose: To investigate the relationship between thyroglobulin doubling time (TgDT) and risk factors at diagnosis and metabolic parameters derived from 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) data in differentiated thyroid cancer (DTC) patients with rising serum thyroglobulin levels. **Subjects and Methods:** A retrospective analysis of 95 DTC patients who had undergone radioiodine therapy in our department between Janu-

ary 1998-December 2015 and had rising serum thyroglobulin (Tg) levels despite negative antithyroglobulin (ATg) was made. Basal demographic and histopathologic risk factors, serum Tg and ATg levels during radioiodine therapy, metabolic tumor volume (MTV), maximum standardized uptake value (SUVmax), SUVmean, SUVpeak and total lesion glycolysis (TLG) were taken under consideration. TgDT was calculated for 28/92 patients who had rising serum Tg levels under T4 suppression. The relationship between TgDT and basal risk factors and metabolic parameters were statistically analysed. **Results:** In 28 patients (15M,13F, mean age: 52.6 ± 17.6) that TgDT could be calculated, I-131 whole body scintigraphy was negative and 18F-FDG PET/CT was performed. In 16/28 patients 18F-FDG PET/CT was also negative. In 12/28 patients, mean MTV, SUVmax, SUVmean, SUVpeak and TLG values were as follows: 28.97 cm^3 , 9.85 g/dL , 5.26 g/dL , 5.87 g/dL and 235.45 . Among metabolic parameters, TgDT was only correlated with SUVpeak ($p < 0.05$). However, median TgDT was found lower in 18F-FDG PET/CT positive patients compared to the patients with normal 18F-FDG PET/CT results ($p < 0.05$). SUVmax was correlated with tumor size ($p < 0.05$) and SUVmean was correlated with tumor size and vascular invasion ($p < 0.05$). SUVmean was higher in patients with vascular invasion ($p < 0.05$). MTV and TLG showed no relationship with any basal demographic or histopathologic risk factors. **Conclusion:** TgDT may be predictive of a positive 18F-FDG PET/CT in DTC patients with rising serum thyroglobulin levels under T4 suppression. Greater tumor size and vascular invasion may be related with higher SUVmax and SUVmean levels. Larger scale studies are needed to confirm results and to calculate a possible cutoff of TgDT for a positive 18F-FDG PET/CT study.

EP-0658

Value of F-18 FDG PET/CT in Medullary Thyroid Cancer Patients with Persistent Elevated Calcitonin Levels

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Purpose: Persistently elevated calcitonin level is indicative for residual or recurrent disease in medullary thyroid carcinoma patients. In this study, we reported our experience with fluorine-18 fluorodeoxyglucose (F-18 FDG) positron emission tomography/computed tomography (PET/CT) in evaluation of this specific group. **Subjects & Methods:** Between October 2011 and April 2018, 41 F-18 FDG PET/CT scans were performed on 23 patients (6 men, 17 women; mean age: 50.3 ± 13.2 years) with medullary thyroid carcinoma and elevated calcitonin levels for localization of residual or recurrent disease. 13 PET/BT scans performed for treatment response on 3 patients were excluded from the study. All F-18 PET/BT scans (28 scans of 23 patients) included in the study were performed for restaging. The results of F-18 FDG PET/CT, histopathological data and other imaging methods such as (neck and abdominal ultrasonography, thorax CT and abdominal magnetic resonance imaging were reviewed retrospectively. The final diagnosis of positive F-18 FDG PET/CT lesions was based on histopathological findings and/or follow-up imaging studies. Because all calcitonin levels were abnormally high defined as persistent disease, negative F-18 FDG PET/CT

scans accepted as false negative. When viewed from this aspect, because there was no true-negative study, only sensitivity and positive predictive value (PPV) were calculated. In addition, calcitonin levels and SUVmax values were assessed by Mann-Whitney U test and ROC curve analysis. Accuracy of the tests was measured by area under the curve (AUC). **Results:** There were 8 true-positive, 7 false-positive and 13 false-negative F-18 FDG PET/CT scans. Because there was no true-negative results, specificity and negative predictive value were not calculated. Sensitivity and PPV were 38.1% and 53.3% respectively. Difference of mean calcitonin level between true-positive cases (815 pg/ml) and the others (508 pg/ml) was nonsignificant ($P=0.23$). In lesion-based analysis SUVmax value of true-positive cases (6.1) were significantly higher than of the others (4.3) ($p<0.05$). AUC of SUVmax was 0.78. **Conclusion:** F-18 FDG PET/CT scan appeared to be less sensitive (38.1%) to find residual or recurrent lesion in medullary thyroid carcinoma patients with elevated calcitonin levels. However, it should be considered that F-18 FDG PET/CT was performed to the patients with only no lesion or a suspicious lesion had been detected by the other imaging modalities in this group. Because F-18 FDG PET/CT was not performed when a residual or recurrent lesion had clearly been detected before, sensitivity of 38.1% was considered to be acceptable.

EP-0659

Preablative stimulated thyroglobulin in predicting dynamic risk stratification after 1 year in patients with differentiated thyroid cancer

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Introduction: In patients with differentiated thyroid cancer (DTC) preablative stimulated thyroglobulin (ps-Tg) has the potential to be used as a predictor of response to therapy but its single level can be affected by remnant thyroid tissue and Thyroid-stimulating hormone (TSH). The aim of the study is to assess the relationship between ps-Tg before radioiodine therapy (RIT) and the dynamic risk stratification 1 year after treatment and to establish the utility of stimulated Tg as a predictor of response to therapy. **Patients and Methods:** A total of 73 consecutive patients who underwent total thyroidectomy and radioactive iodine remnant ablation therapy were reviewed retrospectively. Patients were classified according to the dynamic risk stratification 1 year after initial treatment. The ps-Tg values were compared among the groups. ROC curve analysis was performed. **Results:** The mean age at diagnosis was 43.85 (range: 17–75) with a female-to-male ratio of 4,6. Ps-Tg value after total thyroidectomy and before RIT ranged from 0,1 to 256 ng/ml. When patients were restaged, 74% had excellent response to treatment, 12,3% indeterminate and 13,7% incomplete response 1 year after initial therapy. ROC curve analysis showed that the optimal cut-off for ps-Tg was 15 ng/ml with a sensitivity of 61%; a specificity of 87%; positive predictive value (PPV) of 61% and negative predictive value (NPV) of 87%. **Conclusion:** Ps-Tg before RIT is associated with dynamic risk stratification at 1 year after therapy in patients with DTC. Higher ps-Tg levels were found in patients that had indeterminate, and particularly incomplete, response.

EP-0660

Evaluation Of F-18 FDG PET/CT In Differentiated Thyroid Cancers

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Purpose: The aim of the study is evaluation of F-18 FDG PET/CT in differentiated thyroid cancer (DTC) patients who have increased thyroglobulin (Tg) or anti-thyroglobulin antibody (TgAb) levels and negative I-131 whole body scan (WBS). **Subjects & Methods:** A total of 190 PET/CT scans retrospectively analyzed. All patients received radioiodine therapy and had negative I-131 WBS. 22 scans with hypermetabolic lymph nodes but not confirmed with biopsy were excluded from the study. 168 scans (105 female, 65 male; mean age: 46.9 ± 14.2), which had negative scans or hypermetabolic lesions confirmed with biopsy for lymph nodes or confirmed with CT/MRI for lung and bone metastases, were included in the study. Because all Tg or TgAb values were abnormally high defined as persistent disease, negative PET/CT scans accepted as false negative. When viewed from this aspect, because there was no true-negative study, only sensitivity and positive predictive value (PPV) were calculated. In addition, stimulated Tg levels and SUVmax values were assessed by Mann-Whitney U test and ROC curve analysis. Accuracy of the tests was measured by area under the curve (AUC). **Results:** All patients had undergone I-131 therapy at least one time (median: 350 mCi; range: 30–1550 mCi). Mean follow-up time was 5.7 years (range: 0.8–21 years). 143 were papillary and 25 were follicular DTC with increased Tg levels except for 2 patients who had increased TgAb levels. 70 PET/CT scans were negative that accepted as false-negative because all patients had abnormally high Tg. Among them, 3 cases had non-metabolic metastatic lymph nodes, 12 cases had non-metabolic lung metastases; any lesion was not detected in 55 cases. 85 scans were true-positive and 13 were false-positive. Sensitivity and PPV were 54.8% and 86.7% respectively. Because there was no true-negative results, specificity and negative predictive value were not calculated. Mean Tg level and SUVmax value of true-positive cases (210 ng/ml for Tg; 17.2 for SUVmax) were significantly higher than of the others (41 ng/ml for Tg; 3.5 for SUVmax) ($p<0.01$). AUC of Tg level and SUVmax were 0.75 and 0.92 respectively. **Conclusion:** In identifying metastatic lesions, SUVmax value had high accuracy if any lesion was detected. But, it should be kept in mind that, in many patients, no lesion was detected. For this reason, although PPV of FDG PET/CT was high, sensitivity of it was not adequately high in evaluating DTC patients with negative I-131 WBS and increased Tg levels.

EP-48

e-Poster Area

Clinical -> Diagnostic study -> Paediatric study -> Oncology

EP-0661

Role of 18F-FDG PET/CT in Evaluation of Response to Therapy In Patients With Chloroma

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Aim: Bone marrow or medullary involvement is the most common presentation of acute myeloid leukemia (AML). Though bone marrow biopsy is the investigation of choice for the diagnosis as well as response assessment in patients with AML, extra-medullary involvement will be missed by this method. Chloroma is a type of extra-medullary involvement, which is seen in 2-8% of patients with AML and is associated with poor prognosis and shorter survival. In this study, we evaluated the role of 18F-FDG PET/CT in quantification of disease burden and in the assessment of response to chemotherapy in this particular sub-group. **Materials and Methods:** Eight patients (6 males and 2 females) with histopathologically proven chloroma were included in the study with mean age of 10.87 ± 5.08 years. All patients underwent baseline whole body 18F-FDG PET/CT scan, which were analyzed by 2 experienced nuclear medicine physicians. The lesions were classified as mass lesion, lymph nodal involvement, muscle deposits, para-vertebral deposits, spinal canal lesions, pleural deposits, spleen, skeletal lesions, liver, breast, brain and marrow lesions. Follow-up scans were done in 7 patients. Maximum standardized uptake values (SUVmax) were evaluated for all lesions with threshold 2.5 SUVmax. **Results:** There were a total of 52 lesions in 8 patients (SUVmax 5.08 ± 3.11). Among these, biopsy was done for 10 accessible lesions (SUVmax 5.99 ± 1.58). All of them were found positive. In total 52 lesions, 15 were in head and neck region which was the most common site of involvement. Other sites were lymph nodes ($n=13$), Muscle deposits ($n=5$), para-vertebral deposits ($n=4$), spinal canal involvement ($n=4$), pleural deposits ($n=3$), spleen ($n=2$) and skeletal lesions ($n=2$); with SUVmax($\pm$ SD) were $4.00(\pm 2.25)$, $7.06(\pm 5.08)$, $7.89(\pm 2.82)$, $5.17(\pm 3.49)$, $3.35(\pm 0.70)$, $2.76(\pm 0.25)$ and $4.5(\pm 1.21)$ respectively. One lesion each is noted in liver (SUVmax =4.16), breast (SUVmax =4.10), brain (SUVmax =7.39) and marrow (SUVmax =5.56). Follow up PET/CT scan was done in 7 patients after completion of chemotherapy. One patient died before the follow-up scan. The follow-up scan of 5 patients showed complete metabolic response while in 2 patients were having residual disease. Among these 2 patients, one showed residual disease in 3 lesions of head and neck region with SUVmax $2.55(\pm 0.76)$ and other showed persistent lesion in brain (SUVmax =4.66) **Conclusion:** FDG PET/CT has definite role in detection of chloroma lesions in patients of AML. It is also useful in response assessment after completion of chemotherapy, and during further follow-up.

EP-0662

Effects of insulin and blood glucose on FDG-uptake in a mouse lung tumour model

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Introduction: FDG-PET/CT tumour scans in patients suffering from diabetes can be challenging in terms of blood sugar

control and insulin level, even though guidelines precisely describe the proper procedure. **Aim:** To elucidate the influence of high blood sugar (BS) and low insulin level or low BS and high insulin level on FDG-uptake in tumour, liver, and muscle in a pre-clinical tumour model. **Material & Methods:** Twenty-three mice were allocated to 4 groups: Group DT with diabetes and tumour ($n=8$); group D with diabetes only ($n=5$); group T with tumour only ($n=6$); control group without diabetes and tumour (C) ($n=4$). Type-1 diabetes was chemically induced in 13 mice (groups DT and D) by a single intra-peritoneal injection of Alloxan. Fourteen mice, 8 diabetic (DT) and 6 non-diabetic (T) mice were inoculated subcutaneously with human lung cancer cells 3 weeks prior to imaging. All mice underwent FDG-PET/CT using a Siemens Inveon system. The groups of diabetic mice (DT and D) were scanned on two consecutive days; day 1 with low insulin and high blood glucose level prior to FDG injection and vice versa on day 2. The groups of non-diabetic mice (T and C) underwent 4-hour fasting prior to FDG-injection. FDG uptake in each volume of interest was reported as the mean standardized uptake value (SUVmean). Finally, ex vivo FDG biodistribution was studied in all mice. **Results:** In DT mice there was no significant difference ($p=0.21$) in SUVmean of tumour tissue on day 1 (high BS, low insulin) and day 2 (low BS and high insulin): 0.65 ± 0.20 [range: 0.37;0.88] vs 0.57 ± 0.18 [0.23;0.87], $p=0.21$, whereas SUVmean of both liver ($p=0.017$) and muscle tissue ($p=0.012$) was significantly lower in this group on day 1 than day 2. SUVmean of tumour tissue was significantly lower in diabetic tumour-bearing mice than in non-diabetic mice with regular fasting preparations (day 1: -0.28 ; $p=0.01$; day 2: -0.36 ; $p=0.01$). However, this finding was not significantly supported by biodistribution data. **Conclusions:** FDG-uptake in tumours of diabetic mice was independent of high BS/low insulin and low BS/high insulin levels, possibly reflecting the autonomous nature of cancer cells, even in the presence of significantly lower tumour FDG-uptake than in non-diabetic animals. In contrast, liver and muscular FDG-uptake was clearly lower under diabetic circumstances.

EP-0663

Evaluation of Prostate Specific Membrane Antigen (PSMA) expression in a prostate cancer patient-derived xenograft model (LuCAP PDX) during Androgen deprivation therapy (ADT) using [18 F]DCFPyl PET imaging.

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Purpose: PSMA is over expressed in prostate cancer and has emerged as a potential diagnostic and therapeutic target. PSMA overexpression has been associated with androgen dependent disease and increased malignancy although the underlying biological mechanisms still remain to be elucidated. PET imaging of PSMA with 2-(3-{1-carboxy-5-[(6-[18 F]fluoro-pyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid ([18 F]DCFPyl) would offer a real-time readout of the PSMA status of tumors

as well as monitor changes due to ADT. In these studies [^{18}F] DCFPyL imaging will be used to assess changes in PSMA expression in response to ADT using a genomically defined LuCAP141 PDX model, characterized as responsive to ADT (Castrate sensitive, CS). Control and ADT-treated LuCAP141 PDXs were imaged weekly and concurrently tumor volumes were measured by caliper (tV) over the 3 week ADT paradigm. **Methods:** [^{18}F] DCFPyL was synthesized via coupling of 6-[[^{18}F]fluoronicotinic acid-2,3,5,6-tetrafluorophenyl ester to di-tert-butyl (((S)-6-amino-1-(tert-butoxy)-1-oxohexan-2-yl)carbamoyl)-L-glutamate formate salt. [^{18}F]DCFPyL was evaluated in vitro binding studies using PC3+(PSMA high expressing transfected prostate cancer cell line) and LuCaP141 tumor membranes. Control and ADT (Degarelix) LuCAP141 PDXs were imaged (60 min post [^{18}F]DCF-PyL injection) before treatment (baseline) and Day 7, 14, and 21 following treatment from which tumor:muscle ratios (T:M) were calculated $[\% \text{injected dose}/\text{g}(\text{ID}/\text{g})_{\text{tumor}}/(\% \text{ID}/\text{g})_{\text{muscle}}]$. After imaging tV were determined by caliper and used to calculate % volume increases from baseline at each time. Biodistributions were done after imaging at Day 21 and T:M were calculated $(\% \text{ID}/\text{g}_{\text{tissue}} / \% \text{ID}/\text{g}_{\text{muscle}})$; tumors were then sectioned for immunohistochemistry [IHC, PSMA and androgen receptor(AR)]. **Results:** [^{18}F]DCFPyL exhibited high affinity binding ($K_d \sim 0.7$ nM) to PSMA with both LuCAP141 and PC3+ tumor membranes although LuCAP141 PSMA expression was ~ 10 -fold lower than PC3+. [^{18}F]DCFPyL imaging revealed increased PSMA expression in ADT-treated LuCAP141 tumors compared to controls over the time course. Similarly the Day21 biodistribution T:M ratios showed significant increases (68%) in the treated group (94:1) compared to the controls (56:1) which corresponded to PSMA IHC results. Conversely treated tVs significantly regressed ($\geq 1000\%$) from baseline to Day21 while control tVs steadily increased (100–200%) over the same time. At Day 21 AR tumor expression (IHC) was not significantly different between treated and controls. **Conclusions:** [^{18}F]DCFPyL detected increased PSMA expression in response to ADT in a CS LuCAP PDX model. [^{18}F]DCFPyL imaging of additional LuCAP PDXs which are representative of the phenotypic and molecular heterogeneity in patient tumors may establish the clinical relevance of PSMA expression as a biomarker predictive of ADT response and metastatic potential.

EP-0664

18F-ML-10 Animal PET/CT Imaging Could Predict Response Of Cetuximab In Enhancing Radiosensitivity In Human Nasopharyngeal Carcinoma Xenografts: A Preclinical Study

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Purpose: Because the epidermal growth factor receptor (EGFR) is overexpressed in most nasopharyngeal carcinoma (NPC) patients, the EGFR targeted therapy (Cetuximab) has potential to improve their outcomes. However, not all the patients would benefit from Cetuximab in clinical practice. As previous studies have reported that the radiosensitivity is associated with apoptosis. We aimed to find whether 18F-ML-10 PET/CT (based on

apoptosis), as a noninvasive method, could predict prognosis to guide future individualized treatment of Cetuximab in nasopharyngeal cancer treatment. **Methods:** In our study, the enhancement of radiosensitivity in NPC radioresistant cell (CNE1) by Cetuximab was verified by clone formation experiment. Apoptosis were assayed by Annexin-V analysis. We also observed the impact on EGFR-dependent signaling pathway (PI3-K/AKT) after the combination use of Cetuximab and radiotherapy. Furthermore, we set up xenograft tumor models, and performed 18F-ML-10 PET/CT. We compared the difference of tumor uptake before, 24h and 48h after treatment in serial PET/CT imaging. Additionally, we compared PET/CT parameters with Tunel results. **Results:** In the presence of Cetuximab, the colony of CNE-1 cells decreased significantly after irradiation at 1 and 2 Gy. In addition, Cetuximab increased the cytotoxicity and apoptotic rate of CNE-1 cells to radiation. Mechanism studies demonstrated Cetuximab enhanced radiosensitivity by suppressing EGFR/PI-3K/AKT pathway. In PET/CT imaging, the tumors showed obvious uptake of 18F-ML-10 at 24 h, 48 h after combined treatment, and the value of T/M was significantly higher than the other three groups. The T/M of 18F-ML-10 uptakes showed a positive correlation of 0.926 with apoptosis index ($P < 0.001$). However, the uptake of 18F-FDG in tumors exhibited no trend among the four groups. The T/M of 18F-FDG revealed a positive correlation of 0.926 with Glut-1 intensity ($P < 0.001$). **Conclusions:** Cetuximab could enhance the radiosensitivity of NPC via suppressing EGFR-dependent signaling pathway and inducing apoptosis. 18F-ML-10 animal PET/CT showed its potential to predict its response in NPC.

EP-0665

Vpac1

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Aim: Urothelial Bladder Cancer (UBC) is the second most common genitourinary malignancy. Accurate staging of UBC with conventional imaging is often inaccurate. To improve visualization of primary disease, the extent of loco regional disease and the presence or absence of metastatic lesions, a large number of PET biomarkers have been developed. However serious limitations including urinary excretion of radioactivity compromise their ability to serve the objectives. This ongoing investigation is aimed to validate a hypothesis that VPAC receptors expressed in high density on UBC cells can be targeted to PET image UBC,

its loco regional disease and metastatic lesions. **Materials and Methods:** Cu-64-TP3805, shown in our laboratory to have high affinity (3.1×10^{-9} M) for VPAC was the imaging agent. Patients (M, N=12, 44–80 yrs.) diagnosed with invasive UBC, scheduled for radical cystectomy were administered $148 \pm 10\%$ MBq Cu-64-TP3805 (20 μ g) intravenously. Urine and blood samples were collected at predetermined time points. Patients underwent PET/CT imaging 90 minutes later. Images were read independently by two nuclear medicine physicians. Radical cystectomy and lymphadenectomy was performed 1 to 4 weeks later. VPAC PET images were correlated with final surgical pathology. **Results:** There were no AEs. Pathological results on last two subjects are not available at the time of this writing. Blood clearance $t_{1/2}$ (α) was 22.3 ± 2.7 min ($> 85\%$) and $t_{1/2}$ (β) was 118.2 ± 4.9 min ($< 20\%$). There was no urinary excretion of radioactivity. Final surgical pathology was positive for BCa in 6/10 patients, for PCa in 3, for bone metastasis in 2/6, and there were 4 positive LNs (3 in one, 1 in the other). Cu-64-TP3805 PET scan was positive for 5 BCa, 6 PCa, 3 LNs and for bone lesions. The 5 mm PET resolution may have missed the 4th LN. The results of the remaining patients' images were concordant with histology. **Conclusion:** In this first-in-human pilot study of VPAC PET imaging of UBC, VPAC avid lesions were demonstrated in radical cystectomy patients which correlated with final surgical pathology. While data are limited, further validation of this approach in which VPAC receptors are targeted for PET imaging UBC and its metastatic lesions is warranted. **Acknowledgement:** Supported in part by NIH, NCI R01 157372 (MLT) Dean's Translational Science Award (MLT) and Sidney Kimmel Cancer Center Award (MLT).

EP-0666

CHL1 Gene Differentiates Hurthle Cell Carcinoma From Hurthle Cell Benign Disease

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Purpose: Hurthle cell carcinoma (HCC) is an unusual and relatively rare type of differentiated thyroid cancer. Currently, cytologic analysis of fine-needle aspiration biopsy is limited in distinguishing benign Hurthle cell neoplasms from malignant neoplasms. The aim of this study was to determine whether differences in the expression of specific genes could differentiate HCC from Hurthle cell benign disease by evaluating differential gene expression in Hurthle cell disease. **Methods:** 18 Hurthle cell benign disease samples and 7 HCC samples were performed by whole-transcriptome sequencing. Bioinformatics analysis was carried out to identify candidate diagnostic genes. Then expression of these candidate genes was re-examined by quantitative real-time PCR. Protein expression was quantified by Immunohistochemistry. **Results:** CHL1 gene was discovered

to over-express in HCC. CHL1 was found to have greater than 15-fold higher expression in Fragments per Kilobase Million (FPKM) in HCC compared to benign Hurthle cell tumors. This was confirmed by qRT-PCR. Moreover, the immunoreactivity score of the CHL1 protein was significantly higher in HCC compared to Hurthle cell benign disease. **Conclusions:** CHL1 seems to represent a marker of HCC. Hence, assessment of its expression might represent a novel and useful prognostic biomarker to distinguish HCC from benign Hurthle cell disease.

EP-0667

Multi-tracer PET studies in a murine model of multiple myeloma

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Purpose/Introduction: Multiple myeloma (MM) is the second most common hematological malignancy and despite the therapeutic advances over the last ten years it remains incurable. The objective of this work was to compare the diagnostic performance of three PET radiotracers, 2-[18F]-fluoro-2-deoxy-D-glucose (¹⁸F-FDG), L-[methyl-¹¹C]-methionine (¹¹C-MET) and [N-Methyl-¹¹C]choline (¹¹C-COL) in the detection of MM in a murine model. **Subjects & Methods:** Twelve immunosuppressed mice (Rag2 - / -; γ c - / -) were injected subcutaneously with 5×10^6 MM1S-tomato cells to create xenograft tumors. MicroPET studies were performed (Mosaic, Philips) with ¹⁸F-FDG, ¹¹C-MET, ¹¹C-COL in the same animals in two consecutive days. After qualitative analysis, the parameters maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were calculated by means of VOI drawing (50% SUVmax) using PMOD v3.2 software. The statistical analysis was performed with non-parametric tests (StatCalc 12). **Results:** All mice developed tumors that were visually detected. Qualitatively, the three radiotracers were 100% successful in detection of tumors. However, ¹¹C-COL showed a slight uptake and the physiological uptake of ¹⁸F-FDG in the bladder and muscle made the detection difficult in 3 of 12 tumors. The uptake of radiotracers was heterogeneous in 7 of 12 tumors, showing areas with a concordance between ¹¹C-MET and ¹¹C-COL but discordant for ¹⁸F-FDG signal. Quantitatively, ¹⁸F-FDG uptake (SUVmax: 1.4 ± 0.2) was higher than ¹¹C-MET (SUVmax: 1.0 ± 0.2) or ¹¹C-COL uptake (SUVmax: 0.6 ± 0.1), with statistically significant differences between the three groups ($p = 0.0001$). However, no significant differences were found in the MTV defined by the three radiotracers (¹⁸F-FDG: 1.5 ± 0.9 , ¹¹C-MET: 1.5 ± 0.8 , ¹¹C-COL: 1.1 ± 0.6). TLG values were similar for ¹⁸F-FDG (1.5 ± 1.0) and ¹¹C-MET ($1.2 \pm$

0.8) without statistically significant differences, but significantly lower with ^{11}C -COL (0.5 ± 0.3) ($p < 0.001$). **Conclusions:** All three radiotracers detected all of the tumors. However, the poor up-take of ^{11}C -COL makes its diagnostic performance lower than that of ^{18}F -FDG and ^{11}C -MET in this murine MM model. The different distribution of radiotracers along the tumors may reflect the metabolic heterogeneity of the tumors.

EP-0668

The role of FDG PET/CT in the diagnosis and stratification of non-Hodgkin's lymphomas in paediatric population: the experience of a single center institution

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Aim: The presentation of PET-CT results in the diagnosis, monitoring and outcome of non-Hodgkin's lymphomas (NHL), in pediatric patients, comparison with the corresponding CT results and investigation of the two methods complementarity.

Method: 110 patients (1982–2017) with NHL (85 boys, 25 girls) with median age 7.0 years underwent a whole-body CT for initial staging, after 2 or 3 chemotherapy schemes and at the end of the chemotherapy, in order to estimate the imaging response. In addition, 17/110 patients were evaluated with PET-CT: in the initial study (N=7), after 2 chemotherapy schemes (N=2) and after the end of treatment (N=8), in order to assess the metabolic response. **Results:** 6/7 of the patients, who were submitted to PET-CT during the initial diagnosis were PET-CT positive (Burkitt = 1, B-lymphoblastic = 1, T-lymphoblastic = 1, nodular = 1, DL-BCL = 1 and anaplastic lymphoma = 1). In 4/6 PET-CT positive patients, the use of PET-CT revealed additional initial disease localizations undetectable with the initial CT. In 2/17 patients, PET-CT revealed additional residual disease sites undetectable by re-staging CT. Finally, in 8/17 patients with PET-CT at the end of chemotherapy, 2/8 patients had positive metabolic activity, in areas described in the CT evaluation of the imaging response, at the end of treatment. None of the patients has been upgraded, due to the detection of additional PET localizations, since they were already stratified as high risk (R3 / R4) due to imaging (CT) disease localizations. All patients with PET-CT positivity are in remission. **Conclusions:** FDG PET/CT can be used as a diagnostic tool for baseline and re-staging of NHL in childhood, in addition to the existing imaging methods available. FDG PET / CT, is superior compared to CT in detecting additional initial and residual disease of NHL in pediatric patients.

EP-49

e-Poster Area

Clinical -> Therapy study -> Other treatments -> Bone metastases, pain palliation

EP-0669

Quantitative Assessment of Skeletal Tumor Burden in Bone Scintigraphy as a prognostic biomarker in Radium-223-dichloride Therapy

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Purpose/Introduction: [^{223}Ra]RaCl₂ is a bone therapy agent used in metastatic castration-resistant prostate cancer (mCRPC) patients that, unlike other bone-targeted therapies, has been shown to improve survival. The aim of this study was to investigate the prognostic value of quantitative assessment of skeletal tumor burden on bone scintigraphy (BS) previous to [^{223}Ra]RaCl₂ treatment. **Subjects & Methods:** This was a multicentre retrospective study involving three Nuclear Medicine departments. All mCRPC patients treated with [^{223}Ra]RaCl₂, with pre-treatment BS and baseline and end of treatment laboratory tests, namely PSA, ALP, LDH, haemoglobin, leukocyte and thrombocyte count, were selected. Pre-treatment skeletal tumor burden was quantified using whole body geometric mean BS images, in a **GEXel-eris2.0** station. After the exclusion of areas of physiologic uptake (mainly urinary tract and bladder activity) and contamination (mostly injection site), automatic regions of interest (ROI) were drawn fully encompassing the skeleton (S_ROI) and the bone metastasis (M_ROI). S_ROI and M_ROI were corrected for background activity. Percentage of skeletal tumor burden (%STB) was calculated by dividing M_ROI/S_ROI. The primary end point was death. Baseline and end of treatment PSA, ALP, LDH, haemoglobin, leukocyte and thrombocyte count measurements were recorded, as well as demographic variables, treatment status, and follow up time. The variance between end of treatment and baseline laboratory test measurements, percentage-wise, was calculated. Unfortunately, several clinical variables were not available (e.g. GS, TNM stage, staging PSA). **Results:** A total of 29 patients were selected (71.9 ± 9.1 41–87 years). Median number of completed [^{223}Ra]RaCl₂ cycles was 6 (2 cycles:3.4%, 3cycles:20.7%, 4cycles:13.8% and 5cycles:10.3%). During a mean follow-up of 10.8 ± 7 2–30 months, 9 patients died. A statistically significant correlation was found between %STB and baseline PSA, ALP, LDH, and Hb ($p < 0.05$, r^2 :0.689, 0.697, 0.443 and -0.511, respectively). Also, a statistically significant correlation was established between %STB and the number of treatment cycles ($p < 0.05$, r^2 :-0.486). No statistically significant correlations were found between %STB and end of treatment to baseline laboratory test variance, including PSA, ALP, LDH, haemoglobin, leukocyte and thrombocyte count. In a multivariate Cox regres-

sion analysis only %STB was found to be associated with overall survival ($p < 0.05$). **Discussion/Conclusion:** Baseline skeleton tumor burden quantified by %STB seems to be a promising prognostic biomarker in mCRPC patients receiving [^{223}Ra]RaCl₂. Furthermore, pretreatment %STB was negatively correlated with Hb (bone marrow suppression due to advanced disease), however a greater burden of disease was not associated with a worsening of hematological toxicity.

EP-0670

Radium-223 Dichloride For Castration Resistant Metastatic Prostate Cancer - Usefulness Of The Response Evaluation Using Ra-223 CZT Spect/ct For Quantitative Analysis

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Purpose: Image-based quantitative analysis of Radium-223 dichloride (Ra-223) may be useful in predicting therapeutic response in patients with castration-resistant prostate cancer (CRPC). The aim of this study was to evaluate clinical usefulness of Ra-223 cadmium-zinc-telluride (CZT) SPECT/CT. **Materials and Methods:** CRPC patients with bone metastasis who received Ra-223 treatment from January 2017 to March 2018 were included. All patients underwent bone scintigraphy and F-18 FDG-PET/CT before and after the treatment. Ra-223 CZT SPECT/CT was performed at 2 hours and 4 days after injection. Quantitative analysis was performed by measuring SPECT standardized uptake value (SUV) and bone scan index (BSI). The rate of change of SPECT-SUV (%SPECT-SUV) and the rate of change of BSI (%BSI) were calculated as follows: %SPECT-SUV = (4 days SPECT-SUV - 2 hours SPECT-SUV) / 2 hours SPECT-SUV, %BSI = (after treatment BSI - before treatment BSI) / before treatment BSI. The correlations between these quantitative parameters derived from bone scintigraphy and Ra-223 CZT SPECT/CT were analyzed. **Results:** Fourteen scans were enrolled. Four were excluded because they were not taken care of as an outpatient. A statistically significant negative correlation between %SPECT-SUV and %BSI was observed with a Pearson's correlation coefficient (r) of -0.784 and a p -value of 0.007. FDG accumulation of bone metastases also changed consistent with BSI. **Conclusion:** Quantitative evaluation using Ra-223 CZT SPECT/CT may be effective for predicting Ra-223 therapeutic response.

EP-0671

Assessment In Patients With Bone Metastasis By CPRC Treated With RA-223 Through PET-¹⁸FNa

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Objective: To evaluate the value of PET with ¹⁸FNa in the follow-up of patients with bone metastases by CRPC, treated with Ra-223. **Material and Method:** Ten consecutive patients were studied, with an indication of treatment with Ra-223 due to their CRPC, all of them symptomatic and with confirmed osteogenic

bone metastases. The average age was 70 years, (Range 57-81). PET-¹⁸FNa studies were performed prior to treatment, between the 3rd and 4th doses and between the 1st and 2nd week after the end of the 6th cycle. A qualitative and a quantitative analysis of the images was carried out using Segami Oasis V3.0.1.9000 software. A follow-up study was performed 6th months after the last treatment dose. **Results:** All patients presented a significant decrease in the EVA scale of pain with a reduction of analgesia. Regarding the initial PET-¹⁸FNa, the patients were classified into two categories: oligometastatic ($n=3$, 1 exitus) and disseminated disease, which included countless M1 and diffuse infiltration pattern ($n=7$, 4 exitus). A Flare phenomenon was identified in 3 patients. Visual assessment showed bone progression at the end of treatment in 3/10 patients. The remaining 7/10 showed partial response or stabilization of bone disease. The calculation of tumor metabolic volume (MVT) showed an association between the highest VMT in the baseline study and mortality. The SUVmax showed no evolutionary correlation with the qualitative assessment of the studies. **Conclusions:** PET-¹⁸FNa can precisely evaluate the state of dissemination of metastatic bone disease in patients who are candidates for treatment with Ra-223. There is a high proportion of patients in very advanced stages of the disease. The clinical response to pain did not correlate with the metabolic response. The value of VMT reflected the evolution of the disease throughout the treatment.

EP-0672

Disease Control Rate and Pain Response Rate in castration resistant prostate cancer patients with symptomatic bone metastases treated with ²²³Radium: a unicentric experience

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Aim: ²²³Radium (²²³Ra) has been shown to improve overall survival (OS), to delay skeletal-related events and to reduce pain in patients with castration-resistant prostate cancer (CRPC) and bone metastases. Our retrospective, observational study aims to evaluate Disease Control Rate (DCR), Pain Response Rate (PRR) and OS, in patients underwent ²²³Ra-therapy at Policlinic-University of Bari. **Materials and Methods:** From February 2016 to April 2018, 24 patients (mean age 68 years, range 57-83) with symptomatic bone metastases of CRPC, matching the approved inclusion criteria, were enrolled at our Nuclear Medicine Department to underwent ²²³Ra-therapy. Among them, 14 patients who completed all six scheduled doses of therapy (55 kBq/kg, 4 weeks intervals) were included in the analysis. The time from diagnosis of bone metastases was mean 35.4 months (range 13-72). At the time of starting therapy, each patient had at least 6 bone metastases (tumor burden: 6-20 in 8/14; >20 in 6/14), assessed by bone scintigraphy. Treatment response was evaluated by comparing the number of lesions from pre-therapy to post-therapy bone scintigraphy and classified in: complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD). DCR was calculated as the fraction of patients who had the best response rating (CR+PR+SD). PRR was

also assessed both at the end of the treatment and at follow-up, using a quantitative pain scale (Brief Pain Inventory-Short Form). Finally, the OS was estimated using Kaplan-Meier method. The mean follow-up period was 8.86 months (5–21 months). **Results:** At the end of treatment PR was observed in 2/14 (14.3%) patients, SD in 5/14 (35.7%) and PD in 7/14 (50%). No CR was observed in our sample. The DCR was 50%. At follow up assessment only 1/14 patients died. Although patients referred increasing pain in the first 3 months of ^{223}Ra -therapy, probably due to “flare phenomenon”, PRR resulted 71% (10/14 patients) at the end of treatment, while decreased to 35% (5/14) at follow-up. Mean OS after ^{223}Ra -therapy was 634 days (IC 95%; range 615.79–653.21). **Conclusion:** ^{223}Ra confirmed to be an important treatment option for patients with CRPC and symptomatic bone metastases. Our results demonstrate that it is able to control the disease in a significant percentage of patients and to extend survival with a favorable safety even in the presence of a high tumor burden. ^{223}Ra -therapy has proved also effective in pain control in the majority of patients for a mean period of 8 months.

EP-0673

^{223}Ra -dichloride Treatment In mCRPC Patients: Analysis Of An Elderly Population

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Aim: ^{223}Ra -dichloride in mCRPC symptomatic patients is administered without age foreclosure, but there are no study focused on elderly patients. Study aim is to analyze the subgroup of mCRPC elderly patients treated with ^{223}Ra -dichloride in our Center. **Materials and Methods:** ^{223}Ra -dichloride (55KBq/Kg lq4w) was administered to 38 mCRPC symptomatic patients more than 80 years aged. Previous therapies (Docetaxel, Cabazitaxel, Abiraterone or Enzalutamide), follow-up time, Gleason, BMI and ECOG Performance Status were analyzed. Previous use of diphosphonates was also considered. Moreover, Baseline and “At the End of ^{223}Ra treatment” (ATE) values were recorded, such as Complete blood counts, PSA and tALP. Exploit the Brief Pain Inventory Numeric Rating Scale (BPI 0–10 Scale) and Narcotic Score (NS)(considering medication type and medication frequency), Pain response during treatment was assessed. **Results:** 38 patients more than 80 years aged (mean age 82.83 years, range 80–91) received ^{223}Ra -dichloride therapy. 8 were still receiving treatment at the time of analysis, so it was performed on 30 pts. 21 patients completed all the 6 scheduled administrations while 9 patients discontinued ^{223}Ra treatment for death or progression disease. 10 patients had no previous treatments, 10 patients received only 1 previous therapies while the remaining patients received 2 or more therapies before ^{223}Ra -dichloride. 13 patients received diphosphonates before or during ^{223}Ra therapy. The mean follow-up time was 9.63 months (2–31 months) from the start of ^{223}Ra therapy. ECOG PS was reported as 0 in 5 pts, 1 in 18 pts and 2 in 7 pts. Mean BMI was 26.03 and Gleason median value was 8 (7–10). Baseline PSA mean value was 259.9 ng/ml (2.32–1383) while ATE PSA mean value was 706.5 ng/ml (2.47–1998). Baseline tALP mean value was 291.63 U/l (63–

1188) whereas ATE tALP mean value was 154.75 U/l (41–394). Furthermore, Baseline Hemoglobin mean value was 11.9 g/dl (10.1–14.1) instead ATE Hemoglobin mean value was 10.41 g/dl (8.8–12.7). Finally, Baseline Platelets mean value was $229 \times 10^3/\text{ml}$ (140–331) while ATE Platelets mean value was $181 \times 10^3/\text{ml}$ (98–228). Pain assessment: Baseline BPI mean value 5.4 (2–10) with mean NS 3.73 (0–15), while ATE BPI mean value 3.9 (0–9) with mean NS 2.95 (0–9). **Conclusion:** In mCRPC elderly patients, ^{223}Ra -dichloride is well tolerated, without significant hematological toxicity. The decrease of tALP is emphasized. Pain palliation is also to be underlined, especially because related to lower intake of analgesics. Therefore, even in older population, we recommend the use of ^{223}Ra -dichloride therapy.

EP-0674

Post Therapy Biodistribution and Dosimetric Analysis of Lutetium Zoledronate [^{177}Lu]Lu-DOTA^{ZOL} in Patients with Osteoblastic Metastases : First Results

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Pre-clinical *in vitro* and *in vivo* animal biodistribution and dosimetric analysis of [^{177}Lu]Lu-DOTA^{ZOL} has proposed it to be an upcoming new theranostic therapeutic radionuclide for skeletal metastatic disease. In this study biodistribution and normal organ absorbed doses resulting from therapeutic doses of [^{177}Lu]Lu-DOTA^{ZOL} in patients of skeletal metastatic disease was evaluated. **Method:** Four metastatic skeletal disease patients (mean age $\pm$ SD: 69.25 ± 9.21) secondary to mCRPC and bronchial carcinoma and non-responsive to conventional therapies were treated with mean dose of 5968 MBq of [^{177}Lu]Lu-DOTA^{ZOL}. Patients underwent blood sampling and planar whole body imaging using pre-calibrated Symbia SPECT/CT gamma camera at 20min, 3, 8, 24 and 167 h post injection (p.i) with a known standard source placed between the legs. For dosimetric analysis ROI were drawn manually on source organs (Kidneys, urinary bladder, whole body) as well as for soft tissue background, background outside the body and standard source on first image and copied to later images. MIRD pamphlet no 16 and EANM dosimetry guidelines were used for source organ activity and whole body activity calculations. Bone marrow self-dose was determined by indirect blood based method. Urinary bladder wall residence time was calculated using cloutier’s dynamic urinary bladder model with 4 h voiding interval. OLINDA/EXM software was used to determine residence times in source organs by applying biexponential curve fitting and organ absorbed dose calculations. **Results:** Qualitative analysis revealed early and high uptake in kidneys with fast clearance showing minimal activity by 24 h. Activity in skeleton increased gradually over time starting as early as 2–3 h p.i. Rest of the organs did not show relevant uptake. Mean residence times (MBq-h/MBq) were also found to be highest in bones followed by kidneys. Residence times for skeleton varied with tumor load in patients. Mean organ absorbed doses were highest in osteogenic cells (2.92 mSv/MBq) followed by kidneys (0.495 mSv/MBq), red marrow

(0.413 mSv/MBq) and urinary bladder (0.206 mSv/MBq). Comparison of biodistribution and normal organ absorbed doses for humans computed from animal biodistribution and dosimetry with current study has shown similar pattern of organ absorbed doses with lower doses. **Conclusion:** High uptake in skeleton of [^{177}Lu]Lu-DOTA^{20L} with maximum absorbed dose in skeleton and lower kidney doses as compared to [^{177}Lu]Lu-PSMA proposes it to be a better therapeutic agent for metastatic skeletal disease. However further clinical response studies with tumor lesion dosimetry need to be evaluated.

EP-0675

Early Therapy Assessment of ^{223}Ra -Dichloride by ^{18}F -Fluorocholine PET/CT in Castration-Resistant Metastatic Prostate Cancer: a Single Institution Experience

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Purpose: To evaluate the utility of early assessment of ^{223}Ra -dichloride therapy by ^{18}F -fluorocholine (FCH) PET/CT in patients with symptomatic bone metastases of castration-resistant prostate cancer (mCRPC) to early adjust therapy and predict end-treatment response. **Methods:** We administered ^{223}Ra -dichloride (6 monthly planned injections of 55 kBq/Kg) in 20 symptomatic patients with mCRPC and bone metastases (mean age 69 y, range 54–76 y) from June 2015 to April 2018. Patients were excluded if they had a malignant lymph nodes >3cm in the short-axis diameter. All patients underwent baseline bone scintigraphy before and after therapy and FCH PET/CT at baseline and within 2 wks after the 3rd and 6th ^{223}Ra injections. **Results:** Two patients are still under treatment and 10 patients did not complete the 6 planned cures, because of hematologic toxicity (n=4), disease progression (n=4), or death (n=2). Of 8 patients who received the 6 cures, mid-therapy FCH PET/CT showed a disease control on bone metastases (partial response or stable disease) in 5 and bone progression in 3. A nodal involvement was present in 3 of 5 patients who improved and in 2 of 3 who progressed. One patient who responded on bones had nodal progression. Regarding end-treatment FCH PET/CT, 3 of 5 patients with early improvement demonstrated further improvement in bone disease (1 also improved in lymph nodes), while the remaining 2 progressed in both target sites. Nevertheless, metabolic tumour activity decreased by a half between 1st and 3rd FCH PET/CT assessments. Two of 3 patients with early progression demonstrated further progression and the 3rd one showed bone and nodal stability. One of 2 refractory patients (with initial nodal involvement) progressed with hepatic metastases. Ultimately, 4 patients presented disease control including 3 of 5 early responders and 1 of 3 early refractory patients. **Conclusion:** These preliminary results suggest that early FCH PET/CT imaging has a very interesting predictive value for therapy assessment of ^{223}Ra -dichloride, especially in patients without nodal involvement. Further investigations in larger series are

warranted to determine the predictive value of serial early FCH PET/CT assessment among those cases.

EP-0676

Radium-223: overall survival, disease free survival and response variables during therapy

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Aim: To analyse overall survival (OS) and disease-free survival (DFS) of patients with metastatic Castration Resistant Prostate Cancer (mCRPC) treated with Radium-223, its relation to first-line treatment, and to assess the association of clinical response parameters and DFS during alphatherapy. **Materials and Methods:** 25 patients with mCRPC treated with 3 or more Radium-223 doses were included; 22 of 25 had finished their alphatherapy at the time of this analysis. 9/22 patients received at least Docetaxel prior Radium-223; 13/22 received Radium-223 prior Docetaxel and 7 of those received Radium-223 as first-line treatment. OS and DFS were analysed from the beginning of Radium-223. The overall tendency of lactate dehydrogenase (LDH), alkaline phosphatase (ALP) and Prostate Specific Antigen (PSA) during alphatherapy (upward or stable/downward tendency) was established and their association with DFS during Radium-223 treatment was assessed. **Results:** Median OS was 14 months. Median OS for patients treated at least with Docetaxel prior Radium-223 was 8 months and none of the patients treated with Radium-223 prior Docetaxel were dead at the time of analysis, with statistically significant difference (p=0.05). Median DFS was 7 months, 5 for patients treated at least with Docetaxel prior Radium-223 and 7 for those treated with Radium-223 before Docetaxel, with no statistical significance (p=0.092). 17/25 patients showed upward PSA tendency and 8/25 stable/downward tendency. ALP tendency was upward for 5/24 and stable/downward for 19/24. For LDH, 10/24 patients showed upward tendency and 14/24 stable/downward tendency. No association between PSA or ALP and DFS during treatment was found, but the LDH tendency showed association to progression during alphatherapy, with statistically significant difference (p=0.011). Out of the 8 patients who showed upward LDH and disease progression during alphatherapy, 7 (87.5%), had non-osseous disease. **Conclusion:** Therapy with Radium-223 before Docetaxel treatment improves OS and DFS of mCRPC patients. LDH is a useful tool to monitor the progression of non-osseous disease during therapy with Radium-223.

EP-0677

Clinical experience with radium-223 in the treatment of patients with advanced castrate-resistant prostate cancer and bone metastases

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Aim: To present our clinical experience and to identify baseline features that may predict outcome in ^{223}Ra therapy (^{223}Ra). **Materials and Methods:** We retrospectively reviewed 30 patients (age range 53–86 years) with metastatic castration-resistant prostate cancer with >2 bone metastases and no visceral metastases who were administered in total 112 cycles of ^{223}Ra in our department from August 2016 till March 2018. The following parameters were evaluated prior, during and after ^{223}Ra treatment: blood values, prostate-specific antigen (PSA), alkaline phosphatase (ALP), Eastern Cooperative Oncology Group (ECOG) performance status and pain score (WHO criteria). Skeletal burden on bone scan and use of prior therapies were also evaluated. Patients were followed up for median 6 months (1–13 months range). **Results:** The planned course of six cycles was completed in eleven patients (37 %), was interrupted in thirteen patients (43%), while six patients (20%) were still undergoing ^{223}Ra treatment at the time of analysis. In the group that completed six cycles of ^{223}Ra therapy, PSA and ALP values increased in nine pts (81%) (mean PSAdt=2.6mo, mean ALP increase=47%), did not demonstrate significant alteration in one patient and decreased in one patient with concomitant reduction in pain score. Patients tolerated well ^{223}Ra therapy with mild adverse events. Four patients continued with other therapies after completion of 6 cycles ^{223}Ra due to clear disease progression. Another patient died 3 months after completion of ^{223}Ra treatment due to disease progression and concomitant bone marrow failure. In thirteen patients ^{223}Ra treatment discontinued after median=2 cycles (range=1–4) due to disease progression and one or more of the following: hematologic toxicity (n=8, grade 2 anemia, grade 3 thrombocytopenia), declining ECOG status by two points (n=6) and severe side effects (n=2, nausea, anorexia, fatigue). Four patients were switched to another therapy and five out of thirteen patients died at a mean time of 8 months after cessation of ^{223}Ra treatment due to disease progression. None of the patients presented acute skeletal events. Patients with borderline hematologic values, significant skeletal disease burden (>50foci), short PSAdt during initial evaluation and those who had received external beam radiation therapy, were more susceptible in hematologic toxicity /other adverse events and completed lesser cycles of ^{223}Ra . **Conclusion:** Our initial experience on the use of ^{223}Ra treatment denotes that patients with less aggressive and lower burden of disease having sufficient marrow reserves are more likely to complete ^{223}Ra therapy and achieve better therapeutic outcomes.

EP-0678

Prognostic aim of interim and final bone scintigraphy and ^{18}F -Fluorocholine PET/CT response in patients with prostate cancer treated with ^{223}Ra

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Purpose: To determine the prognostic value of $^{99\text{m}}\text{Tc}$ -HDP bone scintigraphy (BS) and ^{18}F -Fluorocholine PET/CT findings in the

interim and end-of-treatment response evaluation in patients with castration-resistant prostate cancer and bone metastases (CRPC-BM) treated with ^{223}Ra . **Subjects & Methods:** Prospective and multicenter ChoPET-Rad study. 45 patients with CRPC-BM and indication for ^{223}Ra treatment, who received at least 3 doses, were consecutively included. Basal, after 3 (interim) and 6 doses (final) BS and PET/CT were performed. Clinical variables [Gleason score, basal PSA, previous treatments, treatment failure, degree of response (progression or not) of bone metastases in both imaging techniques], progression free survival (PFS) and overall survival (OS) were obtained, after a minimal follow-up of 6 months. The relation between clinical and imaging variables with PFS and OS was analyzed by ROC; Kaplan-Meier and Long Rank (Mantel-Cox) tests. **Results:** Of the patients included, 45% of them had Gleason score ≥ 8 , 84% were post-docetaxel, 80% had multimetastatic disease in BS and 71% in PET/CT. Median $\pm$ SD of PFS and OS of these patients were 3.0 ± 0.2 and 23.0 ± 1.5 months, respectively. 20/45 patients died during the follow-up. Only the final response in BS was related to OS ($\chi^2=6.78$; $p=0.009$), while multiple variables were related to PFS, like interim response in BS ($\chi^2=4.45$; $p=0.035$), interim response in PET ($\chi^2=12.33$; $p<0.001$) and final response in PET ($\chi^2=6.56$; $p=0.010$). Conditioned by the progression of disease, the therapeutic failure (not to complete the 6 doses of treatment) was associated with a higher risk of death (HR=4.8; $p=0.004$). Likewise, the patients categorized as progression in final BS had 11.5 times higher death risk than the rest ($p=0.012$) and the ones identified as progression in interim and final PET presented a 3.5 ($p=0.04$) and 4.4 ($p=0.03$) times higher risk of biochemical progression than the others, respectively. **Conclusion:** Both BS and ^{18}F -Fluorocholine PET/CT at the interim and final evaluation of patients treated with ^{223}Ra were good predictors of PFS. The results of the final BS were related to the OS. An increase of the sample will demonstrate the possible added value of PET/CT in the prognosis.

EP-0679

Survival analysis of castration resistant prostate cancer (CRPC) patients with bone metastasis, without visceral metastatic disease, treated with Ra223

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Aim: The aim of this study was to assess the efficacy of Ra223 treatment in CRPC patients. A survival analysis was conducted, estimating overall survival (OS) and progression free survival (PFS). **Materials and Methods:** CRPC patients treated with Ra223 (28) were assessed in two groups: pre Docetaxel (preD) patients (18) and post Docetaxel (postD) patients (10). A survival analysis was performed in both groups using the Kaplan-Meier method, to determine the therapeutic effectiveness of Ra223, considering if they received or not a complete treatment. **Results:** Of the 28 patients, 12 patients received 6 doses, 3 patients received 5 doses, 4 patients received 4 doses, 2 patients received 3 doses, 5 patients received 2 doses and 2 patients re-

ceived 1 dose. In the preD group, half the patients (9) received 1–4 doses and half received 5–6 doses. In the postD group, 4 patients received 1–4 doses and 6 patients received 5–6 doses. The treatment was suspended in 55.6% of the preD patients and in 40% of the postD patients. The global progression free survival (PFS) was 6.1 months; 6.7 months in the preD group and 5 months in the postD group, with no statistically significant differences between groups. General overall survival (OS) was 11.8 months; 10.1 months in the preD group and 14.4 months in the postD group, with no statistically significant differences between groups. OS was 16 months for patients who completed the treatment and 8.3 months for those patients whose treatment was suspended. This difference was statistically significant ($p=0.02$, 95% IC from 12.1 to 19.9). **Conclusion:** -Ra223 is an effective therapeutic option that improves overall survival for patients who complete the treatment. - No statistically significant differences in OS and PFS were found in relation with a previous Docetaxel treatment.

EP-0680

Ra223 treatment of castration resistant prostate cancer (CRPC) patients with bone metastasis, without visceral metastatic disease

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Aim: We assess the efficiency and impact on the quality of life of Ra223 treatment in CRPC patients performing a clinical follow-up. **Materials and Methods:** We assessed 28 CRPC patients treated with Ra223 (18 preDocetaxel and 10 postDocetaxel), considering clinical aspects (pain relieve, secondary effects, progression, ECOG scale), biomarkers (alkaline phosphatase, prostate-specific antigen, lactate dehydrogenase and blood count), and previous administration of Docetaxel. Mortality and progression free survival (PFS) has been analyzed. **Results:** Most patients reported pain relief after the first dose. The most usual side effects were fatigue and nausea. There wasn't a significant trend on the evolution of the biomarkers. Of the 28 patients, 55.6% of the preDocetaxel patient group and 40% of the postDocetaxel group could not complete the treatment. Patients who suspended treatment had the highest ECOG (66.7% of ECOG 2 and 75% of ECOG 3). General PFS was 6.1 months, 6.7 months for the preD group and 5 months for the postD group. We found progression in the 46.4% of patients: bone (7.2%), visceral (25%) and hematological toxicity (14.2%), with no statistically significant differences between the pre/post Docetaxel groups. 71.4% of exits were in the preDocetaxel group and 28.6 in the postDocetaxel group, with no statistically significant differences between them. **Conclusions:** -Ra223 is an effective therapeutic option in CRPC patients, easing the pain in most cases since the first dose, and initially improving the quality of life. -46.4% of patients had progression, therefore, PFS is regardless of whether they received prior chemotherapy or not.

EP-0681

Two Years Of Clinical Experience Outcome Review On Radium223 Therapy In Bone Metastatic Castrate-resistant Prostate Cancer

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Introduction: In Portugal, Radium 223 therapy (RaT) has been approved for bone mCRPC in pts without visceral metastasis, with previous therapy with docetaxel or not fitted for it. We evaluated biomarkers and bone scan evolution, as well as myelotoxicity in our 2 years clinical experience review. **Subjects & Methods:** twenty pts with bone mCRPC received RaT, seventeen (85%) after previous docetaxel. All had good ECOG performance status. All bone scans revealed focal metastasis (no baseline superscan). Complete blood count, APH, LDH and PSA were determined the week before each 223Ra administration and at 1 (n=18), 6 (n=13) and 12 months (n=7) after last cycle (ALC). Bone scan was performed at 3, 6 and 12 months ALC. **Results:** 107 injections were administered. 12 pts completed the 6 cycles. One is still ongoing and 7 were cancelled prematurely: one for visceral progression, 3 due to thrombocytopenia (tbp) and 3 for other clinical reasons. 3, 4 and 5 cycles were completed respectively by 3, 1 and 3 pts. One month ALC, average decrease (↓) was more pronounced in neutrophils (45%↓, but in normal ranges), platelets (34%↓) and haemoglobin (20%↓). Four pts reached grades 2 and 3 tbp (2+2) and two pts reached grade 2 anaemia. APH 44%↓ and LDH 69%↓. Except for platelets and haemoglobin, the other ↓ were transitory. PSA increased in all patients (75%↑). There was a statistically significant higher tbp in patients with previous docetaxel (27%↓ vs 8%↑ - $p<0.005$). No skeletal events were ever reported. At one month ALC, bone scans showed stable disease in 4 pts and progression in the others (less uptake in the original lesions, but new lesions or mainly a disseminated/medullar pattern). All pts were alive 1 month after the last cycle. 22% (4/18) died before the 6th month evaluation and the 1 year ALC survival rate was 66% (12/18). **Conclusions:** 1. Controllable but irreversible medullar toxicity for haemoglobin and platelets that shortened the therapy in 16% of the pts. 2. Cumulative toxicity only for the platelets line on pts with previous docetaxel therapy. 3. Decrease (>40%) in bone biomarkers (APH and LDH) with increased (75%) PSA. 4. Change in bone scan pattern: from multiple focal disease into less osteoblastic lesions but in a more extensive and diffuse/medullar pattern (different from the usual superscan), suggesting disease progression.

EP-0682

The Relevance Of The Treatment The Prostate Primary Tumour In The Response To Radium-223 In Bone Metastatic Castration Resistant Prostate Cancer

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Introduction: Radium-223 (223Ra) improves survival in patients with metastatic castration-resistant prostate cancer (mCRPC). The primary prostate tumor could progress during 223Ra treatment period, particularly if hematological toxicity, patients compliance and general status and other factors might limit the early start of further therapy. The aim of our study was to evaluate the clinical impact of the presence or absence of primary tumor in terms of progression, death and treatment withdrawal in patients with mCRPC undergoing 223Ra therapy. **Materials and Methods:** The clinical records files of 44 consecutive patients were reviewed. In all patients luteinizing hormone-releasing hormone analogues therapy was maintained. The 223Ra treatment schedule consisted in the administration of 55 kBq/kg every 4 weeks for up to six injections. Patients were stratified according to the presence or absence of the primary prostate tumor. Radium-223 treatment was discontinued at patient's request, on occurrence of CTCAE grade 3 or 4 neutropenia, anaemia or thrombocytopenia lasting longer than 14 days, for visceral progression or for a dose delay of more than 4 weeks. Clinical outcomes in terms of progression, death and treatment withdrawal due to toxicity were analyzed according to the presence/absence of the primary tumor. **Results:** The clinical records files of 44 consecutive patients were reviewed. The Gleason grade of the prostate tumor was 7, 8 and 9–10 in 11 (25%), 13 (29.5%) and 13 (29.5%) patients respectively. Sixteen (36.4%) patients were previously submitted to radical prostatectomy and 5 (11.3%) to prostatic radiotherapy, while in 28 (63.6%) the primary prostate tumor did not receive any local treatment. All patients had bone metastases, the number of lesions was less than 6 in 9 (20.4%), between 6 and 20 in 10 (22.7%) and more than 20 in 24 (54.5%) patients. Twenty-six (59.1%) patients had previously received systemic chemotherapy. 223Ra regimen was suspended in 17 patients (41%): for toxicity in 9 (20.4%), for progression in 7 (15.9%) and for other causes in 1 (2.3%). Out of these 17 patients, 14 (77.7%) had their prostate, previously submitted to radiotherapy in 2 patients. Out of 12 (27.3%) patients showing progression, 9 (75%) patients had their prostate, submitted to previous radiotherapy in 1 case only. Five patients died, 4 of them with their prostate. **Discussion and Conclusion:** In our preliminary experience, the presence of the primary prostate tumor plays a detrimental role in terms of treatment completion and clinical response in 223Ra treatment.

EP-0683

Single Center Clinical Experience With Radium-223 Dichloride In Patients With Metastatic Castrate-resistant Prostate Cancer

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Objectives: From October 2015 National Cancer Institute patients with metastatic prostate cancer started receiving treat-

ment with Radium-223 dichloride. The aim of this study was to evaluate clinical, biochemical and radiological response to treatment. **Methods:** In total between October 2015 until April 2018, 32 patient received treatment with Radium-223 dichloride. Incidence of hematologic, gastrointestinal, and other adverse events were identified for each patient. Changes in bone pain, serum alkaline phosphatase, prostate-specific antigen (PSA) levels and radiological response to the treatment with the bone scan were obtained and evaluated. **Results:** 15 patients received all 6 scheduled doses of Radium-223 dichloride, 2 patients completed 3 doses, 2 patients received 3 doses and 13 patients are still continuing treatment. On average, a single patient received 5.3 doses of Radium-223 dichloride. 4 patients were scheduled for a second treatment with Radium-223 dichloride between 8 to 16 months after the first treatment (after 10.8 months on average). After 6 doses of Radium-223 dichloride 3 patients (20.0%) became pain free, 8 patients (53.3%) reduced painkillers doses and 4 patients (26.6%) did not report any pain-relieving effect. After treatment 3 patients had radiologically stable disease, 4 patients - mixed response, 2 patients - progressive disease, 6 patients - positive effect (decreased osteoblastic activity, disappearance of the metastatic lesions). Falling in serum alkaline phosphatase and PSA was observed in 13 and 4 patients respectively. 2 patients discontinued treatment after receiving at least two doses due to grade III hematological toxicity (required blood transfusions), 2 discontinued treatment due to acute cardiovascular events. 5 patients developed mild gastrointestinal symptoms, 6 developed grade I-II neutropenia. **Conclusions:** From our single center experience with Radium-223 dichloride the treatment was relatively well tolerated amongst the patients. The main reason for cancelation of the therapy was grade III hematological toxicity and acute cardiovascular events. A decrease of serum alkaline phosphatase was more common than a decrease of PSA.

EP-50

e-Poster Area

Clinical -> Therapy study -> Other treatments -> Local radionuclide treatment

EP-0684

Importance of dosimetric parameters in radioembolization of hepatocellular carcinoma

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⁹⁰Y- Selective internal Radiation therapy (SIRT) is increasingly used for the treatment of hepatocellular carcinoma (HCC). A precise dosimetric evaluation is important in clinical practice to improve predicting clinical outcome. The aim of this retrospective study is to determine a threshold dose for radiological response and hence to assess the prognostic importance of dosimetry in HCC. **Methods:** Forty-five patients with mostly multifocal lesions were treated by SIRT using resin or glass microspheres, between 2011 and 2017 in our institution and underwent post-therapy ⁹⁰Y-(TOF)PET. Average tumor dose (TD) and tumor dose volume

histogram (DVH) were calculated using a dose point kernel convolution algorithm. Radiological tumor response was assessed using modified RECIST criteria. Thresholds for dose response were estimated using ROC curves. Progression-free survival (PFS) and overall survival (OS) were analyzed using Cox regression analysis.

Results: Twenty-six patients were treated with glass microspheres (41 lesions) and nineteen with resin microspheres (51 lesions). Median follow-up was 9 months (range 1.8–26 mo). Median doses for tumor response were 194 Gy and 102 Gy for glass and resin microspheres respectively ($p < 0.0001$), corresponding to a dose ratio of 1.9. This ratio was used to calculate an equivalent glass microsphere dose (resin microspheres dose $\times$ 1.9) for the overall survival (OS) analysis. The threshold for tumor response was 116 Gy for glass microspheres (Se: 90%, Sp: 68%, AUC: 0.91 ± 0.06) and 71 Gy for resin microspheres (Se: 84%, Sp: 70%, AUC: 0.82 ± 0.07). The equivalent glass microsphere TD cutoff of 116 Gy correlated with PFS (HR: 4.12, $p < 0.001$) and OS (HR: 4.62, $p < 0.001$). At the voxel level (DHV), when 66% of the tumor received an absorbed dose of 43 Gy, the outcome (OS) was better predicted with an univariate HR for PFS and OS of 3.82 ($P = 0.001$) and 2.50 ($P = 0.026$), respectively. Using multivariate analysis, only the equivalent glass microspheres TD of 116 Gy was strongly correlated with OS (HR: 6.26, $P = 0.005$). **Conclusion:** Dosimetric parameters correlated well with tumor response, PFS and OS. In clinical practice, a systematic dosimetric evaluation using ^{90}Y -PET should be used to predict the clinical outcome.

EP-0685

Impact of scatter fraction on SPECT relative quantification in patients with HCC treated with ^{188}Re SSS Lipiodol

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Introduction: The main objective of this work was, based on preliminary data from the phase 1 Lip Re I trial (NCT 01126463), to compare the impact of scatter fraction on quantification based on SPECT studies in each target organ in patient treated with ^{188}Re -SSS Lipiodol. **Material and Methods:** Description of biodistribution of ^{188}Re -SSS Lipiodol based on tomographic (SPECT) studies performed at 1, 6, 24, 48 and 72 hours post administration. Quantification in % of administered activity of ^{188}Re SSS lipiodol of detected activity using a double headed gamma camera (Symbia T2, Siemens Healthcare) equipped with medium-energy parallel-hole collimators. SPECT images were reconstructed using corrections for attenuation (low dose CT based attenuation), dead time (Freedman methods), and scatter (Double Energy Window based scatter correction). Two k factors of scatter fraction were used: $k=0.5$ and $k=1$. Tumor on Non Tumor (T/NT) higher uptake ratio were also calculated on each abdominal SPECT studies (using a 3 cm³ VOI positioned on the higher-uptake area of the tumor and on the surrounding healthy liver). **Results:** 6 patients were treated with 1581 ± 414 MBq of ^{188}Re -SSS Lipiodol. Uptakes were seen in liver (tumor and healthy liver) and in lungs only. With a scatter fraction of 0.5: a mean of 90.66 ± 1.70 % of the

detected activity was in whole liver (with 66.06 ± 0.55 % and 24.60 ± 2.08 % respectively in tumor and in healthy liver) and 9.33 ± 1.42 % of detected activity was in lungs (5.66 ± 1.14 % in right lung and 3.66 ± 0.57 % in left lung). The mean T/NT ratio was 31.25 ± 4.08 and stable during time. With a scatter fraction of 1, a mean of 90.44 ± 2.00 % of the detected activity was in whole liver (with 67.63 ± 1.01 % and 22.81 ± 1.50 % respectively in tumor and in healthy liver) and 9.55 ± 2.01 % of detected activity was in lungs (7.48 ± 6.04 % in right lung and 4.92 ± 5.53 % in left lung). The mean T/NT ratio was 41.39 ± 5.11 and stable during time. **Conclusion:** the impact of scatter fraction on SPECT studies with ^{188}Re -SSS Lipiodol was minimal on quantification and on tumoral targeting.

EP-0686

Value Of The Multidisciplinary Approach For Planning Treatment Of Liver Lesions With ^{90}Y -Microspheres

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Aim: To present our results of planning Selective Internal Radiation Therapy (SIRT) after combination of diagnostic arteriography and $^{99\text{m}}\text{Tc}$ -MAA scintigraphy. **Materials and Methods:** We analyzed 22 diagnostic arteriographies performed in 14 patients (mean age: 65.1 years) referred for assessment of treatment with ^{90}Y -microspheres (11 hepatocarcinomas and 3 cases of hepatic metastases of colorectal carcinoma). We intend to perform 5 bilobar treatments and 9 unilobar treatments. During the performance of diagnostic arteriography catheter placement point is selected and occlusion of non-interesting arteries is needed to guarantee appropriated/successful tumor treatment. Radioisotopic procedure is jointly performed with interventional radiologist by an intraarterial injection of 259 MBq of $^{99\text{m}}\text{Tc}$ MAA. 30 minutes later, thoracic and abdominal planar images and abdominal SPECT/CT are obtained to calculate lung shunt, ensure hepatic uptake of $^{99\text{m}}\text{Tc}$ -MAA and localize possible extra-hepatic foci. **Results:** In the 22 arteriographies arterial embolization was performed in the gastroduodenal artery (5), the cystic artery (2), gastric branches (2), gastroduodenal and gastric branches (1), and also in 2 cases a balloon microcatheter was placed in the left liver artery to block its flow of blood. After the scintigraphic study, SIRT was dismissed in 3 cases, one due to hypovascular liver lesion and two due to elevated lung shunt (37.5%). Furthermore, a second arteriography was needed when target tissue was not reached by $^{99\text{m}}\text{Tc}$ MAA due to poor placement of catheter (1 case); and to embolize the aberrant arteries (2 cases) when extrahepatic uptake (gallbladder and stomach) was observed. Finally 15 treatments were safely and successfully completed in 12 patients (9 unilobar and 3 bilobar). **Conclusion:** Planning diagnostic arteriography and scintigraphy with $^{99\text{m}}\text{Tc}$ -MAA together is essential to ensure the success of liver lesions treatments with ^{90}Y -microspheres, especially when arterial embolizations are needed after confirmation of extrahepatic uptake in the scintigraphy.

EP-0687**High-energy beta-emitter ¹⁸⁸Rhenium resin application in the treatment of non-melanoma skin cancers patients: preliminary results of a dose-personalized non-sealed brachytherapy**

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Purpose: Surgery is the treatment of choice for basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), grouped in non-melanoma skin cancers (NMSCs). However some patients may show large or multiple lesions located in critical areas (face, scalp, hands, ears or genitals) where surgical excision may be technically difficult and disfiguring. The European Union recently approved the use of a resin containing the high-energy beta-emitter ¹⁸⁸Rhenium (OncoBeta, Rhenium-SCT®) in the treatment of NMSC. The aim of this pilot study was to assess the clinical usefulness and safety of a non-sealed ¹⁸⁸Rhenium brachytherapy in NMSC patients. **Subjects and Methods:** Sixteen consecutive patients (6F, 10M, age range 71-91 y.o.) with nine-teen histologically proven NMSC lesions (14 BCC, 5 SCC) and clinically not eligible for surgical excision, were enrolled. Out of 19 lesions, 11 were located on face and scalp, 6 on the limbs and 2 on the back. Lesion's characteristics were: surface areas ranged from 2 to 13,2cm² (mean 6.1cm²), thickness invasion ranged from 0,2 to 2,0mm (mean 0,9mm). To deliver an empiric dose of 35Gy to the deepest point of neoplastic infiltration (previously assessed by skin biopsy), the administered ¹⁸⁸Rhenium activity ranged from 202 to 1028MBq (mean 452MBq) and the treatment time ranged from 21 to 285 minutes (mean 67minutes). Patients were followed-up after 7, 21, 60 and 180 days when a biopsy was performed. **Results:** Seven days after therapy, all the treated lesions showed a superficial burn (grade-1 radiodermatitis comparable), generally healing in 20-30days without any therapy required except the largest one (grade-2 radiodermatitis comparable) that needed longer time (40days) and topic application of hyaluronic acid to heal. No pain was reported by any patient. Seven out of nine-teen lesions were biopsied six months after treatment and all of them showed a complete histological response. Absence of neoplastic structures was confirmed also by video-dermoscopy. No mid-term, local or systemic side-effects were registered. A dermatological examination showed excellent esthetic results due to the absence of any scar in all the treated lesions. **Conclusion:** Despite the limitation of the small population enrolled, we can conclude that the use of the dose-personalized non-sealed ¹⁸⁸Re-brachytherapy in patients with NMSC is highly effective and it is an alternative when surgery is critical or not recommended. Moreover the procedure is easy and provides excellent aesthetic results. No major side-effects were reported. A larger number of patients and a longer follow-up are needed to confirm our findings.

EP-0688**Quality of Life in patients with Neuroendocrine Tumors Treated With [¹⁷⁷Lu-DOTA 0,Tyr 3]octreotate**

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Introduction: Peptide receptor radionuclide therapy (PRRT) is an effective treatment modality in patients with metastasized neuroendocrine tumors (NETs). We purpose to evaluate the quality of life (QoL) in patients with somatostatin receptor positive inoperable or metastatic NETs throughout therapy cycles. **Methods:** Where included 28 patients followed in our center. Were analyzed overall QoL and specific domains of QoL according to the Organization for the Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30) scoring manual. **Results:** In this sample, 20/28 patients were men with mean age of 67 years (29-81 years). Regarding to origin, 53.7% (15/28 cases) were gastroenteropancreatic NETs. From the 28 patients, 18 completed at least 2 copies of the EORTC QLQ-C30 at different times (before and after the last therapy's cycle). Patients had been treated with mean activity 614mCi of ¹⁷⁷Lu-octreotate (303-1177 mCi). Fourteen patients had progressive disease, twelve had stable disease and two had notable lesions regression during PRRT. Regardless of the treatment outcome, Global Health Status/QoL (GHS/QoL) improved significantly in the total group (p=0.03) with an improvement on score superior to 10 points before vs after therapy (Δ+10.1). Besides GHS, we observed also a favorable impact on cognitive functional scale (p=0.046) after therapy. **Conclusions:** A better health-related QoL in cancer patients with incurable disease is an important outcome of cancer therapy, especially when survival is prolonged. Therapy with ¹⁷⁷Lu-octreotate significantly improved QoL regarding cognitive function and had favorable impact on global health status even on those with progressive disease.

EP-0689**Multimodality imaging analysis improves effectiveness and safety of 90-Yttrium radioembolization in liver tumors**

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Aim: Trans-Arterial-Radioembolization (TARE) using 90-Yttrium microspheres (90Y-spheres) is a well-established therapy option in primary or secondary liver malignancies. To date, there is not a consensus in reference imaging method for the evaluation of the extent of liver disease after TARE. Morphological, metabolic and perfusion tumor characteristics, provided by contrast-enhanced CT (CECT)/trans-arterial CECT (arterial-CT), PET/CT and 99mTc-MAA-SPECT/CT, can highlight different but equally important aspects of the same disease. We present our

multimodality imaging analysis approach in which the TARE planning derived from the different pre-treatment imaging modalities. **Material and Methods:** from May 2016 to March 2018, 54 patients (mean age 69 years, range 38–84) were evaluated as potentially candidates for TARE: 34/54 (63%) hepatocellular carcinoma (HCC), 18/54 (34%) liver metastasis (LM), 2/54 (3%) cholangiocarcinoma. All patients were preliminary subjected to 18F-FDG-PET/CT (in FDG-avid tumors) or 18F-FCH-PET/CT (in well-differentiated HCC) and an abdomen CECT for staging liver disease and to detect the target tumor, both with metabolic and morphological data. Moreover, during the angiographic work-up, arterial-CT was acquired, outlining the perfusion territories of the hepatic artery branches. Finally, 99mTc-MAA-SPECT/CT was performed as TARE simulation. Subsequently, nuclear physician together with radiologist provided an off-line fusion imaging registration of arterial-CT, 99mTc-MAA-SPECT/CT and PET/CT exams on a dedicated workstation in order to integrate volume with perfusion and metabolic target lesion data. When needed, the angiographic work-up and 99mTc-MAA-SPECT/CT simulation were repeated. Mean and max counts in 99mTc-MAA-SPECT/CT and volumes in arterial-CT, both for lesion and healthy perfused liver, were considered to calculate the injected activity. After TARE, 90Y-PET/CT was performed to confirm the preliminary simulation. **Results:** In 21/54 (38%) patients, PET/CT information guided the treatment in the most metabolically active area of the target lesion. In 5/54 (9%) patients, arterial-CT identified more extensive liver involvement with widespread microscopic disease, not detected at staging imaging; they resulted not eligible for TARE. In 7/54 (13%) cases, there was discordance between 99mTc-MAA-SPECT/CT and arterial-CT results and the angiographic work-up was repeated. The remnant cases demonstrated a good match between different imaging methods. In all cases the 90Y-PET/CT post-TARE confirmed the preliminary radiopharmaceutical distribution. **Conclusion:** The multimodality imaging analysis based on the integration of different information develops a “disease liver map” which consider morphologic, metabolic and perfusion aspects. Our experience demonstrates that this approach allow to optimize treatment efficacy (directing more precisely to the target lesion with a better selectivity) and safety (avoiding irradiation to the healthy liver).

EP-0690

Ultrasound Monitoring Of The Synovial Thickness After 166-Holmium-Phytate Radiosynoviorthesis Six years results Phase III prospectiv study

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166-Holmium-phytate produced by us: radiation type beta energy maximum: 1,84 MeV; radiation type gamma energy maximum: 0,66 MeV; soft tissue penetration: maximum 8,4 mm; average: 3,3 mm; half-life: 26,9 hours; particle size: 0,6–2 µm **Study Objectives:** measur the synovial thickness after 166-Holmium radiosynoviorthesis by sonography. **Methods:** Phases III, prospectiv study. 33 patients suffering from chronic synovitis, rheu-

matoid arthritis were examined. The protocol commenced with screening. The patients were selected according to inclusion and exclusion criteria. **Patients:** Gender (male/female): 10–23; Age: 56,79 (37–77) Stage of knee joint x-ray (I / II): 7/26; Duration of synovitis (years): 6,95(0,5–27), Duration of disease (years): 8,55 (1–27); Number of punctures before the Ho-166 treatment: 11,97; Number of steroid injections before the treatment: 12,36. Holmium phytate injectable suspension marked by 600 MBq ¹⁶⁶Holmium phytate injectable suspension, and 40 mg of 1 ml triamcinolone acetonide and 1 ml of lidocaine 1 %. There were 72 months follow-up period after the administration of the isotope. Inflammatory activity of the affected knee-joint was tested prior to treatment, and the 3th and 3, 6 12, 24, 36, 48 and 72 months after treatment. We measured the synovial thickness the following locations: In the midline, lateral and medial, by the condylus of femur medial and lateral. **Results:** During the study period, inflammation decreased. In the first six years excellent and good results were recorded in 84%. Six years after radiosynoviorthesis 83.3% of patients did not need another puncture. The thickness of the synovia decreased significantly. We find a significant correlation between the synovial thickness and the clinical improves. **Conclusion:** The 166-Holmium-phytate is an effective new radiopharmakon in the treatment of synovitis. We detect the clinical improvement by sonography. The effective dose is 555–650 MBq. **References:** Margit Szentesi: Radiosynoviorthesis with Ho-166 phytate. First clinical results EANM Post-Congress Scientific Meeting. Radionuclide therapy in theory and practice. Győr, Hungary. 5. szeptember. 2002. Szentesi M.,¹ Környei J.,² Antalffy M.,² Törkő J.,² Tóth Gy.,² Jánoki Gy.,³ Balogh L.,³: Study of intraarticular application of 166-Holmium IHPP in rabbits. World Journal of Nucl. Med. 1. Suppl. 2. S243. September, 2002. Szentesi M.,¹ Takács S.,¹ Farbaki Zs.,¹ Nagy E.,¹ Környei J.,² Antalffy M.,² Törkő J.,² Tóth Gy.,² Jánoki Gy.,³ Balogh L.³ Géher P.,¹ Comparative study of applying increasing doses of ¹⁶⁶Ho- phytate injectable suspension in chronic synovitis. (Comparative, randomized, single-blind, placebo-controlled study with increasing dosage) Eur. J. Nucl. Med. Suppl. 2. 498. 2003.

EP-0691

Is PET/MRI better than PET/CT for imaging and dosimetry after radioembolization with Yttrium-90 (⁹⁰Y) microspheres in the treatment of hepatocellular carcinoma?

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Purpose: This study aims to compare dosimetry obtained from PET/MRI and PET/CT post-therapy imaging, done after radioembolization with ⁹⁰Y microspheres, for patients with hepatocellular carcinoma (HCC). **Methods:** Retrospective analysis was performed on 32 subjects (25 male, 7 female, mean age 64.7 ± 9.9 years). 25 patients were treated with TheraSphere® (glass microspheres; BTG, London, UK) and 7 subjects were treated with SIR-Sphere® (resin microspheres; Sirtex Medical, Sydney, Australia). After **radioembolization** with ⁹⁰Y, patients were imaged on a TOF mCT PET/CT system followed by a PET/MRI study done on a 3 T Biograph mMR scanner (both systems from Siemens

Medical Systems, Erlangen, Germany). Reconstructed images were transferred to a common platform and used to calculate ^{90}Y dosimetry using MIM 6.6 software (MIM Software Inc.). A Passing-Bablok regression scatter diagram and the Bland and Altman method were used to analyze the difference between dosimetry values. **Results:** For PET/MRI and PET/CT modalities, the mean liver dose for all 32 subjects was 46.5 ± 22.7 Gy and 51.6 ± 24.7 Gy, respectively, with a mean difference of 5.1 ± 5.0 Gy. The repeatability coefficient was 9.0 (18.5% of the mean). The Spearman rank correlation coefficient was very high ($p = 0.97$). The maximum dose to the liver varied remarkably, differing up to 40%. However, the mean liver doses from the two modalities were relatively close, with a difference of 18.5% or less. **Conclusions:** ROI creation is likely the dominant driver of differences in ^{90}Y dosimetry between PET/CT and PET/MRI. PET/CT provides better quantification of PET images, due to better attenuation correction. However, liver contours are typically better delineated in MRI images, due to superior soft tissue contrast. Our results suggest that the dosimetry of ^{90}Y microspheres obtained from PET/MRI and PET/CT in post-therapy studies, are comparable.

EP-0692

Practical and Technical Experience of using ^{32}P -OncoSil™ in treating patients with unresectable locally advanced pancreatic adenocarcinoma, in combination with FOLFIRINOX or gemcitabine + nab-paclitaxel chemotherapies.

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Purpose: To share our experience of treating patients with unresectable locally advanced pancreatic adenocarcinoma using ^{32}P -OncoSil™, an open-label, single arm pilot study, performed by OncoSil Medical Ltd. Imperial College Healthcare NHS Trust is the highest recruiter in the UK/Europe. 26 patients have been treated in Australia, 5 in the UK and 2 in Belgium, a total of 33 participants worldwide. **Method:** The study evaluates the safety and efficacy of ^{32}P -OncoSil™ given in combination with systemic chemotherapy, when implanted directly into pancreatic tumours under endoscopic ultrasound guidance (EUS-FNA) using a 22G needle. The activity of ^{32}P -OncoSil™ was calculated by taking 8% of the CT tumour volume and multiplying by the specific activity concentration of ^{32}P OncoSil™ (6.6MBq/ml); giving an intended average tumour dose of 100Gy ($\pm 20\%$). Blood and urine sampling for radioactivity concentration and safety was conducted. Bremsstrahlung imaging was performed within 4 hours of implantation and on day 7 post implantation. ^{18}F -FDG PET/CT imaging was performed at screening and week 12 to assess metabolic tumour response according to PERCIST criteria. **Results and Discussion:** Four patients have been treated to date (62–84 years, 2 male, 2 female). Tumour access was easy and the intended activity for implantation (4.8–16.4MBq) was successfully delivered for all patients. Two patients had ^{32}P -OncoSil™ implanted into the pancreas head, one in the uncinate, and one in

pancreas head/uncinate. The single deposit method was used for central tumour delivery in two patients with SEMS in situ. In one patient, the tracking deposit method was used because of a cyst in the line of implantation site which was aspirated in single pass prior to implantation. ^{32}P -OncoSil™ distribution in the tumour was estimated to be 26–50% in all patients. In most cases the shielded syringe was easy to attach to the endoscope; there was variable resistance to syringe plunger force during implantation. In one case, resistance encountered required higher plunger pressure and repositioning of the needle. It was easy to disassemble the implantation device and decontaminate the endoscope in all cases. **Conclusion:** ^{32}P -OncoSil™ was successfully delivered for four patients at our centre. Bremsstrahlung imaging confirmed successful delivery of ^{32}P -OncoSil™ in all cases. In two cases where follow-up ^{18}F -FDG PET/CT imaging has been completed; both demonstrated focal photopenia at the site of ^{32}P -OncoSil™ delivery, with one showing reduction in bulk of the pancreatic mass.

EP-0693

Retrospective visualization of the cystic artery on hepatic angiographic images: Is there any risk for radiation-induced cholecystitis after radioembolization with Y-90 microspheres?

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Aim: We evaluated whether the retrospective visualization of the cystic artery (CA) on hepatic angiographic images obtained for radioembolization (RE) with Y-90 microspheres was related to any risk for radiation-induced cholecystitis (RIC). **Materials and Methods:** The cystic artery was retrospectively visualized on hepatic angiographic images in 29 patients who underwent RE with Y-90 glass microspheres. Ten patients had primary, 19 patients had metastatic liver tumors. A total of 34 RE procedures were performed through a transarterial catheter from the right hepatic artery. After injection of 185 MBq of Tc-99m MAA, SPECT/CT images were obtained using iterative reconstruction algorithms. The gallbladder uptakes were assessed visually and quantitatively in patients with positive SPECT/CT fusion images and gallbladder doses were calculated using the unit density sphere model of MIRD. Tumor doses, radiation-injected healthy liver doses (RIHLD), and healthy whole liver doses (HWLD) were also calculated using the multicompartmental partition model. **Results:** Of 29 patients, 11 patients had increased Tc-99m MAA gallbladder uptake on SPECT/CT images. In these groups, mean gallbladder dose was 96.4 ± 53.4 Gy. Two patients complained of abdominal pain and distention within 15 days after RE. None of the patients developed acute cholecystitis. During a mean follow-up of 14 months, hematological blood tests remained normal. The mean tumor dose, RIHLD and HWLD were 204.9 ± 66.8 Gy, 70.5 ± 15.7 Gy and 31.1 ± 12.7 Gy, respectively. **Conclusion:**

Radiation-induced cholecystitis is a rare but serious complication. During the RE procedure, the necessity of coil embolization upon the observation of the CA is still controversial. While coil embolization is routinely used by about 40% of the European centers, several studies have shown that even coil embolization of the CA itself may lead to ischemic attacks. Surprisingly, in the current study, RIC was not observed after RE, probably due to the dose range given. Information is lacking about gallbladder limit doses for radionuclide treatment. For external radiation therapy, gallbladder doses up to 90 Gy can be tolerated. Our findings show that up to 100 Gy of gallbladder doses may be safe and tolerable, obviating coil embolization and prophylactic cholecystectomy.

EP-0694

Non - Carrier Added (n.c.a.) ^{177}Lu -DOTATATE Adjuvant Therapy In Initially Surgically Excised Liver Metastasized Non - Functioning Neuroendocrine Tumours Improves Progression Free Survival And Response Rate

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Introduction: To evaluate the progression-free survival and response rate in a cohort of patients with non-functioning neuroendocrine tumors (NF-NETs), treated with n.c.a. ^{177}Lu -DOTA-TATE as first line therapy, whilst 13 of them were previously subjected to surgical lesion excision as per our institution protocol. **Subjects and Methods:** Twenty one patients (12 females, 9 males, mean age 59 and 63 years, respectively) suffering from advanced, progressive NF-NETs from lung and pancreas primaries were infused i.v. with n.c.a. ^{177}Lu -DOTA-TATE, at a dosage of 7.4 GBq (6 cycles with treatment intervals of 7-8 weeks), supported with LAR-octreotide, administered i.m. at a dose of 30 mg. Thirteen of them were previously subjected to debulking liver lesion surgery. This surgically treated cohort underwent either pancreateo-duodenectomy, or distal pancreatectomy and splenectomy. Intraoperative Liver Ultrasonography was performed to enhance missed lesion detection. Liver metastases were present in all patients. Prophylactic cholecystectomy was also performed to obviate adverse events due to the use of somatostatin analogues. **Results:** The mean progression-free survival for the thirteen, initially surgically treated cohort was 38.3 months (range: 24 to 85 months) vs. 25.8 months (range: 14 to 37 months) for the eight non-surgically managed patients ($p=0.031$). Regarding overall survival, respective values were 53.5 months (range: 27 to 85 months) vs. 35.4 months (range: 16 to 76 months), respectively ($p=0.026$). Regarding the response rates, complete, partial response and stable disease were found in 1, 5 and 7

of the surgically treated patients, respectively. Corresponding numbers for the non-surgically treated patients were 0, 1 and 7; the difference could not reach however statistical significance. Regarding overall survival, at the end of the follow-up period 6 patients (46%) of the surgically treated group and 7 (88%) of the non-surgically treated one, had died. That difference albeit not statistically significant, showed a trend for better survival after surgery ($p=0.15$, Yate's corrected chi-square test). **Conclusion:** NF-GEP-NET patients, initially subjected to surgical liver lesion excision and consecutively treated with n.c.a. ^{177}Lu -DOTA-TATE, as adjuvant therapeutic scheme tend to have longer progression-free and overall survival, as well as higher response rate compared with inoperable cases, treated only with n.c.a. ^{177}Lu -DOTA-TATE. Larger patient cohorts are necessary to elucidate the abovementioned observations.

EP-0695

The effect of selective internal radiation therapy with yttrium-90 resin microspheres on lung carbon monoxide diffusion capacity.

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Purpose: Selective internal radiation therapy (SIRT) with embolization of branches of the hepatic artery is a valuable therapeutic tool for patients with hepatic malignancies; however, it is also associated with lung injury risk due to shunting. Diffusion capacity of the lungs for carbon monoxide (DLCO) is a clinically significant lung function test, and worsening in DLCO is suggested to reflect a limited gas exchange reserve caused by the potential toxicity of chemoradiotherapy or it may be a marker of related lung injury. This study aimed to examine the changes in DLCO during SIRT with resin microspheres in newly treated and retreated patients. **Methods:** Forty consecutive patients who received SIRT for a variety of malignant conditions were included. All subjects were treated with Yttrium-90 labelled resin microspheres. DLCO tests were performed after the procedures. In addition, patients were specifically followed for radiation pneumonitis. **Results:** The mean DLCO did not significantly change after the first (82.8 ± 19.4 vs. 83.1 ± 20.9 , $p=0.921$) and the second treatments (87.4 ± 19.7 vs. 88.6 ± 23.2 , $p=0.256$). Proportion of patients with impaired DLCO at baseline was not altered significantly after the first (37.5 vs. 45.0%, $p=0.581$) and the second treatments (27.3 vs. 27.3%, $p=1.000$). Also, percent change in DLCO values did not correlate with radiation dose, lung shunt fraction, or lung exposure dose ($p>0.05$ for all comparisons). None of the patients developed radiation pneumonitis. **Conclusion:** Our results suggest that no significant change in DLCO in association with SIRT occurs, both after the first or the second treatment sessions. Further larger studies possibly with different protocols are warranted to better delineate DLCO changes after SIRT in a larger spectrum of patients.

EP-0696

First experiences and methodological aspects in the use of ^{188}Re for treatment of non-melanoma skin cancers

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Introduction/Aim: ^{188}Re , a beta emitter with an half life of 17.0 hours, has been already proposed for use in Nuclear Medicine. The maximum energy of the beta emitters is of 2.1 MeV, while its limited gamma ray emission is essentially at 155 keV (yield 15 %). The specific gamma ray constant is $8.2\text{E}-06\text{ mGy/h per MBq at }100\text{ cm}$, that is less than one half that of $^{99\text{m}}\text{Tc}$. Recently, following on an initial work developed by Cipriani et al, a new medical device has been certified in Europe for the therapy of basal and squamous cell carcinomas of the skin. This work presents some methodological aspects relative to our experience in the use of this device. **Materials and Methods:** This study was conducted on a Rhenium-188 compound produced by OncoBeta® GmbH for Rhenium-SCT® therapy. In the compound, ^{188}Re is bound to a fluid matrix that can be applied over the tumor with a dedicated applicator. Even if the device for delivering the therapy includes an activity meter, to provide a back up, calibration of our activity meters for ^{188}Re was checked by comparison with an independently calibrated gamma ray spectrometry system equipped with a HPGe detector (relative efficiency of 30% and resolution of 1.8 keV at 1332 keV). Calibration factors were found for a standard vial (5cc) and for two different activity meters, a Capintec CRC15 and a MecMurphil MP-DC. The level of dose rate at operator position during application of the radionuclide was measured using a calibrated dosimeter. Treatment time was calculated using Varskin 6.0, based on the amount of activity applied and depth of the lesion. Cross-checking against Monte Carlo simulations using FLUKA is ongoing. **Results/Conclusions:** Calibration factor (relative to $^{99\text{m}}\text{Tc}$) for Capintec CRC15 and MecMurphil MP-DC was 2.46 ± 0.10 and 2.47 ± 0.13 respectively. Lesions are treated with an activity in the range of 200-1000 MBq for 20-200 minutes, in order to reach the prescribed dose (35 Grays). Measurement of ambient dose rate at operator position during application gave results in the range 10 - 40 $\mu\text{Sv/h}$, depending on the distance. The absorbed dose to each operator is typically less than 20 μSv for application. Varskin-FLUKA cross-checking shows good agreement (<10% difference), moreover simulations confirm a very localized dose, being the dose less than 5% at 1 mm from the edge of the treatment region. This supports the concept of overall safety of this interesting, new treatment.

EP-0698

Clinical efficacy of radiosynoviorthesis (RS) in cases of large upper limb joints systemic arthritis

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Purpose: The retrospective assessment of the long-term efficacy of RS in patients with systemic arthritis (rheumatoid or psoriatic arthritis) of the shoulder and elbow joints. **Methods:** Thirty-one painful, not responding to systemic treatment, large upper limb joints (29 per shoulder), 30 patients (28 women, 64.7 ± 4 years) underwent RS with ^{186}Re . All joints presented a positive blood pool pattern in a pretherapeutic bone scan, suggestive for local synovitis. The treatment efficacy was determined by assessing the variation of a composite index-CCI calculated in terms of functional disability, a ten-step pain assessment analog scale, joint sensitivity / edema, patients and physician's total assessment prior to and after treatment, with a mean follow-up of 12 months (CCI, from 1-> non-functional joint to 10-> lack of any impairment, $\text{CCI} \geq 6$ being considered a success term treatment). **Results:** Twenty-six (83%) 2-arm joints showed significant ($\text{CCI} \geq 6$) improvement (17 with good and 9 with moderate response) at the end of the 12 month control vs 71% (15 good and 7 moderate <span title="απάντηση" στο follow up των 6 μηνών, p response) in the follow-up of 6 months, $p < 0.05$. No statistically significant difference in treatment efficacy was observed with respect to the underlying systemic disease. **Conclusion:** RS is an effective treatment option in the management of patients with active systemic arthritis of the large upper limb joints

EP-0699

Tumor response assessment in ^{90}Y resin microspheres treatments: effect of tumor dose and tumor volume.

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Purpose/Introduction: The aim of this study was to correlate local tumor response of treated lesions with tumor absorbed dose and tumor size. **Subjects & Methods:** A retrospective analysis was performed on 31 consecutive patients affected by unresectable HCC and treated with ^{90}Y resin microspheres. All patients underwent a $^{99\text{m}}\text{Tc}$ -MAA SPECT before treatment to assess microspheres distribution and to calculate average tumor, healthy liver and lung absorbed doses, using a three compartmental MIRD model, assuming uniform distribution inside each compartment. Tumor response to treatment was established, from follow-up CT/MR imaging at 3 or 6 months, as CR (complete response), PR (partial response), SD (stable disease) or PD (progressive disease). **Results:** 4 patients (pts) were excluded from the analysis because they didn't perform any follow-up imaging in our institution. The average tumor dose and volume of the 27 pts included in the analysis were respectively 248 cc [Range: 30.4 - 977.3 cc] and 244.1 Gy [53.8 - 1055.7]. 12/27 pts had CR (44.4%), 7/27 pts PR (26%), 2/27 pts SD (7%) and 7/27 pts PD (26%). 13/27 pts received less than 200 Gy to the target

lesions: 4/13 pts had CR (31%), 5/13 pts PR (38%), 1/13 pt SD (8%) and 3 pts PD (23%). 14/27 pts received more than 200 Gy to the target lesions: 8/14 pts had CR (57%), 2/14 pts had PR (14%) and 4/14 pts had PD (29%). From a tumor volume point of view: a) 7/27 pts with lesions smaller than 100 cc received an average dose of 410,3 Gy: 4/7 pts had CR (57%) and 3/7 pts PR (43%); b) 3/27 pts had very big lesions, greater than 500 cc, which received an average tumor dose of 107,6 Gy: 2/3 pts had PD (67%) and 1 pt PR; intermediate lesions received an average dose of about 199,7 Gy with 4/17 CR (23%), 8/17 PR (47%), 2/17 SD (12%) and 3/17 PD (18%). **Discussion/Conclusion:** As very well-known tumor dose and tumor volume play an important role in tumor response. Small lesions received high dose values and showed very good local response, while, on the other hand, big lesions, probably because of their heterogeneity, deserved higher doses than the ones delivered. Intermediate volume lesions showed not unique results and the high number of partial response (8/17) indicate the fact that higher doses could be preferable and allow more CR.

EP-0700

Feasibility, safety and advantages of high dose-personalized brachytherapy using a non-sealed ¹⁸⁸Rhenium paste in patients with non-melanoma skin cancers

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Aim: Aim was to evaluate the feasibility, safety and potential advantages of high dose-personalized brachytherapy using a non-sealed ¹⁸⁸Re-paste in patients with NMSC. **Materials and Methods:** The European Union recently approved the use of a resin containing the high-energy beta-emitter-¹⁸⁸Rhenium-paste in the treatment of non-melanoma skin cancers (NMSC) (OncoBeta® GmbH for Rhenium-SCT®). ¹⁸⁸Re is a Beta-emitter with an half-life of 17 hours and an energy spectrum of 1.9-2.1 MeV; ¹⁸⁸Re-beta particles deliver 92% of the dose within the first 3 mm human tissue. ¹⁸⁸Re-resin is applied over the lesion surface with a special shielded brush, while the lesion is protected by a surgical foil avoiding any direct contact of the resin with the lesion. After application, the required amount of time to deliver an empiric estimated dose of 35Gy to all the thickness of the lesion is calculated, considering lesion surface and thickness, using a simulation software (VARSKIN 5.2). After that, the protective foil with ¹⁸⁸Re-matrix is removed. Patients were followed-up after 7, 21, 60, 180 days when a biopsy has been performed. **Results:** Nine-teen lesions (14 Basal-cell Carcinoma, 5 Squamous-cell Carcinoma) in six-teen consecutive patients have been treated from Sept 2017 to March 2018: 11 lesions were located on face and scalp, 6 in upper and lower limbs and 2 in the back. Mean surface was 6.1cm² (range: 2-13.25cm²), mean thickness 0.9mm (range 0.2-2mm); mean administered dose 452Mbq (range 202-

1028), mean time of treatment 67minutes (range 21-285). No mid-term, local or systemic side effects have been observed. Seven days after therapy, 16/17 lesions showed a grade-1 radio-dermatitis, generally healing in 20-30days without any therapy; 1/17 lesion showed grade-2 radiodermatitis that needed longer time (40days) and topic application of hyaluronic acid to heal. Main advantages: 1) ¹⁸⁸Re-resin can be easily applied directly over the exact shape of the lesion and security margin can be covered performing a conformational personalized radiotherapy; 2) dosimetry is calculated on a lesion basis and the delivered dose can be easily controlled by varying the time of treatment 3) no pain, local or systemic side effects for the patients; 4) simple and fast outpatient procedure. **Conclusions:** Despite the limitation of the small population enrolled, we can conclude that the dose-personalized brachytherapy using a non-sealed ¹⁸⁸Re-resin in patients with NMSC is feasible and safe and may offers many advantages over other local treatments.

EP-0701

Personalized medicine: method of in vitro determination of receptor binding for Lu-177 radio-pharmaceuticals therapy efficacy estimation

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Introduction: Lu177-PSMA and Lu177-DOTA-TATE are currently used for treating mPC and mNET when other therapeutic approaches fail. However, there is interindividual heterogeneity even of a specific cancer type, e.g., among patients with mPC, 5-10% there is no profound PSMA expression on metastatic cancer cells. The aim is to develop a simple, sensitive and accurate in vitro test system that is based on the determination of receptor binding affinity of synthesized radionuclides to be used for functional quality control and further as the reference for accurate prediction of the targeted radionuclide binding potential to individual patients' cancer cells. **Materials and Methods:** Lu177-DOTA-TATE, Lu177-PSMA-617 were synthesized. For quality control, methods suggested by European Pharmacopeia have been used. The test system was based on the usage of stable cancer cell lines: mPC PC3(PSMA+/-) and LNCaP(PSMA+), NCI-H69(SSTR2+) and CorL23(SSTR2-) were seeded in triplicates in 6-well plates, Radioactive labelling of cells was done in serum-free medium adding 0.5-5MBq. Cells were incubated in standard conditions for 1h at 37°C, medium was withdrawn, and cells washed with PBS. Cells were collected by centrifugation or lysing, samples were measured in gamma spectrometer. The level of the specific receptor expression on cancer cells was visualised by immunocytochemistry using mouse monoclonal antibody against human PSMA and SSTR2 and visualised by anti-mouse-Cy5-labelled secondary antibody. Results were assessed by fluorescence microscopy. **Results:** Quantitative and qualitative assessment of RP receptor binding reaction dynamics was performed. By differentiating activity fractions (bound/

unbound) and observing changes in value dependant on added RP amount and type of cells, various parameters were obtained: (i)confirmation of receptor expression, in regard to respective RP; (ii)receptor binding constant K_d via Wolf plot; (iii) practically achievable maximum saturation value of cell surface receptors and lowest plateau of detectable added radionuclide activity; (iv)unspecific binding values; (v)absolute deviation for measured values. For the specific receptor-negative cell lines, activity measurements yielded values less than 300Bq while for cell lines positive for specific receptors it was up to a maximum of ~15kBq. **Conclusions:** Study shows that in vitro test can be used for the express quality control of the synthesized Lu177-RPs, the results are comparable with the receptor expression levels in corresponding cell lines determined by immunocytochemistry. By using Lu177-RPs, it is possible to qualitatively and quantitatively assess the binding capacity on live cells. Further elaboration of this methodology would enable the prediction of the efficacy of the molecularly targeted radionuclide diagnostics and therapy in individual patients.

EP-0702

⁹⁰Y TOF-PET based EUD reunifies patient survival prediction in resin and glass microspheres radioembolization of HCC tumours

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Purpose: Many clinical studies reported a ratio of about 2 between the toxicity of resin spheres and of glass spheres, as well as between their efficacy. Monte Carlo simulations of spheres transport in liver arterial tree and also liver biopsies post radioembolization evidenced that glass spheres give a more heterogeneous dose distribution quantitatively explaining the difference in liver toxicity (Handbook of radioembolization. CRC press 2016). Our aim is to investigate whether the same mechanism could explain the different efficacy in tumor response. **Method:** Jones-Hoban equivalent uniform doses (EUD) and absorbed doses (D) of HCC tumors were computed in 45 patients. Attenuation and scatter compensated OSEM reconstruction was used with 4 iterations, 8 subsets and without post-filtering. The resulting ⁹⁰Y TOF-PET/CT distribution was iteratively de-convoluted with the measured ⁹⁰Y PSF and afterwards convoluted with the ⁹⁰Y dose deposition kernel. 19 and 26 patients were treated with resin and glass spheres, respectively. Kaplan-Meier (KM) survival curves for a 40 Gy threshold were computed for resin and glass spheres. 9 patients were still alive and censored with a current follow up ranging from 6 to 23 months. Mean and maximal uncensored patient survivals were 9.7 and 26 months, respectively. **Results:** In order to fit the glass spheres KM curves with those of the resin spheres, the absorbed dose D had to be converted into an effective dose (D_{eff}) by applying a 2.5 fold dose reduction factor (median survival (<40Gy, >40Gy): resin (5.6m, 10.1m), glass (5m, 12.2m)). On the other hand, using EUD with a HCC cell radiosensitivity of 0.05 Gy⁻¹, a nice matching between glass and resin KM curves was observed (median survival (<40Gy, >40Gy): resin (6.2m, 14m), glass(5.5m, 12.5m)). Furthermore, the lower and upper 40 Gy threshold KM curves were better separated

using EUD, than using D_{eff} . For tumors with absorbed dose D below 120 Gy (n=26), i.e. with D_{eff} around the 40 Gy threshold, the EUD/D slope was 0.59 and 0.39 for resin and glass spheres, respectively, proving a higher observed dose heterogeneity using glass spheres. **Conclusion:** These results clearly support the fact that the heterogeneity observed in ⁹⁰Y TOF-PET post radioembolization does not only result from low statistics only, but also reflect the actual heterogeneity of the spheres distribution, that when taken into account by the EUD formalism, reunify the efficacy of the two devices.

EP-0703

Transarterial radioembolization treatment for unresectable intrahepatic cholangiocarcinoma: dose-response relationship and estimate of the radiobiological α parameter

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Aim: A relation between tumor absorbed dose and outcome of transarterial radioembolization (TARE) in patients with unresectable intrahepatic cholangiocarcinoma (ICC) has been investigated. The radiobiological α parameter from a simplified Linear Quadratic Model (LQM) has been estimated for 14 patients with unresectable ICC submitted to this kind of procedure. **Material and Methods:** Since 2012 up to now, patients with unresectable ICC, previously selected by MRI or CT scans, had pre-TARE planning angiography and Tc-99m-MAA SPECT/CT. TARE procedure with Y-90 resin microspheres was performed 7-14 days later followed by PET/CT imaging within 24 hours. The administered activity was determined using the BSA method. Post-treatment 3D dosimetry based on PET-CT images was performed to calculate tumor average absorbed dose. Response to TARE was evaluated in terms of reduction of the treated tumor volume based on CT scan at 4-6 weeks after treatment and then every 3 months. The radiobiological α parameter of a simplified LQM was then calculated in selected cases. **Results:** Twenty patients (15 males and 5 females) were recruited and considered fit for TARE treatment. Thirty TARE procedures were performed (including dual-lobe treatments in 8 patients and retreatments in the same lobe in 2 patients because of local relapse). Patients non-submitted to PET-CT or lost during follow-up were excluded from the calculation of α . Thus, 16 procedures in 14 patients have been considered. The mean of average absorbed dose to the tumor was 346±135 Gy and the mean tumor volume before treatment was 83±51 ml. We observed a volumetric increase of four treated tumors (88±44 ml as basal measurement and 129±85 ml after treatment) and a stable tumor volume in one case. In the remaining 11 procedures, we recorded a significant volumetric reduction of the treated tumors (91±56 ml pre-treatment vs 44±32 ml post-treatment; p=0.003) and a moderate correlation between the rate of this reduction and

average absorbed dose to the tumor ($r=0.59$; $p=0.05$). The mean of the estimated radiobiological α parameter in the 11 procedures was 0.002 ± 0.002 Gy⁻¹. **Conclusions:** In our experience TARE with Y-90 microspheres is an effective option for patients with unresectable ICC. We found in our series a correlation between tumor absorbed dose and outcome of TARE. However, the α parameter calculated by the simplified LQM seems to be variable in this tumor setting. Further evaluations are needed to establish which factors could affect the variability of the radiobiological parameter.

EP-0704

Transarterial Radioembolization (TARE) in Hepatocellular Carcinoma (HCC) using ⁹⁰Y Resin and Glass Microspheres

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Purpose: To evaluate the efficacy of treatment with TARE in HCC in terms of overall survival (OS), progression free survival (PFS), and radiological response (RR). **Subjects and Methods:** It is a retrospective review of HCC patients treated between December 2009 and May 2017 with a minimum follow-up of 9 months. Efficacy (OS, PFS, RR) was analyzed according to baseline clinical, analytical and radiological characteristics, previous therapies and treatment characteristics (dose, particle type, among others). Time to liver progression was recorded and response was classified as good / poor responder (GR / PR) according to radiological/clinical evolution at 6m. Adverse effects (AE) and follow-up (additional treatment / outcome, among others) were also monitored. **Results:** 80 procedures were performed in 57 patients. The BCLC stage was A: 3.57%, B: 64.28% and C: 32.14%, mostly Child-Pugh A (71.42%). 64.3% were treated with resin microspheres and 35.7% with glass particles. 89.4% did not show relevant AE. The median OS and PFS were 21.2 and 9.4 months respectively. The RR was 78.7% (complete + partial response). There were no differences in terms of OS, PFS, RR or AE between particles. GR was associated with better OS (HR 0.34, $p = 0.019$). A higher dose administered to the tumor was associated with better PFS (HR 0.96, $p = 0.000$) and associated to being a GR with a sensibility of 63.2% and a specificity of 77% for 119.5Gy. A partial response / stable disease was a risk factor versus complete response for OS and PFS (HR 16.6, 9.58 and 9.21, 9.5 respectively). Bilobar involvement predicted worse OS (HR 2.37, $p = 0.021$) and malignant thrombosis (MT) was associated to being a PR ($p = 0.011$). **Conclusion:** The results for OS, PFS, RR and AE for our center are concordant and in some cases, superior to the published series. There are no significant differences in terms of OS, PFS, RR and AE between both particles. A good RR predicts OS and PFS. A greater tumor dosimetry is in turn associated with better RR and PFS. Bilobar involvement and MT are predictors of poor prognosis.

EP-0705

Progression free survival after selective internal radiation therapy with ⁹⁰Y resin microspheres in primary and secondary liver tumours: experience in 70 patients

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Purpose: The aim of this study was to assess the impact on progression free survival (PFS) of selective internal radiation therapy (SIRT) using ⁹⁰Y resin microspheres in liver tumours.

Methods: We retrospectively analyzed the results of SIRT in patients with primary and secondary liver tumours, treated in our hospital between November 2008 and March 2018. Data about gender, age, histological diagnosis, anatomical characteristics of the tumour, administered doses and the subsequent follow-up were collected. Pretreatment planning based on ^{99m}Tc-MAA planar image and SPECT-CT was carried out one week before the planned treatment, and lung shunt and extrahepatic depositions were evaluated. The dose was adapted according to the lung shunt, liver lobe to be treated, as well as in cases of previous treatment. Patients were imaged using CT, MRI or PET-CT to monitor treatment response 3-8 weeks after radioembolization.

Results: We analyzed the data from 86 patients, being finally included 70 (50 male, 20 female; mean age 66.5), in which all the relevant information was achieved. In 60% (42/70) patients the diagnosis was hepatocellular carcinoma (CHC), in 21.4% (15/70) colorectal liver metastases and others tumours with liver metastases in 18.6% (13/70). Patients previously treated (chemotherapy, radiofrequency, chemoembolization or surgery) were included. Fifty-five patients were treated with SIRT once, 9 patients twice, 4 patients underwent three treatments and 2 patients 4 treatments. Overall, 93 SIRT procedures were performed. The mean dose delivered was 1065.6 MBq (range 407-1750 MBq). Patients were followed up for a mean of 16 months (range 1 to 88 months). We observed progressive disease in 57 patients, stable disease in 4 and complete response in 5. Four patients died before the first radiologic control was carried out. Finally, we obtained an overall mean PFS of 8.12 months after SIRT (range between 0-82 months, 95% CI 5.23-11.03 months). In patients with progressive disease, the mean PFS was 6.3 months (range 1-27, 95% CI 4.66-7.87). Patients with stable disease or complete response after SIRT were followed up for a mean of 23.4 months (range 4-82, 95% CI 3.00-43.89). Once divided according to the histological diagnosis (CHC or secondary tumours), no differences in PFS were obtained in the group with primary or secondary tumours (mean 7.4 and 8.3 respectively, t-Student no significant, $p=0.76$). **Conclusion:** After ⁹⁰Y-SIRT, a mean PFS of 8 months has been achieved in our population. No significant differences seem to exist in the group with primary or secondary lesions.

EP-0706

Hepatocarcinoma, our experience with radioembolization treatment

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Objective: Analysis of progression-free time (PFT) and survival, global and by groups according to BCLC and Child-Pugh (CP).

Material and Method: Retrospective study of 53 patients with hepatocarcinoma treated from March 2009 to December 2016 with radioembolization. The average age was 62.7 years (range 28–86 years). The mean follow-up was 16.2 months. 70% of patients suffered from HCV alone or in association with other causes of HCC. Classification: CP: 45 stage A patients and 8 stage B. BCLC: 30 stage B patients and 23 stage C. In each procedure, hepatic arteriography and injection of 185 MBq of ^{99m}Tc -MAA were performed, followed by acquisition of thorax and abdomen static images and abdominal SPECT / CT (Gammacamera BrightView XCT). After analyzing the images, the required activities were calculated, proceeding in a second time to the infusion of ^{90}Y microspheres. Subsequently, images of Bremsstrahlung were obtained and from May-2013 PET / CT (Philips Gemini TF) images to evaluate the distribution of the microspheres and to analyze concordance with the initial arteriography images.

Result: A total of 61 procedures were performed, given that bilobar treatment was performed in 8 patients. The average activity administered by procedure was 2.8GBq (0.7–6.4GBq), with a mean tumor dose of 229.9Gy (74–425.9Gy). There was progression of disease in 41 patients (77.4%), 35 died. The overall PFT was 16.2 months (CI 95% 9.6–22.8). No statistically significant differences were found in the study by groups. The average time of overall survival was 18.9 months (CI 95% 5.6–20.1). Statistically significant differences were found in the CP group ($p = 0.003$), shortening the average survival time in those patients with CP B versus CP A (A = 21 months B = 7.6 months). There was a case of RILD (1.6%) during the first month after treatment with death result in a patient in BCLC-C stage (portal thrombosis) and high tumor burden. No other severe adverse effects were observed.

Conclusions: Radioembolization is a safe and effective treatment in the treatment of hepatocarcinoma, significantly increasing survival in those patients with preserved liver function.

EP-0707

The Effect Of Spillover Artefact And Pulmonary Movement To The Calculation Of Hepatopulmonary Shunt Ratio

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Aim: In radioembolization, the lung shunt fraction (LSF) is one of the important parameters directly affecting the treatment dose and radiation dose to the lung. Although SPECT-CT imaging is accepted to be superior to planar imaging in calculating LSF, there are also problems with SPECT-CT imaging. The purpose of this study was to investigate the effect of spillover artefact due to activity in the liver tumor and pulmonary motion during ventilation on lung counts in calculating LSF ratio. **Method:** One hundred and five patients (69 males, 36 females) who had undergone radioembolization in our clinic between 2015–2018 were evaluated retrospectively. Whole body and SPECT-CT im-

aging were performed approximately 90 minutes after Tc-99m macroalbumine aggregate (MAA) was injected to the patient during hepatic catheterization for pre-treatment evaluation. After attenuation and scatter correction of SPECT-CT images, total right lung, total left lung, and liver ROIs were drawn and LSF was calculated. Firstly, the ratio between total right lung count to that of left lung, which we named as Total Lung Count Ratio (TL-CR) was checked. Then the relationship between TL-CR and the segments to be treated in the liver was examined. Afterwards, pulmonary counts were calculated starting from 5 cm above the upper liver border to exclude spillover artefact and the effect of pulmonary movement to the lung counts. Using the values obtained, Half Lung Count Ratio (HL-CR) was calculated as TL-CR. We also compared count/volume ratios from the lower, middle and upper regions of the left lung. **Results:** The mean value ± standard deviation for LSF and TL-CR were 6.51 ± 3.51 and 3.55 ± 3.51 , respectively. When the images of the 41 patients who had liver tumors in segments 1, 2, 3, 5, 6 that were not adjacent to the lung were examined, TL-CR and HL-CR were calculated as 1.43 ± 0.36 and 1.08 ± 0.18 , respectively which were very similar, proving the minimal affect of spillover and motion artefacts in these regions. When the images of the 64 patients who had tumors in segments 4, 7, 8 that were adjacent to the lung were examined, TL-CR and HL-CR were calculated as 5.15 ± 3.83 and 1.55 ± 0.81 , respectively which proved the effect of spillover and motion artefacts to the lung counts. On the other hand, count/volume ratios in the left lung showed homogeneous distribution of MAA. **Conclusion:** Lung counts is affected significantly from spillover and motion artefacts when the tumor activity in the liver is close to the lungs and this situation can alter LSF calculations. Instead of using right+left lung counts for LSF calculations, only left lung counts that are not affected by spillover and motion artefacts can be used.

EP-0708

Assessment of the quantitative accuracy of ^{177}Lu SPECT reconstruction for Peptide Receptor Radiotherapy (PRRT)

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Purpose: An increasingly common clinical protocol is the use of ^{177}Lu -DOTATATE post-treatment imaging to determine the absorbed dose and assess whether any organ has reached a maximum tolerable activity. To determine how much activity was delivered to certain target tissues over time, multiple SPECT/CT scans over several days may be taken to determine the time integrated activity coefficient (TIAC) from which absorbed dose can be calculated. Accurate calculation of dose thus depends on accurate quantification of SPECT images. This work examines the accuracy of SPECT quantification using an OSEM-based SPECT reconstruction tool (SPECTRA QuantTM, MIM Software Inc.). **Methods:** A SPECT image with 64 projections was simulated using the SIMIND Monte Carlo program based on relative activity levels in an existing ^{177}Lu -DOTATATE scan and using a real patient geometry. The relative activity levels were 100 for the lesion regions, 26 for the liver, 49 for the spleen, 33 for the kidneys, 5 for the lungs, and 3 for the rest of the body. Projection images

were similarly simulated for a 20cm x 24cm cylindrical calibration phantom of uniform activity concentration and density to determine a quantitative conversion factor (CF) for the reconstruction. The calibration phantom was decay corrected to acquisition time and then reconstructed using a protocol of 16 iterations and 8 subsets, including attenuation correction, scatter correction, and resolution recovery. The CF in counts/second/MBq was calculated based on the known simulated activity and the number of recorded counts within the image. The patient-based SPECT projection images were reconstructed using the same reconstruction protocol and parameters, and the CF was applied to convert the resulting SPECT image into units of Bq/ml. **Results:** The errors between the known simulated activities and measured activities were: field of view, -4.2%; liver, 7.3%; spleen, 1.7%; kidneys, -19.6%; lungs, 9.0%; 135ml spherical liver lesion, 2.9%; and 16ml spherical liver lesion, -21.0%. **Discussion:** The reconstructed image produced high quantitative accuracy (<10%) for large structures (liver, spleen, lungs, and the 135ml spherical lesion), while smaller regions (kidneys, 16ml spherical lesion) had lower quantitative accuracy as expected due to partial volume effects. The quantitative accuracy of reconstruction using the MIM SPECTRA Quant™ tool allows users to generate accurate time activity curves and TIACs for dose calculation. *May not be available in all countries. Contact MIM Software for details.

EP-0709

A prospective assessment at 1, 3, 6 and 12 months investigating radiation synovectomy in patients with severe and chronic rheumatoid arthritis (RA): an ongoing study

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Purpose: To ascertain the outcome of *Phosphorus-32* radiation synovectomy at 1, 3, 6 and 12 months in patients with knee *rheumatoid arthritis* unresponsive to systematic or local medical therapy. **Materials and Methods:** Nineteen knees in 13 patients with *severe, chronic rheumatoid arthritis* (RA) were treated by the instillation of an intra-articular radionuclide (*Phosphorus-32*-³²P). They were prospectively evaluated at 1, 3, 6 and 12 months. The Western Ontario and McMaster Universities *Arthritis* Index (*WOMAC*) consists of 24 items divided into 3 subscales: pain (5 items) stiffness (2 items) and physical function (17 items), as well as Visual Analogue Scale (*VAS*) and also Health Assessment Questionnaire (*HAQ*) were assessed. The effect of radiosynovectomy was classified in 4 categories. Excellent response (no symptoms), good response (significant reduction of symptoms), moderate response (slight decrease), and no response (no change or worsening), of pain or/ and swelling or/and tenderness in treated joint over a year after procedure. **Results:** Excellent response or good response was observed in 57.89% ; moderate response 5%; and bad response 36.84%. Side effect associated to the RSO observed in 1 patient with slight erythema that resolved within 3 days. In short follow up during 3 months, all cases depicted some clinical improvement. The

WOMAC score before 51.44, one month after injection 31.94; 3 months 42.57; 6 month 43.53 and also 12 months after administration 43.15 . The pain scale rating before administration 6 out 10; one month 2 out 10; 3 months 3 out 10; 6 months 4 out 10 and also 12 months 4 out 10 . The quantitative *VAS* before administration 59 mm; one month 17 mm; 3 months 36 mm; 6 months 37 mm and also 12 months after administration 38 mm. In addition, *HAQ* showed significant difference through the study. **Conclusion:** Radiosynovectomy is an advantage therapeutic procedure in a considerable proportion of patients with *severe* and *chronic rheumatoid arthritis* suffering from knee synovial inflammation, inefficiently controlled by pharmacotherapy.

EP-0710

Success Prediction Of SIRT Based On Tumor ROI Activity Of The Pretherapeutic MAA Study

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Introduction: If patients experience a minor therapeutical effect after SIRT time in which they could have commenced alternative treatment options is irrecoverable. And since a complete SIRT procedure also requires high expenses and efforts concerning staff and logistics the aim of the study was to ascertain whether pre-therapeutic MAA studies can be used to predict the outcome of a SIRT. **Subjects and Methods:** Our study retrospectively compared pre- and post-therapeutic VOI values with the corresponding MRI sizes of 23 SIRT patients suffering from HCC, CCC and Colon-C. The SPECT/CT images using a GE NM640 were carried out directly after the intervention and iteratively reconstructed with attenuation correction. For regional evaluation the Freeware program AMIDE (Vers. 1.04, sourceforge.net) was utilized. The liver uptake was considered to be 100% and the individual VOI uptake of the tumor entity was determined by a 3D-isocontour cut-off level of 50% for both the Tc-99m and the SIRT data. The resulting dose was calculated according to the partition model provided by SIRTEX. Considering the inferior spatial resolution of Y-90 images (compared to Tc-99m) the measured counts of the SIRT-VOI were reprojected into the outlines of the corresponding MAA-VOI. **Results:** In 4 of the 23 cases post-therapeutic MRI studies detected increasing tumor volumes. They were thus recognized as non-responders. In 10 cases the tumor volumes remained stable and in 9 cases they shrunk up to 69% in diameter. The regional SIR-sphere-concentration in kB/cc was principally lower than that of the corresponding MAA-spheres. Calculated doses of >100 Gy in the pre-therapeutic MAA VOIs were associated with stable and regressive tumor volumes. Post-therapeutic doses of >60 Gy for SIRT-VOIs showed the same effect. Therapy response was neither correlating with the different tumor types (HCC, CCC, Colon-C) nor with the level of sphere accumulation in the tumor region. **Conclusion:** Though the number of patients evaluated is considerably small, a correlation between calculated pre- or post-therapeutic dose and therapeutical SIRT effect is evident. If MAA study results deliver a dose >100 Gy or if post-therapeutic values of the SIRT data show >60 Gy the probability for a positive response to the intervention (stable or regressive disease) is expectably high.

EP-0711**Influence of previous treatment on the result of radioembolization of hepatic lesions with yttrium-90 spheres. Preliminary results**

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Purpose: To evaluate the influence of previous treatment (chemotherapy or transarterial chemoembolization) on the response of hepatic lesions treated by radioembolization with yttrium-90 spheres. **Subjects and Methods:** Prospective longitudinal study, which included patients diagnosed with hepatocellular carcinoma or colorectal cancer metastasis treated by radioembolization with yttrium-90 spheres, between November 2015 and December 2017. The response was evaluated 3 months after radioembolization, by abdominal CT, applying the RECIST criteria. The influence of previous therapy was analyzed by distinguishing 2 subgroups: 1) patients without previous treatment and, 2) patients with previous chemotherapy or transarterial chemoembolization. **Results:** We included 14 patients (mean age=65.4 years), 8 with a diagnosis of hepatocellular carcinoma and 6 with metastasis of colorectal cancer. Seven patients did not receive previous treatment and the remaining 7 patients had been previously treated (2 with transarterial radioembolization and 5 with chemotherapy). Two patients died before evaluating the response. Overall, 3 patients had a complete response (25%), 4 patients a partial response (33.3%), 3 patients a disease stabilization (25%) and 2 patients a disease progression (16.7%). The bivariate analysis showed differences, tending to statistical significance ($p=0.051$), between the previous treatment group and the response to radioembolization, so that none of the patients who had been previously treated made a CR. Distinguishing by subgroups, we appreciate statistical significance for the group with colorectal cancer metastasis ($p=0.015$), whereas it does not occur for the hepatocellular carcinoma group. **Conclusion:** Despite the small number of patients evaluated, our results suggest that previous treatment of hepatic lesions may have a negative influence on the response to radioembolization with yttrium-90 spheres.

EP-0712**Careful SPECT/CT evaluation of ^{99m}Tc -macroaggregated albumin uptake is essential in Selective Internal Radiation Therapy workup for a reliable prediction of 90Y-resin-microspheres distribution and response. A preliminary single center experience.**

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Purpose/Introduction: Primary aim was, in patients (pts) undergoing Selective Internal Radiation Therapy (SIRT), to compare

^{99m}Tc -labeled-macroaggregated-albumin distribution at hepatic artery perfusion scintigraphy and SPECT/CT (MAA scan) with 90Y-resin-microspheres PET/CT distribution. Secondary aim was to correlate scan results with treatment response (at 6 months).

Subjects & Methods: a retrospective single center analysis was performed including pts who underwent MAA scan and 90Y-PET/CT, pre and post-SIRT respectively, between November 2016–October 2017, with available clinical and imaging (CT/MRI/PET) follow-up of at least 6 months. All scans, performed according to standard guidelines, were reviewed by at least two expert nuclear medicine physicians (ET, ELR, LZ). The following parameters were evaluated: a) absent/partial/complete distribution match between MAA and 90Y-resin-microspheres on target hepatic lesion and, when present, on neoplastic thrombosis; b) response to treatment at 6 months of follow up. **Results:** Overall 20 consecutive pts were included (5 females, 15 males; mean age 59 ± 10 [39–75]). Diagnosis was primary hepatocellular carcinoma (HCC) in 16/20 pts, cholangiocarcinoma (CC) in 2/20 pts, HCC+CC in 1/20 pts and liver metastasis from colon cancer in 1/20 patients. At least one treatment between surgery, chemotherapy, TACE/TAE or radiofrequency was previously received by 12/20 pts. In 1/20 PET post-yttrium was not available for technical issues. In all cases (19/19, 100%) there was a good distribution match between MAA and 90Y-microspheres, with complete target lesion correspondence (to note: in 3/19 pts target was only partially covered). Among the 12/20 pts with neoplastic thrombosis, 11/12 presented a complete MAA-90Ymicrospheres correspondence. Extra-hepatic activity in 90Y-PET was detected in 3/19 (1 diffuse lung; 2 inconclusive: 1 multiple lung, 1 gastro-duodenal spots). No significant complications were observed during/early after SIRT procedure (1 infective/not post-actinic pneumonia; 5 faint symptoms i.e. fever, nausea, abdominal pain, solved with medical therapy within 24–48h). 6 months after SIRT, response was: complete (CR) in 12/20 pts (60%) (1/12 patient then addressed to liver transplantation), partial (PR) in 3/20 (15%), stable disease (SD) in 1/20 (5%) and progressive disease (PD) in 4/20 (20%). Overall 2 cases presented with target CR+ thrombosis SD whereas a single case target CR+ thrombosis PD. **Discussion/Conclusion:** Our preliminary results confirm that a careful MAA scan evaluation reliably reflects 90Y-resin-microspheres distribution and therefore impact on SIRT response. Further analyses are ongoing in order to establish a possible prognostic value in terms of progression free survival and to search for potential clinical and imaging predictive factors of treatment response.

EP-0713**Lung shunting in therapy with Y-90 labeled glass microspheres for liver cancer**

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Purpose: Lungs are critical organs in therapy with Y-90 labeled glass microspheres if yttrium spheres are deposited in the lung and this absorbs doses higher than 30 Gy limit above which pneumonitis, fibrosis and respiratory insufficiency occurs. Although the lung shunting fraction LSF is defined as the per-

centage of activity shunted into the pulmonary circulation, the current standard for analysis of [99mTc]-MAA shunt studies is to estimate the LSF from the AP and PA planar images of lung and liver of the treatment planning study with [99mTc]-MAA, as the ratio of the total accounts in lungs between the sum of the lungs and liver counts. This method is subjective and highly variable, due to failure to consider the different attenuation of Tc-99m in lung and liver and the lack of a precise definition in the delimitation of the ROIs to quantify in the planar images. As a result, an overestimation of LSD can occur in values that may compromise the viability of the treatment. In this study, the results obtained for the LSF are compared according to the standard method (M1), M1 corrected for attenuation (M2) and the gold standard method using the SPECT-CT image (M3). **Subjects and methods:** Fifteen patients treated with 90Y-microspheres (1-5 GBq) and planned ~15 days before with MAA-99mTc (107-340 MBq) have been studied. All images are acquired using a SYMBIA T2 gammacamera with LEHR collimator and analyzed with ImageJ software. **Results:** The SPECT-CT image-based methodology M3 obtains similar LSF results to the attenuation-corrected planar image-based methodology M2. However, the standard method M1 overestimates the LSF in values up to four times higher than the results for M2 and M3. With M2 and M3 very similar values are obtained. There is extensive variability in the LSF measured: Ten patients (75%) has an LSF lower than 11%, and only four patients (25%) has an LSF higher than 11% (M1). On the other hand only four patients has an LSF higher than 4% and 11 patients has an LSF lower than 4% (M2/M3) Median (%) and range (%) LSF are 7(3-37) and 2(1-21), for M1 and M2 respectively. **Conclusion:** M2 seems to provide the best approach to gold standard M3 with less cost since M3 requires a dedicated SPECT acquisition with the FOV centered in lungs.

EP-0714

Treatment With 90Y-RESIN Microspheres In Radioembolization Of Hepatic Tumors

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Introduction: Liver tumors (hepatocarcinoma and metastasis) are susceptible to local treatments with minimally invasive techniques such as intraarterial radioembolization (RE) with microspheres of resin marked with yttrium-90 to inhibit its progression or reduce size. We present our experience in this therapy. **Material and Methods:** We administered (January 2016-February 2018) 34 RE in 27 patients (21 men-6 women) with hepatocarcinoma (single lesion (SLH): 10, multicentric (MH): 8 or metastasis (M): 5. Age 53-84 y/old (68 ± 8). We performed selective angiography 6-22 days before treatment, with evaluation of hepatic vascularization and arterial embolization if necessary (5 cases), administering 99mTc-MAA in the hepatic artery. We obtained planar thoracic-abdominal images, SPECT and SPECT-CT fusion (predictable treatment distribution and detection of

possible extrahepatic activity), calculating hepato-pulmonary shunt (HPS) and tumor/non-tumor index (TN) to calculate activity-absorbed dose. Treatment administration involved the nuclear medicine physician introducing the isotope alternating with the radiologist introducing iodine contrast. We acquired post-treatment images (three energy peaks-MEGP collimator) after 24h. We evaluated previous treatments, initial tolerance to treatment, follow-up (3-18 months in 23 cases), partial response (PR), stable disease (SD) or progression (P) (using MRI and/or CT). **Results:** Average size (if SLH) 71.28 ± 44mm. Mean tumor volume: 355.3 ± 469.48 cc. Total hepatic volume: 1924.83 ± 540.40cc. Mean HPS: 6.41 ± 2.83% (1.6-12.5). Average administered activity: 1.56 ± 0.71 GBq (0.6-2.9), if PR + SD: 1.34 GBq and P: 1.61 GBq. One patient received 3 treatments in 2 years. Three patients with bilobar involvement received 2 lobar treatments. The post-treatment images confirmed adequate distribution without extrahepatic activity (except one). There were 13 PR, 2 SD and 8 P. In PR + SD, there were no statistical difference between single and multiple lesions (53.3% vs 46.6%), previous treatments (50%) or not (50%), follow-up time (3-12 months: 46.2%, 12-18 months: 53.8%). Two cases with SD: 1 SLH, 1 MH. Eight with P: 4M, 2SLH, 2MH. Mean tumor size (if SLH) was higher in PR + SD (87.2 ± 32.78 mm) with respect to P (53.00 ± 31.05 mm) (NS). Good initial tolerance except 6/27 cases (mild digestive symptomatology). **Conclusions:** Radioembolization with 90Y-resin microspheres in liver tumors is a safe and effective treatment with good initial tolerance. In 15/23 cases there was PR or SD. Careful preparation and treatment planning is essential, being multidisciplinary this collaboration.

EP-51

e-Poster Area

Clinical -> Therapy study -> Other treatments -> mIBG and peptides therapy

EP-0715

Impact of Lutetium-177 DOTA-NOC therapy on Karnofsky Performance Score in patients with Neuroendocrine tumor with skeletal involvement

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Introduction: Stage IV neuroendocrine tumors (NETs) have limited treatment options where Lutetium-177 (Lu-177) labelled PRRT (DOTA-TATE & DOTA-TOC) has shown to improve the Quality of Life (QoL) and progression-free survival. In this study, we aimed to evaluate the impact of Lu-177 DOTA-NOC therapy in patients of histologically proven Stage IV NET with skeletal metastases. **Subjects and Methods:** Patients of histologically proven Stage IV NET with skeletal metastases in baseline Ga-68 DOTA-NOC PET/CT were enrolled. Baseline Karnofsky Performance Score (KPS) was noted and Lu-177 DOTA-NOC therapy was administered as per EANM guidelines. KPS was recorded at the end of therapy. The change in KPS was graded as follows, i) decrease of 21 or more - significant deterioration, ii) decrease of 11 to 20

- moderate deterioration, iii) decrease of 6 to 10 - mild deterioration, iv) decrease or increase upto 5 - no significant change, v) increase of 6 to 10 - mild improvement, vi) increase of 11 to 20 - moderate improvement and vii) increase of 21 or more - significant improvement. **Results:** A total of 7 patients enrolled for the study. The primary site of NET was medullary carcinoma thyroid (post radical total thyroidectomy) in 3(43%), anterior mediastinal NET in 3(43%) and ileal carcinoid in 1 patient (14%) (Both without any surgical resection). A median of 2 cycles (range: 1-4) of Lu-177 DOTA-NOC was administered. Median baseline KPS was 70 (range: 50-80) and post therapy was 60 (range: 20-70). Maximum improvement in KPS was increase by value of 20 while maximum deterioration was fall by a value of 50. 2 out of 7 (28%) patients had severe deterioration, 2 moderate deterioration (28%) and 1(14%) mild deterioration in the post treatment KPS, and 1 (14%) each showed mild- moderate improvement. However, no statistically significant difference was noted in pre- and post-therapy KPS. Of the 7 patients, 5 (71.4%) succumbed within 2 cycles of therapy. Additionally, 1/7 patient(14%) had Grade IV Hematotoxicity and 4/7 (57%) had Grade I Hematotoxicity. **Discussion:** Our study shows that Lu-177 PRRT in Stage IV NETs with predominant skeletal involvement is associated with significant marrow suppression and is less likely to lead to improvements in QoL or progression-free survival.

EP-0716

Response to Single Low-dose ^{177}Lu -DOTA-EB-TATE Treatment in Patients with Advanced Neuroendocrine Neoplasm: A Prospective Pilot Study

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Objective: ^{177}Lu -1, 4, 7, 10-tetra-azacyclododecane-1, 4, 7, 10-tetraacetic acid-Evans blue-Tyr³-octreotate (^{177}Lu -DOTA-EB-TATE) is a theranostic agent based on octreotate that uses an Evans blue structure to bind albumin to improve the pharmacokinetics and pharmacodynamics. This pilot study aims to evaluate the efficacy of a single low-dose treatment using ^{177}Lu -DOTA-EB-TATE in patients with advanced neuroendocrine neoplasm (NEN). **Methods:** With IRB approval and informed consent, 4 NEN patients were enrolled to undergo ^{177}Lu -DOTA-EB-TATE treatment with a single low dose of $0.66 \pm 0.06 \text{ GBq}$ ($17.8 \pm 1.7 \text{ mCi}$); 3 other NEN patients were enrolled as controls to undergo ^{177}Lu -DOTA-TATE treatment with administered activity of $3.98 \pm 0.17 \text{ GBq}$ ($107.6 \pm 4.6 \text{ mCi}$). One primary tumor and 62 metastatic lesions in the 7 patients were evaluated by ^{68}Ga -DOTA-TATE PET/CT immediately before and one or three months after the treatment. Maximum SUV (SUV_{max}) of the tumors $\geq 2.0 \text{ cm}$ in diameter were measured and percentage of change (ΔSUV) after treatment were calculated. **Results:** All 4 patients subjected to ^{177}Lu -DOTA-EB-TATE treatment tolerated

the administered activity without significant adverse effects and showed symptomatic remission. Among the patients, 40 tumors were found with diameter $\geq 2.0 \text{ cm}$, with the baseline SUV_{max} varied from 1.5-82.9 (35.9 ± 21.0) and the $\Delta\text{SUV}_{\text{max}}$ of before and three months after the treatment from -75.1-26.3% ($-38.9 \pm 25.5\%$). Thirty-two(80.0%) of the tumors showed $>15\%$ decrease of SUV_{max} ($\Delta\text{SUV} = -75.1\% - 17.1\%$). There was a significant negative correlation between the baseline SUV_{max} and the ΔSUV after treatment ($r = -0.852$, $P < 0.001$). Compared with the control ^{177}Lu -DOTA-TATE therapy, the ^{177}Lu -DOTA-EB-TATE treatment using approximately 1/6 the dose showed no significant difference in ΔSUV ($-7.9 \pm 5.4\%$ vs. $-5.8 \pm 3.9\%$, $P = 0.189$) as demonstrated by the tumors with comparable baseline SUV_{max} from 10.0-35.0. **Conclusion:** A single low-dose ^{177}Lu -DOTA-EB-TATE treatment appears to be safe and effective in the treatment of NENs with high ^{68}Ga -DOTA-TATE uptake. This pilot study merits further investigation with increased dose and frequency of ^{177}Lu -DOTA-EB-TATE administration with potential advantages over ^{177}Lu -DOTA-TATE.

EP-0717

New Model For Lu-177 Dotatate Guide Decisions For Patient Restrictions And Release From Hospital

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Introduction: London Health Science Center (LHSC) is a frequent user of Lu-TATE for the treatment of Neuroendocrine Tumors NET. We began using this therapy as an in-patient procedure, where patients were released at 20 hours' post therapy administration with minimal restrictions. Lu-TATE practices in Canada require patients to be placed on major restrictions for their first 20hrs after each dose administration. Therapy of Lu-177 clearance was based on radioactive decay only. Over the course of 2013, we worked to transform this therapy into an out-patient procedure, where patients were released at 4-6 hours' post therapy administration with major restrictions. **Methods:** LHSC new proposed model combines our experimental results with results from literature. The model will state the dose rate from discharge can be modeled as a decaying double exponential function. The early phase clearance is dominated by protocol and patient-specific variables. Conversely, late-phase clearance is usually from disease-specific uptake. We designed an experiment to measure dose reduction factor (DRF) due to patient self shielding (R); DRF due to patient voiding (V); and four parameters, λ_1 , λ_2 , α & β , of our clearance model, CLR (t). Six patients were administered Lu-TATE. Activity range: 3700 - 5500MBq. Dose rate was measured at different time points post therapy. **Results:** In six patients one hour pre-void & post-void, 5 hour & 20 hour mean dose rate was 5.6uSv/hr, 4.4uSv/hr, 2.28uSv/hr and 1uSv/hr respectively. We can determine dose reduction factor due to patient self-shielding (R) value which found to be 0.87. We determined fraction of radiotherapy product due to patient voiding by comparing pre- and post-void dose-rate measurements to be 0.87. Both predicted & experimental measurements dose rate for administered activities of

3700MBq at 1.9m plot with time data on the graph. **Conclusion:** In correlation with our previous data from 2013, we described an experiment where we measured cumulative doses from 14 patients. Dosimeters were placed in various locations in patients' rooms and measured over different time periods. Our 2013 data shows variability and there are differences compared with our proposed model ranging from 3 - 32%. Overall, when we consider the 2013 results and our current model, predictions are reasonably close, especially considering differences may be due to the patients of 2013 moving around their hospital rooms. Our intention is to eventually use our new model to guide decisions for Lu-TATE patient restrictions and release from our institution.

EP-0718

Equivalent dose rate at 1m from patients after ^{177}Lu -octreotate peptide receptor radionuclide therapy and its predictive factors

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Introduction: A new radiopharmaceutical ^{177}Lu dotatate (Lutathera®, Advanced Accelerator Applications), has been approved recently for use in the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) in several European countries and USA. The radiation safety after treatment is barely studied; especially the radiation exposure of the entourage of patients treated remains a subject of controversy. This study aims to improve the management of these patients by analyzing the decrease of the external dose rate in order to predict how long a patient need to stay in a nuclear medicine department. **Subjects and Methods:** An observational prospective study was conducted in two hospitals for a duration of two years. Patients with GEP-NETs treated with Lutathera® were included. After collecting informed consent, clinical and paraclinical data, including those from PET/CT, equivalent dose rate at 1m (EDR-1m) measurements were performed repeatedly seven times after the end of treatment, until the 4th hour post-treatment, on two different anatomical areas (thorax and pelvis). Then a multivariate analysis between the decrease of equivalent dose rate and the clinical and paraclinical data in search of statistical correlation. **Results:** From May 2016 to April 2018, thirty eight series of measurements from twenty different patients were carried out. The EDR-1m at the end of measurements (the 4th hour post-treatment), is less than 40μSv / h for all of them and less than 25μSv / h for 29 of them. The EDR-1m becomes less than 40μSv / h generally in one hour. The average half-life of decrease is about 2h30 with a considerable inter-individual variability, varying from 1h to 4h. The thorax seems to be the site which has the best reproducibility of the measurements, compared to the pelvis. There is a statistically significant correlation between the average half-life of decrease and the creatinine clearance value on the one hand and the tumor burden (quantified by the metabolic volume of patients who had PET / CT) on the other hand. **Conclusion:** This study suggests that most patients treated with Lutathera® do not need to stay in the nuclear medicine department only for radiation safety. Renal function and tumor

burden appear to be correlated with the decrease of equivalent dose rate and could be useful to predict possible duration of hospitalization.

EP-0719

Rechallenge ^{177}Lu -PSMA radioligand therapy: First assessment in patients with metastatic prostate cancer

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Aim: Radioligand therapy (RLT) with ^{177}Lu -PSMA is gaining more and more interest as a therapeutic option for advanced prostate cancer. For chemotherapy there are examples where patients responded to reintroduction of the same therapy (drug rechallenge) after drug holiday following disease relapse. No previous work has described PSMA-targeted RLT in a rechallenge setting. Hence, our aim was to analyse the feasibility of rechallenge ^{177}Lu -PSMA RLT. **Material & Methods:** We retrospectively analysed the efficacy and safety profile of ^{177}Lu -PSMA I&T therapy in patients with metastatic prostate cancer who underwent multiple lines of treatment. The antitumor effect was assessed using serum-PSA levels and imaging by ^{68}Ga -PSMA-11 PET/CT according to PERCIST 1.0 criteria. Non-hematological and hematological adverse events were analysed from the clinical reports and were graded according to the Common Terminology Criteria for Adverse Events (CTCAE v5.0). PSA progression-free survival (PSA-PFS) and overall survival (OS) were calculated beginning with the date of first rechallenge cycle. **Results:** Nine patients received rechallenge ^{177}Lu -PSMA I&T RLT with a median number of 2 cycles (range 1-4). During initial ^{177}Lu -PSMA I&T, all patients had at least 50% maximum PSA decline, of whom 66.6% (6 of 9) had at least 90% maximum PSA decline. During rechallenge, a maximum PSA decrease of at least 30%, 50% and 90% was achieved in 66.6% of patients (6 of 9), 33.3% (3 of 9) and 11.1% (1 of 9), respectively. Partial response was present in 3 out of 7 patients who have completed ^{68}Ga -PSMA-11 PET imaging prior and after treatment. 4 patients exhibited progressive disease with new lesions. No grade 4 toxicity was observed. Grade 3 hematological toxicity occurred in 3 patients, including anemia (n=1) and thrombopenia (n=2). Renal toxicity (grade 1) was noticed in 1 patient. Xerostomia (grade 1) was noticed in 3 patients. The median PSA-PFS was 3.3 (95% confidence interval: 1.5-10.4) months. The median OS was 6.1 (95% confidence interval: 1.7-24.4) months. Four patients (44%) were still alive at last follow-up. **Conclusion:** Our results in a small patient cohort with initial excellent response during ^{177}Lu -PSMA I&T RLT indicate that this treatment is effective even in rechallenge setting at low toxicity levels. To confirm our findings further analyses in large patient cohorts are warranted and promising.

EP-0720

Peptide Receptor Radionuclide Therapy (PRRT) in Patients with Grade 3 Neuroendocrine Neoplasms: Safety and overall survival in 69 patients

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Objectives: To date, limited data are available concerning peptide receptor radionuclide therapy (PRRT) of grade 3 (G3) neuroendocrine neoplasms (NENs) with a Ki-67 proliferation index of >20%. The purpose of this study was to analyze the long-term outcome, efficacy and safety of PRRT in patients with SSTR-expressing G3 NEN. **Methods:** A total of 69 eligible patients (41 males, 28 females; age 28–81 y, mean age 58.1 ± 12.9 y) with pathologically confirmed G3 NEN were consecutively enrolled. All subjects received PRRT with Lutetium-177 (^{177}Lu) and/or yttrium-90 (^{90}Y) labeled somatostatin analogs (DOTATATE or DOTA-TOC). Kaplan-Meier analysis was performed to calculate progression-free survival (PFS) and overall survival (OS), defined from start of PRRT, including a subgroup analysis for patients with a Ki-67 index of $\leq 55\%$ and $>55\%$. Treatment response was evaluated according to RECIST 1.1 as well as by molecular imaging criteria (EORTC). Short and long-term toxicity was documented (CTCAE v.5.0) using a prospective database with over 250 items per patient. **Results:** Forty-six patients had pancreatic, 11 CUP, 6 midgut, 3 stomach and 3 rectum NEN. FDG-avid disease was present at baseline in 86.7% patients. DCR at 3 months post-PRRT was 78.2%, encompassing PR in 30.9% and SD in 47.3%, respectively. 56 of 69 (81%) patients died with a median follow-up time of 94.3 months (range 0.1–114.4 months). The median PFS was 9.6 months and median OS 19.9 months. For G3 NEN with a Ki-67 $\leq 55\%$ ($n=53$), the median PFS was 11 months and median OS 22 months. Patients with a Ki-67 $> 55\%$ ($n=11$), has a median PFS of 4 months and a median OS of 7 months. For those patients with positive SSTR imaging but no FDG uptake, the median PFS was 24 months and median OS was 42 months. PRRT was tolerated well by all patients; no grade 3 or grade 4 myelotoxicity occurred and no clinically significant decline in renal function was observed. There was no hepatic toxicity. **Conclusion:** PRRT is efficacious in G3 NEN, even in patients who have failed chemotherapy, and was tolerated well without significant adverse effects. This treatment approach results in promising clinical outcome especially in patients with a Ki-67 index of $\leq 55\%$. Baseline FDG along with SSTR molecular imaging is useful to stratify those G3-NEN patients with high uptake on SSTR PET/CT and no or minor FDG-avidity, a mismatch pattern which is associated with a better long term prognosis.

EP-0721

Pregnancy and delivery after PRRT without sequelae - report on 4 cases

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Peptide receptor radionuclide therapy (PRRT) with radiolabelled somatostatin analogues has been proven very useful in the management of advanced, well differentiated neuroendocrine neoplasia (NEN). Till date, there have been no reports

about pregnancy outcomes in NEN patients, who have received therapeutic activities of radiolabelled peptides, keeping in mind probable negative radiation effects. We present here the first report on pregnancy outcomes in NEN patients, who have received several cycles of PRRT. **Methods:** Clinical features, treatment parameters, pregnancy and birth outcomes in four young NEN patients (3 females and 1 male, age 28–39 y, mean age 33.0 ± 4.7 y), who successfully gave birth to (or fathered) a child after having received PRRT with ^{177}Lu or ^{90}Y labelled DOTATATE/DOTA-TOC/DOTA-JR11 between 2008 and 2017. **Results:** All patients had well-differentiated (G1/G2) NEN, 1 pancreatic NEN with liver metastases, 1 pancreatic NEN with liver, lymph node and cardiac metastases, 1 jejunum NEN with liver metastases, and 1 female patient having NEN origin in the ovary with extensive peritoneal, lymph node and liver metastases. Prior treatments included surgery in two, octreotide LAR in two, and transarterial chemoembolization in one patient. Baseline (pre-treatment) SUVmax on ^{68}Ga -DOTATATE PET/CT was 47.5 ± 24.7 (range 12.3–71.3). 2 patients were treated with ^{177}Lu -DOTATATE/TOC, whereas the other 2 patients received DUO-PRRT with sequential administration of ^{90}Y - and ^{177}Lu - DOTATATE/DOTATOC/DOTA-JR11. The median administered activity was 20 GBq (range 13–27 GBq) in 3–4 cycles. Treatment was tolerated extremely well by all patients without significant adverse effects. At 3 months post-PRRT based on molecular imaging criteria (EORTC), 1/4 patients had CR, 2/4 PR and 1/4 SD, and by RECIST, 1/4 had PR and 3/4 had SD. After 3–4 cycles of PRRT, CR was achieved in 2/4 and PR in 2/4 by both, EORTC and RECIST criteria. Disease Control Rate was 100%. Conception in one female patient was by in-vitro fertilization, whereas the mode of conception was natural in the other 3 cases. All the new-borns were healthy and exhibited no malformations. The intervals from first PRRT to birth were 20, 37, 52 and 83 months, whereas that from the last PRRT cycle to birth were 12, 27, 42, and 67 months, respectively. All patients were alive with a follow-up period of 61–114 months after first PRRT. **Conclusion:** Pregnancy as well as birth without sequelae is possible in patients with neuroendocrine neoplasia, who have been treated with PRRT.

EP-0722

Preliminary results of a Peptide Receptor Radionuclide-Therapy (PRRT) trial: prognostic role of baseline ^{68}Ga -DOTATOC PET/CT and tumour dosimetry

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Aim: This work is addressed to explore the predictive value of baseline ^{68}Ga -DOTATOC PET/CT and lesion dosimetry. **Material and Methods:** In a phase II trial for PRRT, patients with progressive NET underwent PRRT with ^{177}Lu / ^{90}Y -DOTATOC. All pts

had baseline 68Ga-DOTATOC PET/CT. The most representative lesions (max 5) for each patient were chosen. Each patient underwent a dosimetry study for organs at risk and for lesions. The red marrow dose couldn't exceed 2 Gy and the kidney Biological Effective Dose (BED) could not exceed 48 Gy. The absorbed dose for every selected lesion was calculated. The selected patients were the first 22 patients (89 lesions) who completed PRRT and were evaluated with a post-treatment 68Ga-DOTATOC PET-CT. SUVmax for each lesion was measured in the basal and post-treatment PET-CT. Baseline SUVmax values were divided into 3 classes (low uptake: SUV < 20; medium uptake: SUV 20–30; high uptake: SUV > 30). SUVmax variation between baseline and post-treatment value was calculated. SUVmax variations were used to define the lesion response according to PERCIST criteria creating 3 groups (complete/partial response-CR/PR, stable disease-SD and progression-PD). Absorbed doses estimates to lesions from dosimetry were divided into 3 classes (D<50Gy; D50–100Gy; D>100Gy). **Results:** PERCIST classification versus basal SUVmax values provided: for SUVmax >20 PR=8%, SD=38%, PD=54%; for 20<SUVmax<30 PR=38%, SD=50%, PD=12% ; for SUVmax>30 PR=63%, SD=32%, PD=3%. The contingency table provided a p-value < 0.00001 for Chi-square test (significant test at p < 0.05), showing an association between PERCIST classification and basal SUV max. Correlations between basal SUVmax values and SUV max variations were considered: Pearson's correlation test showed a weak correlation between patient outcome and basal SUV max (R= -0.436). The PERCIST classification versus lesion doses provided: for D <50 PR=55%, SD=26%, PD=19%; for 50<D<100 PR=47%, SD=43%, PD=10% ; for D>100 PR=48%, SD=48%, PD=4%. Chi-square test did not provide any significant association and no correlation was identified. **Conclusion:** Preliminary results showed that basal PET/CT has a predictive value for the therapy outcome in PRRT. A larger cohort of patient should be considered to confirm this result. The lack of association and correlation of PERCIST response with lesion doses is probably due to the punctual characteristics of SUVmax. Besides, absorbed doses take into account the kinetics of the radiopharmaceutical, unlike PET/CT examinations. Other parameters such as SUVmean in the lesion volume and the product of SUVmean and lesion volume might be much more reliable for this purpose.

EP-0723

PRRT using the radiolabelled somatostatin receptor antagonist Lu-177 DOTA-LM3: First Results of biodistribution and dosimetry in comparison with Lu-177 DOTATOC

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Aim: PET/CT using somatostatin receptor (SSTR) antagonists demonstrates a higher sensitivity and tumour detection rate than using SSTR-agonists, because of the higher receptor affinity. The aim of this study was to determine the kinetics and

dosimetry of Lu-177 labelled SSTR antagonist DOTA-LM3 in comparison to DOTATOC. **Methods:** Nine patients were treated with 5.9±1.3 GBq Lu-177 DOTA-LM3 after confirmation of high uptake using Ga-68 NODAGA-LM3 PET/CT. The biodistribution was determined based on planar whole-body scans & SPECT/CT and dosimetric calculations were performed using OLINDA software (MIRD Scheme). The kinetics were represented in terms of median effective half-life (hours) and median uptake (%IA, fraction of injected activity), which were calculated using the fit of the time-dependent activity curve to a mono- or bi-exponential function. The results were compared with SSTR agonist in 308 patients receiving 7±1 GBq Lu-177 DOTATOC. **Results:** The median uptake of Lu-177 DOTA-LM3 20h p.i. was significantly higher than Lu-177 DOTATOC - in whole body: 73% vs 19%, in kidneys: 6% vs 1.7%, in the spleen: 4% vs 1% as well as in the tumour: 0.2%/ml vs 0.1%/ml. DOTA-LM3 revealed a longer whole-body effective half-life (76h) as compared with DOTATOC (50h), which was concordant for kidneys (LM3 81h, TOC 62h), spleen (LM3 90h, TOC 73h) as well as metastases (LM3 106h, TOC 73h). Longer effective half-life and higher uptake resulted in higher mean absorbed organ and tumour doses (Gy/GBq) using DOTA-LM3 as against DOTATOC - in whole body: 0.13 vs 0.03, in kidneys: TOC 2.4 vs 0.6, in the spleen: 4.0 vs 0.7 and in tumour: 20.0 vs 6.0. Liver metastases demonstrated the highest uptake and longest effective half-life of DOTA-LM3 (0.15%/ml and 110h, respectively). The highest tumour dose in liver metastases was therefore achieved when using DOTA-LM3 (26Gy/GBq), significantly higher than for DOTATOC (7Gy/GBq). **Conclusions:** DOTA-LM3 revealed a higher accumulation in tumour lesions, which is in agreement with molecular imaging using SSTR antagonists. Therefore despite the higher mean absorbed organ doses, PRRT using Lu-177 DOTA-LM3 seems to be promising because much higher tumour doses could be achieved in comparison with Lu-177 DOTATOC. Further studies in a larger number of patients are necessary to confirm these preliminary results.

EP-0724

Chronic Kidney Disease and Hematologic Toxicity one Year after Four Cycles of Radionuclide Peptide Therapy (RNPT)

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Purpose: Renal and hematologic long-term side effects after RNPT have been described in heterogeneous studies using various cumulative activities, number of treatments or radiolabeled peptides. We analyzed long-term side effects for a homogenous treatment schedule in RNPT-patients. **Methods:** From our database we extracted 384 patients having RNPT from April 2005 to June 2017. Patients were analyzed if the same radio-peptide (177Lu-DOTA-TATE or 90Y-DOTA-TOC) was applied four times within a 10 to 12 week-interval. Follow-up data were analyzed at 12 months after fourth treatment cycle. 89 from 384 patients fulfilled inclusion criteria. One patient had three and 11 patients had two times four RNPT-cycles resulting in 102 cases. Glomerular filtration rate (GFR), hemoglobin (Hb), white blood cells (WBC)

and platelets before first and one year after the fourth therapy cycle were compared. GFR-Grading is according to chronic kidney disease classification (CKD). GFR above 60 ml/min/1.73m² was summarized as Grade 1-2, all other values according to CKD-classification. Grading of hematotoxicity is according to Common Terminology Criteria for Adverse Events (CTCAE). Impact of subgroups (age, gender, cumulative activity, type of RNPT) on long-term-toxicity was assessed. **Results:** One year after the fourth therapy cycle 71 (69.6%) cases had GFR Grade 1-2 compared to 87 (85.3%) cases prior to therapy ($p<0.001$), Grade 3a in 13 (12.7%) cases, Grade 3b in 2 (2.0%) cases, and one year after the fourth treatment cycle Grade 3a in 25 (24.5), Grade 3b in 5 (4.9%), and Grade 4 in 1 (1%). Anemia prior to RNPT and one year after was Grade 0 in 63 (61.8 %) versus 48 (47.1 %) ($p<0.001$), Grade 1 in 36 (35.3%) versus 48 (47.1%) ($p<0.001$), and Grade 2 in three (2.9%) versus six (5.9%) cases. White blood cells Grade 0 in 89 (87.3%) versus 83 (81.4%), Grade 1 in 12 (11.8%) versus 13 (12.7%), and Grade 2 in 1 (1%) versus 6 (5.9%). Platelets were Grade 0 in 92 (90.2%) versus 84 (82.4%), Grade 1 in 10 (9.8%) versus 18 (17.6%), and none Grade 2 or higher. Subgroup analysis: only age above 65 years showed a higher incidence for anemia: Grade 0 was found in 31 (70.5%) cases initially versus 18 (40.9%) after RNPT ($p=0.002$). **Conclusion:** The majority of patients shows no or only mild to moderate kidney disease or hematotoxicity one year after completion of standardized RNPT using four treatment cycles. RNPT does not preclude future oncologic treatment in case of progressive disease.

EP-0725

Evaluating single point measurement for dosimetry in ¹⁷⁷Lu-DOTATATE therapy

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Radionuclide therapy for malignant disease is a continuously developing field. Peptide Receptor Radionuclide Therapy has proven to be a valuable and safe treatment alternative for neuroendocrine tumors. Next steps are further optimization according to patient selection, efficacy as well as safety monitoring including dosimetry. This study evaluates if single point measurement of activity concentration after therapy correlates with obtained absorbed doses for kidney, bone marrow and tumors. **Materials & Methods:** Forty-five patients with somatostatin receptor positive advanced NET were treated with 3.7 to 7.4 GBq of ¹⁷⁷Lu-DOTATATE at 1 to 6 occasions at Sahlgrenska University Hospital, Gothenburg. Risk organ and tumor dosimetry was performed by activity quantification in planar images at 2, 24, 48 and 196 hours and a SPECT at 24 hours p.i. The relationship between obtained absorbed doses and the activity concentration in kidneys, bone marrow and tumors at different times for single point measurement (2, 24, 48 or 196 hours) in planar images were then evaluated. **Results:** Single point measurement of activity concentration in kidneys, bone marrow and tumors at 24, 48 or 196 hours p.i. showed a linear relationship with dose estimates from four point hybrid image quantification. R² values were 0.83, 0.87 and 0.88

for kidneys and 0.83, 0.77 and 0.77 for bone marrow at 24, 48 and 196 h.p.i. respectively. For tumor dosimetry 196 h.p.i. imaging showed a R² of 0.95. Single point measurement of activity concentration in 2 hour p.i. images gave R² values of 0.32 (kidneys), 0.5 (bone marrow) and 0.66 (tumor). **Conclusion:** Single point measurement of activity concentration at 24, 48 or 196 h.p.i. may be a surrogate for dose estimates in ¹⁷⁷Lu-DOTATATE therapy though variation is observed. For high accuracy, kinetics of the radiopharmaceutical should be obtained by 3 or 4 point measurement of activity at first treatment. As individual radiosensitivity varies it should always be completed with biomarkers for renal and bone marrow function.

EP-0726

Response Assessment of ¹³¹I-mIBG-therapy in high-risk neuroblastoma patients: SIOPEN or Curie score ?

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Introduction: ¹³¹I-mIBG-therapy is an established treatment option in high-risk neuroblastoma. Its effect on the SIOPEN and Curie score has not been investigated so far. **Patients & Methods:** 121 ¹²³I-mIBG scans of 48 patients who received ¹³¹I-mIBG therapy at our center between 2004 and 2017 were scored according to SIOPEN and modified Curie score before (t1; n=48), during (t2; n=43) and 3 - 6 months after (t3; n=30) ¹³¹I-mIBG-therapy. The effect of ¹³¹I-mIBG-therapy on the scores from ¹²³I-mIBG scans was analyzed and correlated to risk factors and clinical features. **Results:** At t1, SIOPEN score was 0 in 15 patients while Curie score was 0 in 6 patients, indicating 9 patients with soft tissue metastases only. Five patients had ¹²³I-mIBG-positive primary tumors only and 1 patient received ¹³¹I-mIBG therapy without unequivocally ¹²³I-mIBG-positive lesions. After exclusion of ¹²³I-mIBG scans with a score = 0, median SIOPEN score was 13 at t1 [range 1 - 52], 16 at t2 [range 1 - 56] and 8.5 at t3 [range 1 - 54]. For the same cohort Curie scores were 5.5 [t1; range 1 - 24], 5 [t2; range 1 - 25] and 4 [t3; range 1 - 26] respectively. Of 43 patients with available ¹²³I-mIBG scans at both time points, scores were higher at t2 than at t1 in 20 (SIOPEN; median 27 vs. 18; $p<0.001$) and 21 (Curie; median 12 vs. 8; $p<0.001$) patients respectively. However, none out of 12 patients with a pre-treatment SIOPEN score = 0 and only one out of 4 patients with a pre-treatment Curie score = 0 showed a score > 0 in the posttherapy ¹³¹I-mIBG scan. Of 30 patients with available ¹²³I-mIBG scans at t3, reduction of the scores were seen in 10 patients (SIOPEN; median 16 vs. 4.5; $p=0.005$) and 14 patients (Curie; median 7 vs 0.5; $p=0.001$) respectively and was neither correlated with status of MYCN or 1p nor with age at initial diagnosis or at mIBG-therapy nor with mIBG-score at t1 nor with concomitant therapy. **Conclusion:** After ¹³¹I-mIBG-therapy, 33 - 50% of patients showed a reduction of scores in ¹²³I-mIBG scans 3 to 6 months after ¹³¹I-mIBG-therapy. Patients with negative diagnostic ¹²³I-mIBG-scans are unlikely to show mIBG-avid metastases in posttreatment ¹³¹I-mIBG-scans. As to the methodology, SIOPEN scores were higher than Curie scores, and both scoring systems are useful for response assessment.

EP-0727

Combined Peptide Radio-Receptor Therapy (PRRT) And Liver Selective Internal Radiation Therapy (SIRT) In Patients With Metastatic Neuroendocrine Tumors: Which Is The Best Sequence?

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Purpose: Nuclear medicine treatments for neuroendocrine tumors (NETs) are gaining increasing acceptance among clinicians, but optimal treatment sequence remains controversial. Aim of this work was to investigate safety, tolerability and activity of sequential treatment with Peptide Radio-Receptor Therapy (PRRT) and Selective Internal Radiation Therapy (SIRT) in patients with liver-only metastatic NETs. **Subjects and Methods:** Records from metastatic NET patients being treated with at least one cycle of both PRRT and SIRT in Nuclear Medicine Unit of Milan National Cancer Institute, from March 2008 to January 2018, were retrospectively reviewed. Safety and tolerability of sequential treatments were assessed with scheduled blood tests. Treatment activity was evaluated in terms of instrumental response according to RECIST criteria (version 1.1) for PRRT and RECIST plus mRECIST criteria for SIRT. A treatment-specific Progression-Free Survival was evaluated using descriptive statistics. **Results:** Eight patients who underwent both ⁹⁰Y-radioembolisation and PRRT were identified. Patients had G1-G2 GEP-NETs with unresectable liver-only metastatic disease. Five patients (Group 1) underwent SIRT procedure before PRRT, three patients (Group 2) received PRRT followed by SIRT. A single SIRT procedure was performed in three patients; five patients underwent two consecutive radioembolisations with a median time interval between procedures of 11 months (range 3-32). Considering PRRT, three patients completed the 6 scheduled cycles, three patients discontinued treatment due to disease progression and one due to pulmonary embolism. In one patient, PRRT treatment was ongoing at the time of analysis. Both therapeutic combinations showed a limited toxicity profile, with no delayed G3-4 adverse effects. Symptomatic benefit was observed in syndromic patients after both treatments. The best instrumental response was observed at 1-month follow-up CT after SIRT (DCR 75%) and 3-months follow-up CT after PRRT (DCR 100%). Median follow-up from the first nuclear medicine treatment to the date of last contact or death was 52 months (range 14-65). In Group 1, median follow-up was 29 months (range 14-65) vs 55 months of Group 2 (range 52-57). Median Post-PRRT PFS was 16 months (Group 1=12 months vs Group 2=20 months). Median Post-SIRT PFS was 14 months (Group 1=14 months vs Group 2=15 months). **Conclusions:** This study on a small case series of liver-only metastatic GEP-NETs patients treated with sequential

radionuclide therapies found no cumulative toxicity issues for the combined approach and could suggest to adopt PRRT as an upfront treatment followed by SIRT.

EP-0728

Towards dose-response relationship in gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs) treated with ¹⁷⁷Lu-DOTATATE peptide receptor radionuclide therapy (PRRT)

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Introduction: PRRT with ¹⁷⁷Lu-DOTATATE is an established treatment for metastatic well-differentiated GEP-NETs. Even though combining patients with different GEP-NET primary sites could improve the statistical power, dose-response relationship might depend on the tumour primary site. This work aims to study the relationship between absorbed dose at first ¹⁷⁷Lu-DOTATATE administration (D_{1A}), tumour primary site and GEP-NET response to PRRT. **Materials and Methods:** Fifteen consecutive patients with well-differentiated GEP-NETs underwent PRRT with 3-5 cycles of ¹⁷⁷Lu-DOTATATE, each of them followed by three post-PRRT-SPECT/CTs (4, 24, 168 h post-administration). Baseline and end-of-treatment ⁶⁸Ga-DOTATATE-PET/CTs were performed; image quality was assessed using predefined criteria (administration-to-imaging delay, injected activity...). Patients were classified in three groups—pancreatic, intestinal or rectal—according to tumour primary site. Lesion-based dosimetry was performed on post-PRRT-SPECT/CTs (PMOD® 3.4 software). Peak specific activity was measured in a sphere surrounding the lesion on each image. These results were fitted over time with a biexponential function. Dose in lesion was computed assuming local energy deposition and homogenous specific activity. Response assessment was performed on baseline and end-of-treatment ⁶⁸Ga-DOTATATE-PET/CTs (AWserver 3.2 software, GE-Healthcare®). Lesions were delineated with a threshold equal to the baseline normal kidney cortex uptake measured in a 2 cm diameter sphere (Marin et al, EANM 2016). Lesion-based response to PRRT was assessed by decrease in lesion-uptake-volume (LUV). Data normality was checked with D'Agostino-Pearson normality test. The variability of D_{1A} and LUV-decrease in function of GEP-NET group was evaluated respectively with Kruskal-Wallis and one-way ANOVA test, according to normality test results (GraphPad software 7.1, Prism®). **Results:** This study included 61 GEP-NET lesions of which 20, 25 and 16 were classified respectively as pancreatic, intestinal and rectal. D_{1A} did not pass normality test. [first quartile; median; third quartile] was [19.8; 38.5; 59.5], [22.5; 48.6; 68.1] and [24.0; 72.4; 105.3] Gy for pancreatic, intestinal and rectal GEP-NETs respectively. D_{1A} distributions were not significantly different ($p=0.19$). LUV-decrease passed normality test. Mean±SD was 58.8±41.6, 33.8±30.6 and 79.5±21.6 % for pancreatic, intestinal and rectal GEP-NETs respectively. LUV-decrease distributions were significantly different ($p<0.001$). Pancreatic and rectal GEP-NET LUV-decreases were significantly different from intestinal ($p<0.05$ and $p<0.001$ respectively). The difference between pancreatic and rectal LUV-decreases was not statistically significant

($p=0.3$). **Conclusion:** This study indicates that GEP-NET response to PRRT highly depends on tumour primary site (despite similar lesion absorbed doses at first administration), reflecting different degrees of radiosensitivity of these tumours.

EP-0729

In-vivo stability of ^{177}Lu -DOTATATE during peptide receptor radionuclide therapy

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Introduction: ^{177}Lu -DOTATATE has recently been approved by the FDA for peptide receptor radionuclide therapy (PRRT) of neuroendocrine tumours based on the results of the NETTER-1 trial. Both analysis of urine samples from patients during the NETTER-1 trial, showing radiochemical purity close to 100% up to 48 h after administration, and in-vitro studies using human hepatocytes, similarly showing no hepatic metabolic degradation, suggest a high level of in-vivo stability of ^{177}Lu -DOTATATE¹. The aim of the present study was to assess the in-vivo stability of ^{177}Lu -DOTATATE using blood sampling and high performance liquid chromatography (HPLC) in patients undergoing PRRT.

Methods: Six neuroendocrine tumour patients were included. ^{177}Lu -DOTATATE (7.4 GBq) was administered as a 30 min infusion combined with 2 h of amino acid solution infusion for kidney protection starting 30 min before administration of radioactivity. Blood samples were taken immediately after end of ^{177}Lu -DOTATATE infusion and at 4 h, 24 h, and 96 h, centrifuged and injected onto an Xbridge BEH130 C18 HPLC column after protein precipitation and filtering. Samples were eluted at 6 ml/min for 15 min using a gradient of TFA 0.1%: TFA 0.1% in acetonitrile and collected into 30 fractions, and radioactivity concentrations were measured using an automated gamma counter. **Results:** The fraction of intact ^{177}Lu -DOTATATE decreased from 100% immediately after infusion to $96\pm3\%$ at 4 h p.i., $48\pm7\%$ at 24 h p.i. and $5\pm3\%$ at 96 h p.i. Three radioactive metabolite fractions could be consistently identified at 3, 9 and 12 min retention time, with parent fraction at 8 min. Plasma to whole blood ratio was constant and similar across patients and time points at around 1.65, indicating that all blood radioactivity was contained in plasma rather than blood cells. Between-patient variability in metabolism was small. **Conclusion:** Our results suggest that in-vivo stability of ^{177}Lu -DOTATATE is much lower than previously hypothesised, with the major part of radioactivity in plasma consisting of ^{177}Lu -labelled metabolites already at 24 h p.i.. The possible impact of this finding on ^{177}Lu -DOTATATE-therapy and of using different preparations needs to be further assessed. **References:**

¹Lutathera European public assessment report, EMA, 2018

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Prognostic importance of serum PSA response in patients who received Lutetium-177 prostate specific antigen treatment for castration resistant prostate cancer

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Aim: We aimed to analyze the prognostic importance of serum PSA response in patients who received Lu-177 PSMA treatment for castration resistant prostate cancer. Additionally we analyzed if there is a difference in survival rates between patients who have bone only metastases and those have bone and soft tissue metastases. **Material and Methods:** Thirty patients (mean age 68 ± 10) who received Lu-177 PSMA treatment were included to the study. All the patients have histopathologically proven prostate adenocarcinoma diagnosis and have received androgen deprivation and taxan based chemotherapy. Before treatment all the patients underwent Ga-68 PSMA PET/CT. Two hundred mCi Lu-177 PSMA was given in each cycle between 6 weeks period. In patients who were responder and have normal hematological parameters, treatment was completed to four cycle. Additional doses were administered in patients who have good response in Ga-68 PSMA PET/CT after four cycle. Treatment response was evaluated with serum PSA measurements, life quality questionnaires, radiological imaging modalities and Ga-68 PSMA PET/CT. Relationship between overall survival and PSA decline in 50% or any degree was analyzed by Kaplan-Meier method. Additionally overall survival of patients who have bone only metastases and those have bone and soft tissue metastases was compared by same method. **Results:** Totally 12 patients had underwent radical prostatectomy. Gelason scores was ranged between 7 and 9. In pretreatment Ga-68 PSMA PET/CT while 23 (77%) patients had bone and soft tissue metastases (lymph nodes (17), liver (3) and lung (4)), 7 (23%) had bone only metastases. Pretreatment serum PSA levels were ranged between 11.06 and 2044 ng/ml. After first cycle 50% PSA decline was detected in 10 (33%) patients. In same period, any PSA decline was observed in 15 (50%) of patients. After completion of all cycles, 50% and any PSA declines were seen in 13 (43%) and 14 (46%) of them. During mean 11 months follow-up period 20 (67%) patients were died. Mean overall survival time was calculated as 12.8 ± 2.2 (8.4–17.4, %95 CI) months for all patient group. Fifty percent PSA decline after first cycle ($p=0.012$) and 50% ($p=0.024$) or any PSA decline after last cycle ($p=0.016$) was found significant parameters to estimate overall survival. There was not any significant difference in overall survival of patients between patients who have bone only or bone and soft tissue metastases ($p=0.06$). **Conclusion:** Serum PSA decline during and after Lu-177 PSMA treatment are significant parameters to estimate overall survival.

EP-0731

Preliminary Results of Lu-177 PSMA I&T Therapy in Patients with Metastatic Castration-Resistant Prostate Cancer

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Purpose: The aim of this study is to present our preliminary results of Lu-177 PSMA I&T therapy in patients with metastatic

castration-resistant prostate cancer (mCRPC). **Subjects & Methods:** Nineteen patients with mCRPC (mean age 70.7 ± 10 years old) who underwent at least two cycles of Lu-177 PSMA I&T therapy between August 2016 and January 2018 were investigated retrospectively. Mean administered activity per cycle was 4.9 ± 0.6 GBq. Ga-68 PSMA I&T PET/CT was performed before therapy and repeated four weeks after every two cycles. All patients had laboratory tests including complete blood count, renal function and serum prostate-specific antigen (PSA) levels before and after four weeks of every cycle. Therapy response was evaluated by Ga-68 PSMA PET/CT scans and PSA levels. Adverse events were classified according to Common Terminology Criteria for Adverse Events (CTCAE) v4.0. **Results:** A total of 65 cycles of Lu-177 PSMA I&T therapy (2–6 per patient) and 43 Ga-68 PSMA PET/CT studies were performed. Gleason score of all patients was greater than or equal to 7. Initial mean PSA level was 103.10 ± 223.43 ng/mL (2–981). 5 (26.3%) out of 19 had a history of radical prostatectomy. 17 (89.5%) patients had bone metastasis, 12 (63.2%) patients had lymph node metastasis, 4 (21.1%) patients had visceral organ metastasis and 10 (52.6%) patients had both bone and lymph node metastasis. According to follow-up Ga-68 PSMA PET/CT scans, 8 patients had progression while 11 patients had partial response. 8 patients had Grade 2 and 3 patients had Grade 3 hematologic toxicity after therapy. Neither Grade 3 nor 4 nephrotoxicity was observed. **Conclusion:** Lu-177 PSMA therapy is a safe and promising treatment option in metastatic castration-resistant prostate cancer.

EP-0732

Nauseas and Vomiting in PPRT, are females a particularity?

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Purpose/Introduction: Peptide receptor radionuclide therapy (PRRT) is a targeted radiation therapy involving the systemic administration of a radiolabeled peptide designed to target with high affinity and specificity the somatostatin receptors overexpressed on neuroendocrine tumors (NET). The kidneys are the dose-limiting organ, and absorbed dose is significantly reduced by the pre-treatment administration of positively charged amino acids (aa). However, nausea and/or vomit, caused by the aa solution and not controlled by antiemetic therapy, are a common but not ubiquitous side effect. The aim of this study was to assess what patient specific characteristics, if any, may predict the occurrence of these side effects. **Subjects & Methods:** All patients submitted to at least one [¹⁷⁷Lu]Lu-DOTA-TATE PRRT at our center were selected. Nausea and/or vomits occurrence was recorded, in addition to, tumor type, height and weight, body mass index (BMI) and body surface area (BSA). **Results:** A total of 30 patient treated at our center, 20 men and 10 women, with an average age of 64.7 ± 11.6 years were selected. Weight, BMI and BSA were recorded (69.9 ± 12.7 Kg, 25.2 ± 3.1 Kg/m² and 1.8 ± 0.2 m², respectively). Lung carcinoid was the most common tumor (36.7%), followed by pancreatic (30%), gastrointestinal

tract (23.3%), and prostate, insulinoma and medullary thyroid carcinoma. Fourteen patients presented with nausea and/or vomits (46.7%). Of all the variables tested, gender, age, tumor type, weight, BMI and BSA, only gender was statistically significant (Pearson Chi-square, $p < 0.01$, odds ratio: 0.107 - higher risk for female patients). **Discussion/Conclusion:** In our sample, a statistically significant difference was found between side effect incidence (nausea and/or vomit) and gender, females being more prone to their occurrence. No statistical significant differences were found among the other variables tested.

EP-0733

Prognostic factors in patients with advanced neuroendocrine tumors treated with 177Lu-DOTATATE

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Aim: To assess the prognostic value of several variables in patients with an advanced neuroendocrine tumor (NET) treated with 177Lu-DOTATATE (Lu-PRRT). **Materials and Methods:** The data come from the SEPTRALU national registry of patients with advanced NET treated with Lu-PRRT. A multidisciplinary research team from nine spanish hospitals have recruited 82 patients. We analyzed clinico pathological variables proven to predict survival in NET: tumor grade, Ki67 index, primary tumor and metastasis location, number of metastatic sites, chromogranin A levels, ECOG performance status (ECOG-PS), previous tyrosine kinase inhibitor (TKI) treatment, number of previous treatments, surgery or other locoregional metastasis treatment, tumor status and somatostatin receptor scintigraphy (SRS) Krenning score. Univariate and multivariate analyses were performed to identify risk factors using a Cox proportional hazards model. **Results:** The median progression-free survival (PFS) was 18.4 months (95% confidence interval (CI), 14.6-NA) and overall survival (OS) was 28.1 months (95%CI, 19.4-NA). Median follow-up was 19.2 months (range, 3.4-54.9) and at the time of analysis, there were 28 progression events and 21 deaths. Lu-PRRT treatments were started at a median of 37.8 months (range 1.2-287.8) since the diagnosis of metastatic NET. Most of patients had received 1 or 2 previous treatments, somatostatin analogues (n=80), everolimus (n=37), TKI (n=26), interferon (n=7). Most of them were in progression to these treatments and had a tumor with a SRS score ≥ 2 (75%). In the univariate analysis, in addition to the variables with prognostic value in the multivariate study, a ITK treatment prior to PRRTs was associated with an increase in mortality, hazard ratios (HR) 2.65 (95%CI, 1.06-6.58, $p=0.0353$), OS 18.7 months (95%CI, 10.1-NA) vs 28.1 months (95%CI, 26.0-NA),

in the patients who received ITK vs. those who did not. Other prognostic factors like ECOG-PS2-3 with HR 6.85 (95%CI, 2.41–19.45, p 0.0003) and treatment administered in progression with HR 1.99, (95%CI, 1.52–94.55, p 0.0183) were significant independent prognostic factors for PFS in multivariate analysis. For OS, ECOG-PS2-3 (HR 4.94, 95%CI, 2.41–19.45, p 0.0003) and SRS score 4 (HR 2.99, 95%CI, 1.07–8.39, p 0.036) had an adverse prognostic effect. **Conclusion:** Treatment with Lu-PRRT demonstrates a similar clinical benefit in our patients to that reported by other groups, being the ECOG-PS the variable with the greatest impact on survival.

EP-0734

Radiological, clinical, scintigraphic and serum markers response of advanced neuroendocrine tumors treated with ^{177}Lu -DOTATATE

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Aim: To know the radiological, clinical, scintigraphic and serum markers response in patients with an advanced neuroendocrine tumor (NET) treated with ^{177}Lu -DOTATATE (Lu-PRRT). **Materials and Methods:** The data come from the SEPTALU national registry of patients with advanced NET treated with Lu-PRRT. Nine Spanish hospitals have participated and data from 82 patients are available. **Results:** 82 patients, half were women ($n=41$), median age was 57 years (range 22–89) and 29% over 65 years old. 90% of patients had good performance status (ECOG-PS0-1). Regarding to NET, the most frequent locations of the primary tumors were pancreas (38%), gastrointestinal tract (44%), lung (8%), others (10%) and locations of metastases were liver (79.2%), nodes (51.2%), bone (18.2%), peritoneum (17.0%) and lung (2.4%). The number of metastatic sites was: one ($n=33$), two ($n=30$), three ($n=18$) and four ($n=1$). 41% ($n=34$) were functioning tumors. The median Ki-67 index was 5% (range, 1–55), grade 1 (31.7%), grade 2 (58.5%) and grade 3 (9.8%). The median cycles of Lu-PRRT administered was 4 (range 1–4) and more than 93% of the cycles were performed at doses of 7.4 GBq. The reason for suspension of ^{177}Lu -Lutetium was progression or death at 35%. Acute toxicity symptoms were nausea (27%), vomiting (21%), haematological (8%) and renal toxicity (1 case, 3rd cycle). During follow-up, hematologic toxicity (worst grade) was grade 1 ($n=2$, 3.7%), grade 3 ($n=3$, 5.6%) and renal toxicity (worst grade) was grade 2 ($n=1$, 1.8%) and grade 3 ($n=1$, 1.8%). The best response according to RECIST criteria was stabilization (44.4%), progression (28.8%), partial response (24.4%) and complete response in 2.2% of patients. In 22 patients there were recurring

measurements of chromogranin A showing normalization of serum levels (22%), $\geq 50\%$ reduction (40.9%), $< 50\%$ reduction (13.6%), increase (13.6%), and no change (9.0%). Regarding the clinical response of initially symptomatic patients ($n=54$), an improvement (57.4%), stabilization (14.85), and worsening (27.7%) was observed. The scintigraphic response could be measured in 40 patients with stabilization in 23 (57.5%), improvement in 15 (37.5%), and progression in 2 (5%). The median progression-free survival was 18.4 months (95% confidence interval (CI), 14.6–NA) and overall survival 28.1 months (95%CI, 19.4–NA). **Conclusion:** In this national series of advanced NET patients (mostly GEPNET, grade 2 with liver metastases), the response rate was 26% radiological, 37% scintigraphic, 57% clinical and 77% by serum markers, and it stayed during 18 months.

EP-0735

Long-term Results of Peptide Receptor Radionuclide Therapy (PRRT) using an Individualized Therapy Approach

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Aim: To evaluate clinical results of patients treated with the most commonly used radiopharmaceuticals, ^{90}Y -octreotide and ^{177}Lu -octreotate, with special consideration of the long-term outcome. **Methods:** This retrospective clinical study included a total of 44 consecutive patients (27 men) with advanced tumors having enhanced SSTR Expression as assessed by ^{68}Ga -DOTA-TOC PET-CT. The mean age at initial diagnosis was 60.0 years (SD 11.3), the youngest person (minimum) was 40 years, the oldest 84 years. Normally, the ^{90}Y -labelled compound was used as the first choice. However, if individual lesions were smaller than 2 cm in diameter ^{177}Lu -DOTA-TATE was preferred. This compound was also used in cases of re-treatment after therapy with ^{90}Y -DOTA-TOC and progression as second choice tracer due to lower radiation dose to the kidneys. In case of progression after initial successful therapy re-treatment was a common procedure. The available data were used to statistically analyze relationships and differences, e.g. gender distribution, number of organ systems involved, type of first PRRT used, initial response to therapy. **Results:** The overall survival (OS) has been found 81.7 months (SD 51.0) on average. The least duration of illness was 8 months, the longest 155 months. Fourteen of 44 patients (32%) are still alive. Severe side effects (WHO grad III and IV) were seen in 9 / 14. Severe long-term nephrotoxicity in combination with anemia was the most common finding in these patients. Nevertheless, the majority of these patients are in still very good clinical condition. A very poor prognosis was found in patients who showed progressive disease after initial PRRT (Log-Rank, $p<0.001$) while women and patients with limited disease seem to benefit in particular from PRRT. **Conclusion:** Individualized PRRT, meaning the application of different radiopharmaceuticals and retreatment in case of progression, is very encouraging in terms of long-term outcome, so that nearly of quarter of patients with metastatic or inoperable disease are still alive after more than 12 years of follow-up with high quality of life.

EP-0736

Impaired kidney function is associated with higher absorbed dose to organ-at-risk (OAR) in ^{177}Lu -DOTATATE peptide receptor radionuclide therapy (PRRT)

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Introduction: In patients addressed for PRRT, prior treatments or underlying pathology may decrease kidney function. Kidneys and bone marrow (BM) are classically considered as dose limiting organs/OAR. Impaired kidney function might be associated with higher doses to OAR due to reduced ^{177}Lu -DOTATATE renal clearance. This work aims to study the impact of renal function, assessed by glomerular filtration rate (GFR), on absorbed dose to OAR in ^{177}Lu -DOTATATE PRRT of patients with well-differentiated neuroendocrine tumours (WD-NETs). **Materials and Methods:** 26 consecutive patients with WD-NETs underwent PRRT with 3-5 cycles of ^{177}Lu -DOTATATE, administered intravenously every 12 weeks with four-hours concomitant nephroprotective aminoacid solution. Patients underwent serial Cr-EDTA tests before each administration for renal function assessment (GFR), and 3 post-PRRT-SPECT/CTs (4, 24, 168 h post-administration) and 5 post-PRRT blood samples (0, 1, 4, 24, 168 h post-administration) for dosimetry purposes. Activity in kidneys was computed by multiplying volumic activity measured on SPECT images by the anatomical CT volume (PMOD® 3.4 software). For BM, volumic activity measured in blood samples was multiplied by OLINDA BM volume normalized by patient height. Measures were fitted over time with a biexponential function. Absorbed doses to OAR were computed following MIRD formalism (OLINDA/EXM 1.1 software) and normalized by the injected activity. Mean GFR values (GFR_{mean}) and dose per injected activity (D_{mean}) were computed for each patient. Descriptive statistics [first quartile; median; third quartile] were performed. Correlation coefficients (R^2) between GFR_{mean} and both kidney and BM D_{mean} were computed using linear regression model (GraphPad 7.01, Prism®). **Results:** Descriptive statistics for GFR_{mean} , kidney D_{mean} and BM D_{mean} were [64.0; 71.8; 87.4] ml/min/1.73m²/day, [0.72; 0.97; 1.2] Gy/GBq and [0.023; 0.281; 0.033] Gy/GBq respectively. GFR_{mean} was linearly correlated with D_{mean} in kidneys ($R^2=0.24$) and D_{mean} in BM ($R^2=0.43$). Linear regressions had a negative slope significantly different from zero ($p=0.01$ for kidneys and $p=0.0003$ for BM). **Conclusion:** This study demonstrates that an impaired kidney function (lower GFR) is correlated with higher absorbed doses to kidneys and BM in patients treated with ^{177}Lu -DOTATATE. This relationship could be explained by a decreased ^{177}Lu -DOTATATE clearance from blood. This conclusion might suggest a potential predictive value of GFR for OAR toxicity.

EP-0737

Progression Free Survival And Response Rate Differences Between Non-Carrier Added (n.c.a.) And Carrier Added (c.a.) ^{177}Lu -DOTATATE In Non-Functioning NET (NF-NET) Liver Metastasized, Treated Patient

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Introduction: To evaluate the progression-free survival and response rate in a cohort of patients suffering from well-differentiated non-functioning pancreatic neuroendocrine tumors (NF-GEP-NETs) metastatic to the liver, initially treated with n.c.a. ^{177}Lu -DOTA-TATE as first line therapy and after their relapse, consecutively infused with c.a. ^{177}Lu -DOTA-TATE. **Subjects and Methods:** Thirteen patients (8 females, 5 males, mean age 59 and 63 years, respectively) suffering from advanced, progressive NF-GEP-NETs originated from lung and pancreas were infused i.v. with n.c.a. ^{177}Lu -DOTA-TATE, at a dosage of 7.4 GBq (6 cycles with treatment intervals of 7-8 weeks), supported with LAR-octreotide, administered i.m. at a dose of 30 mg. A second treatment cycle of 6 sessions, followed their relapse was applied, this time using c.a. ^{177}Lu -DOTA-TATE i.v., at the same dosage and treatment intervals between them. Mean cumulative dose was 40 and 42 GBq for the n.c.a. and c.a., respectively. Dosimetric calculations were performed to all patients using the patient specific scintigraphic data by the OLINDA /EXM/ 1.0 code. **Results:** For i.v. infused n.c.a. DOTATATE calculated absorbed doses for a liver tumor of 10 gr spherical mass was 33.0 mGy/MBq, for blood 0.030 mGy/MBq and for kidneys 0.46 mGy/MBq. For i.v. infused c.a. DOTATATE, the calculated tumor dose was 4.4 mGy/MBq and for blood and kidneys 0.1 mGy/MBq and 0.9 mGy/MBq, respectively. The mean progression-free survival for the first therapeutic scheme with n.c.a. ^{177}Lu -DOTA-TATE was 34.3 months (range: 16 to 50 months) vs. 20 months (range: 4 to 41 months) for the c.a. radiocomplex ($p=0.0034$). The response rate was 100 % (13/13) in the n.c.a. cohort (one patient had complete response, seven had partial response and the rest five had stable disease) vs. only 23 % (3/13) in the c.a. cohort (ten out of thirteen patients had progressive disease). In both treatment schemes WHO Grade II to III erythro-, leuko- and thrombopenia occurred in 2 (15 %) cases, after the 3rd session in the n.c.a. and after the 2nd session in the c.a. treated arm, respectively. **Conclusion:** First line treatment of NF-GEP-NET with n.c.a. ^{177}Lu -DOTA-TATE, resulted in a markedly longer progression-free survival compared with c.a. ^{177}Lu -DOTA-TATE after relapse. A significantly higher response rate was also observed in the n.c.a. treated arm vs the c.a. one.

EP-0738

Exploring SPECT/CT and PET/CT Imaging Quantification in Molecular Radiotherapy with ^{177}Lu -DOTATATE for Treatment of Neuroendocrine Tumours

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Aims: To assess the feasibility and accuracy of the quantification of SPECT/CT images with ^{177}Lu -DOTATATE for potential comparison with quantitative ^{68}Ga -DOTATATE PET/CT in neuroendocrine tumours (NETs). Quantification of tumour response was based on SUVmax values with incorporation of an isocontour threshold to aid delineation of tumour volumes-of-interest (VOIs). **Materials and Methods:** Four patients with inoperable, metastatic NETs who underwent ^{68}Ga Gallium DOTATATE PET/CT prior to 7.4 GBq ^{177}Lu -DOTATATE radiopeptide treatment (PRRT) were identified. Post treatment whole body and SPECT/CT imaging was performed. The number of PRRT cycles ranged from 2 to 4, and was dependent on the patients' treatment outcomes. 13 SPECT/CT images and 4 PET/CT images were analysed. For the generation of SUVs, 3D VOIs of the tumours were defined using a semi-automatic region growing segmentation technique based on a 41% threshold (established in FDG PET studies). SUVs were determined for the PET studies while the relative SUVs were calculated from the SUV formula in SPECT studies. Three VOIs were identified in each patient from the initial SPECT/CT image and were followed throughout the subsequent scans at each therapy cycle. The same was performed for the corresponding PET/CT images. **Results:** There were similarities in the relative uptake of the identified VOIs in terms of SUVmax in both SPECT and PET imaging. VOIs generally had a decreased uptake of radiotracer over the course of PRRT treatment. Analysis of the use of an isocontour threshold suggested that this might improve tumour delineation. However, in some lesions (33.3 % of all identified VOIs) threshold had to be locally adjusted suggesting that more investigation is needed in determining the appropriate threshold for NETs imaging. **Conclusion:** The use of SUVs to quantify tumour response with ^{177}Lu -DOTATATE SPECT and ^{68}Ga -DOTATATE PET in NETs imaging shows promising results. SUV, as a quantitative measure, is valuable in monitoring changes in radiotracer uptake over time with potential use to monitor therapy response. Further investigation is required to determine and optimise an appropriate threshold for functional SPECT imaging in NETs with the goal of correlating SPECT SUV changes with clinical outcome.

EP-0739

Preliminary Results of Lu-177 DOTA-TATE Therapy in Patients with Neuroendocrine Tumor

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Purpose: The aim of this study is to present our preliminary results of Lu-177 DOTA-TATE therapy in patients with neuroendocrine tumor (NET). **Subjects & Methods:** Twelve patients with NET (mean age 51.67 ± 13.2 years old; 5 female, 7 male) who underwent at least two cycles of Lu-177 DOTA-TATE therapy between August 2016 and January 2018 were investigated retrospectively. Mean administered activity per cycle was 5.6 ± 0.5 GBq. Ga-68 DOTA-TATE PET/CT was performed before therapy and repeated four weeks after every two cycles. All patients had laboratory tests including complete blood count, renal function and tumor markers before and after four weeks of every cycle.

Therapy response was evaluated by Ga-68 DOTA-TATE PET/CT scans and tumor marker levels. Adverse events were classified according to Common Terminology Criteria for Adverse Events (CTCAE) v4.0. **Results:** A total of 41 cycles of Lu-177 DOTA-TATE therapy (2-6 per patient) and 27 Ga-68 DOTA-TATE PET/CT studies were performed. 4 (33.3%) patients had medullary thyroid carcinoma while 8 (66.6%) had NET (3 liver, 2 duodenum, 1 pancreas, 1 colon, 1 small intestine) diagnosis. 7 (58.3%) patients had bone metastasis, 6 (50%) patients had lymph node metastasis, 8 (66.7%) patients had visceral organ metastasis and 3 (25%) patients had bone, lymph node and visceral organ metastasis together. Among 10 patients who had a follow-up Ga-68 DOTA-TATE PET/CT, 3 patients had progression, 5 patients had partial response and 2 patients had stable disease. 3 patients had Grade 2 and 3 patients had Grade 3 hematologic toxicity after therapy. Neither Grade 3 nor Grade 4 nephrotoxicity was observed. **Conclusion:** Lu-177 DOTA-TATE therapy is a safe and promising treatment option in neuroendocrine tumors which have a few therapy options.

EP-0740

^{177}Lu -DOTATATE Treatment In Unresectable Neuroendocrine Tumors: Our Experience

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Objectives: Our aim was to evaluate the results after treatment with ^{177}Lu -DOTATATE in patients with unresectable neuroendocrine tumours (TNEs) in four years follow-up. **Materials and Methods:** We performed a retrospective-descriptive study of 24 patients with unresectable progressive neuroendocrine tumors, somatostatin receptor scintigraphy positive, treated with ^{177}Lu -DOTATATE between April 2014-2018. Previous to the treatment it was checked that the hemogram, the renal function and the hepatic function were inside the parameters recommended by the Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors peptide receptor radionuclide therapy (PRRT). The administered average activity of ^{177}Lu -DOTATATE was 8,0 GBq (217.8 mCi), with a treatment periodicity of approximately 7 weeks, with a 24 hours hospitalization. One patient was hemodialized. The follow-up time average was 18 months (6-48 months). All patients treated with previous treatments: surgery, somatostatin analogues (SA) and/or systemic therapies or several of these. **Results:** 68.3% were women, with a mean age of 55 years (range 20-73y.). The most frequent tumoral histology was: 19/24 TNE well differentiated (79%) 8 of them in the pancreas. 4/24 were paragangliomas (PG) and 1 iode-refractory metastatic differentiated thyroid cancer. 23/24 patients had metastatic disease and one had unresectable PG. The **liver** was **the most common** site of **metastasis** 70.8% (17 patients). 10/24 patients presented side effects, 9/24 were mild (asthenia, abdominal pain, nausea and throw up, transient leukopenia) with recovery within 2 - 3 weeks; and 1/24 showed a serious haematological event, thrombocytopenia after one cycle, with slow

recovery. 17/24 (70.8%) patients completed ^{177}Lu -DOTATATE treatment and have stable disease and 3 are under treatment. One patient was ruled out because lack of uptake of the lesions. 5/24 patients died. 3/5 during the treatment and 2/5 at the end (1 due to a complication not related to the disease and 1 due to progression). **Conclusions:** ^{177}Lu -DOTATATE treatment is well tolerated and safety, and reaches stable disease with a good quality of life in a high percentage of patients. In our experience is an excellent therapy to consider in somatostatin receptor scintigraphy positive patients, to consider in earlier phases of the disease.

EP-0741

Lesion segmentation in Somatostatin Receptor Imaging with ^{111}In -Pentetreotide and ^{177}Lu -Octreotate for Response Monitoring of Neuroendocrine Tumors (net) treated with ^{177}Lu -Octreotate

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Purpose: To monitor lesion evolution of NETs treated with Lutetium-octreotate in terms of average counts (Cmed), maximum counts (Cmax), total counts (Ctotal) and lesional volume on images of ^{111}In -Pentetreotide pre-post-treatment (In1-2) and ^{177}Lu -Octreotate (Lu1-4), during therapy. Correlation between both techniques and with radiological follow up. **Subjects and Methods:** It is a retrospective review of 9 patients treated with Lu-octreotate. We reviewed SPECT-CT images of In1-2, and Lu1-4 (acquired 24h after the administration of 200 mCi of Lu-octreotate) implementing lesion segmentation methods with MIM software. Cmed, Cmax, Ctotal and Volume of each lesion were recorded. The % decrease was calculated between In1-2 (dIn), between each Lu dose and between Lu1-4 (dLu). Radiological follow-up was performed on those patients who completed the treatment. **Results:** We analyzed 12 Indium studies (In1 = 8, In2 = 4) and 23 Lutetium studies (Lu1 = 8, Lu2 = 6, Lu3 = 4, Lu4 = 4). The median dIn for Cmed, Cmax, Ctotal and Volume was 87.78%, 92.44%, 97.41% and 60.11% and 44.56%, 90.14%, 97.97% and 75.63% for dLu, respectively. When comparing In1 and Lu1, the median of Cmed and Cmax were similar (Cmed = 452.7 vs 415 and Cmax 1214 vs 1412 respectively), in In1 Ctotal tended to be lower than in Lu1 (60214 vs 135532 respectively) and tumoral Volume was also lower for In1 (76.6 vs 190.17 p = 0.002). In Lu2 the median of Cmed and Cmax rose slightly. Ctotal descended exponentially, more sharply between Lu1-3. The volume decreased progressively from Lu1 to Lu4. 4 patients completed the treatment; the follow up CT described stable disease of most lesions, sclerosis of bone involvement and partial response in a pancreatic lesion. **Conclusion:** Lesional segmentation of somatostatin receptor imaging with indium and lutetium allows to monitor disease response to treatment by detecting metabolic improvement (of up to 90% activity reduction) despite a poor anatomical response. Lu-octreotate imaging detects more disease than In-pentetreotide; Ctotal seems to be the best marker for follow-up.

EP-0741a

Renal Function Evaluation in PRRT Retreatments

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PRRT is an effective option for patients with inoperable and/or metastatic NEN. However, due to the mainly renal excretion of the tracer, renal toxicity is the most limiting factor over time. We retrospectively evaluated renal toxicity of PRRT salvage therapy in patients affected by NEN. **Methods:** 10 patients (3 female and 7 male, mean age 56,7 y, range 43-75) with NEN (4 pancreatic, 2 of unknown origin, 2 ileal, 1 pulmonary and 1 meningioma) with progressive disease, who had benefit from a previous PRRT (at least stable disease, according to RECIST 1.1 criteria), were selected for re-treatment. 8/10 suffered for comorbidity (6 hypertension, 4 diabetes, 2 dyslipidemia). The cohort underwent at least two PRRT (range 2-4) between 01.02.2006 and 01.10.2017 with high activities of ^{90}Y -, ^{177}Lu - and/or ^{111}In - labeled peptides. Globally, were administered 83 cycles (41, 21, 21 with ^{90}Y , ^{177}Lu , ^{111}In indium, respectively), activity range for cycle was 0,93-7,4 GBq (1,11-2,405 GBq, 1,75-7,4 GBq, 0,93-7,4 GBq for ^{90}Y , ^{177}Lu , ^{111}In indium, respectively). Intravenous infusion of aminoacids was performed at any cycle of PRRT in order to reduce tubular peptide uptake and minimize renal damage. Renal function was assessed through $^{99\text{m}}\text{Tc}$ -DT-PA GFR measurements. We compared GFR% variations after each PRRT and for each radiopharmaceutical. GFR values before the beginning and after last PRRT were also compared. **Results:** Baseline GFR ranged from 50 to 113 ml/min at baseline (mean value 82,9 ml/min) and from 40 to 152 ml/min at last follow-up (mean value 72,9 ml/min). At baseline, according to Cyto-toxic criteria (CTC), 4/10 patients had grade 1 and 6/10 had grade 2 nephrotoxicity. At last follow-up, no-one experienced severe nephrotoxicity (grade 3-4) and 9/10 had grade 2 (moderate nephrotoxicity). According to chronic kidney disease classification (CKD), at baseline 5/10 had normal GFR value, 3/10 had stage 2, 2/10 had stage 3. At last follow-up, 3/10 had still normal GFR value, 2/10 had stage 2, 5/10 had stage 3 toxicity. No-one of our cohort experienced grade 4 (severe impairment) or 5 toxicity (renal failure). No statistically significant difference of GFR before and after treatments was found; no statistically significant difference was found between GFR% variations before and after treatments using different radiopharmaceuticals. Renal toxicity trend seems to reduce with progressive PRRT. **Conclusion:** PRRT salvage therapy is a feasible and tolerable option in patients with a good response after initial therapy. The occurrence of renal toxicity in re-challenge patients is not higher than previously reported.

EP-52

e-Poster Area

Clinical -> Therapy study -> Other treatments -> Radioimmunotherapy

EP-0742

Peptide receptor radionuclide therapy with ^{177}Lu -DOTATATE for patients with somatostatin receptor-expressing neuroendocrine tumors

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Objective: Therapy with ^{177}Lu -LUTATHERA (^{177}Lu -Dotatate) represents a new therapeutic route for those neuroendocrine tumors (NET) that express somatostatin receptors that progress to other treatments and that present limited therapeutic options. The objective of this preliminary study is to present our experience in metabolic therapy with ^{177}Lu -Dotatate and evaluate its tolerability and its short-term efficacy. **Methods:** We evaluated a total of 15 patients (8 men and 7 women) with metastatic NET with a variable grade and proliferation index Ki67 2–30%. The most frequent metastases were found in the liver, peritoneum and bone. The primary tumor was surgically removed in 8 patients. All cases were treated with somatostatin analogues, 11 with Everolimus, 4 with tyrosine kinase inhibitors, 5 with Sunitinib, 3 with interferon and 2 with chemotherapy prior Dotatate treatment. After being evaluated by a multidisciplinary committee and fulfilling RECIST progression criteria, were referred to ^{177}Lu -LUTATHERA treatment (4 bimonthly cycles of 7.4 GBq). **Results:** The most frequent location of the primary tumor was midgut in 10 patients, followed by 3 pancreatic tumors, 1 pulmonary, 1 unknown and 1 thymus. 9 patients presented toxicity to previous treatments to ^{177}Lu -LUTATHERA, whose most common manifestation was diarrhea. Of 15 patients, 6 completed 4 cycles, 8 patients are currently receiving treatment and 1 patient suffered death after the second dosage. No patient presented severe early toxicity and only 2 cases had resolved hematological toxicity. Of the 6 patients who completed the treatment, 3 currently have stable disease, 1 progression and 2 died. **Conclusions:** The treatment with ^{177}Lu -LUTATHERA presents a high safety profile in this study group. However, the increase in the number of patients, as well as a longer follow-up, would allow a better definition of its safety and efficacy.

EP-0743

Evaluation of Response to Radioimmunotherapy with FDG-PET in Follicular Lymphoma: Prediction of Survival Using IHP and D5PS Criteria

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Background: The aim this study is to compare two criteria for evaluation of response on 18F-FDG-PET (PET) after radioimmunotherapy with 90Y ibritumomab tiuxetan (RIT) on patients with non-Hodgkin follicular lymphoma (FL). **Materials and Methods:** We retrospectively analyzed the data on 27 relapsed or refractory FL patients treated with 90Y-ibritumomab tiuxetan (Zevalin) in three different nuclear medicine departments of Germany, who had a PET study carried out before and after RIT. Response was assessed on PET, performed 3 months after RIT using the international harmonization project (IHP) and Deauville (D5PS) Criteria. Progressions-free survival (PFS) and overall

survival (OS) were correlated with the response to RIT, derived from the two criteria stated above. **Results:** Out of 27 patients, 9 were non-responder (Group I), 12 were responder based on both criteria (Group II) and 6 patients were responders based on IHP but non-responders based on D5PS (Group III). All responders based on D5PS were also responders based on IHP criteria. Patients were followed for 8 to 150 (median= 50) months. PFS of Groups I, II and III were 7.3 ± 1.9 months, 94.0 ± 18.7 months and 7.5 ± 0.7 months, respectively. OS of Groups I, II and III were 42.6 ± 8.2 months, 140.9 ± 9.6 months and 79.9 ± 28.4 months, respectively. Kaplan-Meier Survival analysis was used to compare the PFS and OS of these groups, which were significantly shorter for Group I and III compared to those for Group II. There was no statistically significant difference between the PFS or OS of Group I in comparison to those of Group III ($p=0.98$ and 0.54). **Conclusions:** The response to radioimmunotherapy of refractory or recurrent FL using FDG-PET-Scan based on D5PS Criteria predicts PFS/OS more accurately than the evaluation based on the IHP Criteria.

EP-53

e-Poster Area

Clinical -> Therapy study -> Thyroid treatment -> Thyroid treatments, malignant I

EP-0744

Assessment of the role of radioiodine therapy in thyroid cancer patients and the onset of a second primary malignant neoplasm

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Objective: Administration of ^{131}I has been implicated with the onset of second primary malignancies (SPMs). Aims of the current study are: a) to estimate the incidence of second primary malignancy in patients with thyroid cancer b) the timing of occurrence in relation to thyroid cancer and c) to investigate the causal association between radioiodine and second primary malignancies. **Methods:** All records of patients of our hospital with thyroid cancer from January 1990 to December 2015 were retrospectively analyzed. Patients' inclusion criterion was the presence of two or more primary malignancies, one of which was thyroid carcinoma. Second primary malignancies were confirmed by histopathological examination in 165 patients (40 male). Patients were categorized into 3 groups: group A with thyroid cancer as the first diagnosis, group B who initially diagnosed with primary malignancy other than thyroid cancer and group C patients diagnosed and treated simultaneously for both thyroid cancer and other primary malignant tumors. **Results:** Group A included 61 patients (37%), group B 75 (45.5%) and group C 29 patients (17.5%). The whole population mean age ($\pm$ SD) at diagnosis of the first diagnosed cancer (thyroid or

any other cancer) was 51.6 ± 12.5 years and for the second primary, the mean age was 58.4 ± 11.8 years. The other primary tumor was detected mainly in the breast (41.2%), skin (8.5%), larynx/vocal cord (6.1%) and large bowel (5.5%). The primary tumor site differed between two sexes; larynx/vocal cord, prostate and lung cancer were the most common types in males. Radioiodine therapy was administrated to 96 patients (62.3%): 38 from group A, 42 (56%) from B and 16 (55.2%) from group C ($p=0.422$). The mean age of thyroid cancer varied (group A: 49.3 ± 12.4 , group B: 60.5 ± 10.7 , group C: 55.2 ± 13.5 years, $p < 0.001$). The second primary tumor appeared 9.6 ± 7.1 years after thyroid cancer onset (group A). Thyroid cancer occurred 8.4 ± 7.3 years after the second primary tumor (group B). **Conclusions:** There was no statistically significant risk for SPM after radioactive iodine treatment in patients with DTC. Patients who initially developed thyroid cancer were younger. Thyroid cancer more often is preceded by other malignancies or occurs simultaneously rather than appears as the first malignant neoplasm. The appearance of a second primary tumor appears to be independent of complementary treatment with radioactive iodine. Genetic abnormalities are probably responsible for the appearance of a second primary tumor.

EP-0745

Effects of I-131 ablation/metastasis treatment on DNA damage parameters in patients with differentiated thyroid cancer

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Aim: Radioactive iodine therapy (RAIT) is a treatment of differentiated thyroid cancer (DTC) after thyroidectomy. I-131 performs the cytotoxic effect on thyroid cells by forming chain fractures in DNA. The effect of RAIT on peripheral blood cells is controversial. The aim of this study was to determine the effect of RAIT on DNA damage in lymphocytes in patients with DTC. **Method:** Totally 21 DTC patients were included in our study (mean age 45.09 ± 10.02 years). Of the 21 patients; 6 (28.6%) were treated with a low (30 mCi) RAIT dose, 11 (52.4%) with ablation (100 mCi) dose and 4 (19%) with higher dose (>100 mCi). Venous blood samples were taken from each patient before treatment, 7 days and 6 months after the treatment. DNA damage was assessed using COMET assay following lymphocyte isolation from venous whole blood. COMET assay is a sensitive, rapid and easy gel electrophoresis method currently used to demonstrate single and double strand DNA breaks. Seventy-five cells per slide per sample were scored to evaluate DNA damage. Several parameters including head length, tail length, head intensity, tail intensity, tail moment were evaluated for quantitative analysis of DNA damage. Data were analyzed with the SPSS 21.0 program. Repeated Measures Analysis of Variance was used when parametric test assumptions

were provided; and the Friedman test was used when parametric test assumptions were not provided. $p < 0.05$ was considered statistically significant. **Results:** Tail intensity values were significantly lower after treatment (1st week and 6 months) 18.30 ± 6.48 vs. 18.06 ± 5.58 compared to before treatment (23.83 ± 9.82) ($p=0.002$). The head intensity values were statistically significantly higher after treatment (1st week and 6 months) (81.69 ± 6.48 vs. 81.93 ± 5.58) than before treatment (76.16 ± 9.82) ($p=0.002$). The tail moment was lower at 6 months following treatment compared to pretreatment (5.24 ± 2.51 vs. 8.04 ± 3.86) ($p=0.005$). **Conclusion:** The increase in head intensity and decrease in tail intensity and moment followed by treatment have shown that treatment has a positive effect on peripheral blood cells. Our results demonstrate that, RAIT does not cause significant DNA damage in peripheral blood cells. It can be conceived that, RAIT may have activated protective effects on lymphocyte DNA by activating repair mechanisms. **Key words:** Differentiated thyroid cancer, I-131, radioactive iodine therapy, DNA damage, COMET assay

EP-0746

Pulmonary Metastases in Children and Adolescents with Papillary Thyroid Cancer in China: Prognostic Factors and Outcomes from Treatment with 131I

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Purpose: Thyroid carcinoma is rare in children and adolescents. Unlike adults, limited data are available on children with this disease. The incidence of pediatric well-differentiated thyroid cancer (WDTC) cases is rising, most of which are papillary thyroid carcinoma (PTC). Thus, this study evaluated the therapeutic efficacy and prognostic factors of individuals less than 21 years of age with pulmonary metastases from PTC during 1998–2017. **Subjects & Methods:** Seventy-six children and adolescents with pulmonary metastases from PTC treated with 131I were retrospectively analyzed. Therapeutic efficacy was evaluated by changes in serum thyroglobulin (Tg), chest computed tomography (CT) and post-therapeutic 131I whole-body scan (WBS). Factors predictive of overall survival were measured by the Kaplan-Meier method and Cox's proportional hazards. **Results:** Serum Tg concentration increased in 53.9% (41 of 76), decreased in 19.7% (15 of 76) and remained stable in 26.3% (20 of 76) of patients. Changes on anatomical imaging suggested complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) in 3.9%, 63.2%, 15.8% and 17.1% of individuals, respectively. Univariate analysis showed that size and doubling time of pulmonary metastases were independent factors affecting therapeutic efficacy. The 15-year overall survival rate was 89.5%. Eight patients died before the end of the follow-up period. Tumor doubling time (<3 years) and tumor diameter (>1 cm) were significant risk factors associated with a poor prognosis. **Conclusion:** Radioactive iodine therapy is an effective treatment for children and adolescents with pulmonary metastases from PTC. Tumor doubling time and tumor diameter were the main factors influencing patient prognosis.

EP-0747

Comparison of salivary gland functions on the salivary gland scan in differentiated thyroid cancer patients underwent radioactive iodine ablation; Recombinant human thyroid-stimulating hormone versus thyroid hormone withdrawal

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Purpose: Recombinant human thyroid-stimulating hormone (rhTSH) have been widely used for pre-therapeutic stimulation in differentiated thyroid cancer (DTC) patients but there has been no study comparing salivary gland function after radioactive iodine (RAI) ablation according to preparation (rhTSH versus thyroid hormone withdrawal (THW)) on the salivary gland scan (SGS). Thus, we evaluated salivary gland function after RAI therapy with rhTSH and THW preparation using the dynamic SGS.

Methods: A total of 136 DTC patients who underwent postoperative RAI therapy with 3.7 GBq from 2012 to 2015 were enrolled in this retrospective study. 77 patients with rhTSH and 59 patients with THW methods performed dynamic SGS at a median follow-up of 16 months after RAI therapy. Using time-activity curves, 5 scintigraphic parameters were calculated for each parotid gland (PG) and submandibular gland (SMG): time at maximum counts (Tmax), time at minimum counts (Tmin), maximum accumulation (MA), maximum secretion (MS), uptake ratio (UR).

Results: 15 patients (19.48%) of rhTSH group and 13 patients (22.03%) of THW group complained of dry mouth or related symptoms ($p=0.831$). On the patient-based analyses using visual assessment of SGS, salivary gland dysfunction was observed in 27 patients (35.06%) of rhTSH group and in 22 patients (37.29%) of THW group ($p=0.858$). There were no significant differences in all PG parameters between rhTSH and THW groups (Tmax, 22.34 ± 2.89 in rhTSH group vs. 23 ± 2.52 in THW group, $p=0.052$; Tmin, 27.30 ± 1.29 vs. 27.15 ± 1.66 , $p=0.423$; MS, 69.90 ± 24.74 vs. 69.96 ± 25.72 , $p=0.980$; UR, 2.48 ± 1.41 vs. 2.61 ± 1.53 , $p=0.449$), except the MA (69.44 ± 12.03 vs. 74.07 ± 14.44 , $p=0.004$). After 21 patients (15 patients in rhTSH group, 6 patients in THW group) showing early, unstimulated saliva excretion were excluded from the SMG analysis, 5 scintigraphic parameters were also assessed and there were no significant differences in all SMG parameters between rhTSH and THW groups (Tmax, 21.44 ± 18.90 vs. 19.13 ± 6.09 , $p=0.229$; MA, 54.60 ± 14.77 vs. 51.93 ± 15.87 , $p=0.191$; MS, 63.57 ± 12.23 vs. 60.61 ± 10.51 , $p=0.052$; UR, 3.02 ± 0.92 vs. 2.80 ± 0.84 , $p=0.061$), except the Tmin (27.36 ± 1.30 vs. 26.94 ± 1.11 , $p=0.010$). **Conclusion:** This study demonstrates comparable salivary gland function in patients prepared for RAI therapy with 3.7 GBq by either administering rhTSH or THW.

EP-0748

Epidemiopronostic study of differentiated thyroid microcarcinoma

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Introduction: Differentiated thyroid microcarcinoma is reputed to be a tumor with a very good prognosis and a slow evolution-

ary potential. Its therapeutic management is still controversial because of the existence of certain cases where a maximalist attitude is used. The main object of this study was to evaluate its therapeutic management by analyzing prognostic and epidemiological factors. **Methods:** Descriptive, retrospective, monocentric study of 112 MCDT observations. All patients underwent complementary irradiation after total thyroidectomy. The criteria considered for poor prognosis in this study were lymph node involvement and nonresponse to treatment. **Results:** The average age of our patients was 44.4 ± 12.3 years with a female predominance (sex ratio = 0.1). Sixty-three patients had a familial and / or a personal history of thyroid pathology. Multinodular goiter (GMN) was noted in 46.4%. The circumstance of discovery was incidental in 45.5%. The papillary type was the most frequently encountered (94%) with 19.6% of multifocality. Incidental discovery ($P = 0.009$), TNM ($p = 0.001$) and postoperative thyroglobulin (Tg po) ($p = 0.006$) had an influence on remission after the first cure. The study of the impact of epidemiological data on prognosis showed, in univariate analysis, significant relationships with sex ($p = 0.03$), presence of GMN ($p = 0.03$) Family history ($p = 0.009$) and the incidental discovery circumstance ($p = 0.007$). Only the Tg po (OR=0.03, CI 95%:0.00-0.99) and multifocality (OR=0.05, CI 95%:0.00-0.93) were independent predictors of complete response after the 1st cure and the personal history of a GMN (OR=0.34, CI95%:0.12-0.91) for lymph node metastasis. **Conclusion:** The MCDT reaches mostly patients less than 50 years, especially females. It's characterized by epidemiological and clinical parameters that may affect its prognosis. The GMN as a predictive factor of aggressive progression and multifocality and Tg po as predictive factors of a non response to the treatment seem to justify a maximalist surgical and isotopic attitude.

EP-0749

The effect of salivary gland massage to prevent salivary gland dysfunction after high dose radioactive iodine therapy for differentiated thyroid cancer: a prospective, randomized, controlled trial

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Introduction: Salivary gland massage is one of the suggested methods for prevention of salivary gland dysfunction, which is one of the most frequent chronic complications after high dose radioactive iodine (¹³¹I) therapy for differentiated thyroid cancer. To evaluate the effect of salivary gland massage for salivary gland dysfunction, we prospectively investigated the serum amylase value and salivary gland scintigraphy (SGS) in each patient. We also analyzed the effect of using recombinant human thyrotropin (rhTSH) for preparation of the therapy and dose of ¹³¹I (2.96 GBq to 7.4 GBq). **Subjects & Methods:** The serum amylase value was obtained before (pre-amylase) and 24 hours after an ¹³¹I therapy (F/U amylase) in all 96 subjects, and the SGSs were also taken just before (baseline SGS) and at 8 months after the ¹³¹I therapy (F/U SGS). Change in serum amylase was defined as two indices, difference of absolute value

[(Post-therapy serum amylase)/(pre-therapy serum amylase)] and difference ratio [(Post-therapy serum amylase)/(pre-therapy serum amylase)]. The scintigraphic changes in salivary glands were assessed by direct comparison of both pre-SGS and F/U SGS. **Results:** Worsening on SGS was observed in 42 (44.7%) of 94 patients. The incidence rate of abnormality on F/U SGS was significantly lower in patients who received salivary gland massage (odds ratio=0.3846, $P=0.252$). Both difference value and difference ratio of serum amylase were significantly higher in non-massage group ($P=0.0054$ and 0.0056 , respectively). On multiple regression analysis, the PG massage status significantly affected the abnormality of 8-month F/U SGS after adjusting for clinical variables (age, sex, TNM stage, preparation methods (THW vs. rhTSH) for ^{131}I therapy, and dose of ^{131}I). **Conclusion:** The salivary gland massage significantly reduced the incidence rates of salivary gland dysfunction on 8-month F/U SGS and the serologic marker of salivary gland destruction after the ^{131}I therapy. Therefore, the salivary gland massage procedure could alleviate salivary gland dysfunction related to the ^{131}I therapy.

EP-0750

Can ATA high risk thyroid cancer patients with undetectable pre-ablation stimulated thyroglobulin be reclassified as low risk?

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Background: The role of undetectable pre-ablation stimulated thyroglobulin (sTg < 1 ng/mL) has been well documented in low- and intermediate-risk thyroid cancer patients with a high negative predictive value of disease recurrence. The prevalence and implication of undetectable pre-ablation sTg is less described in high risk thyroid cancer patients. The present study was aimed to investigate the prognostic value of undetectable pre-ablation sTg in high risk thyroid cancer patients. **Methods:** Institutional review board approval was obtained and informed consent was waived. Consecutive differentiated thyroid cancer patients referred to our department for remnant ablation were retrospectively studied. Patients with the following characteristics were analyzed: differentiated thyroid cancer; classified as high risk by ATA criteria; without persistent tumor after operation; pre-ablation s-Tg < 1 ng/mL with negative TgAb. The initial therapy was evaluated 6-12 months after ablation by sTg, TgAb and ultrasonography. Then annual measurement of Tg during L-T4 therapy (Tg/T4) and TgAb, neck US, and other imaging methods (if necessary) were evaluated during followed up. **Results:** From January 2009 to December 2014, 432 high risk thyroid cancer patients were ablated, and 44 (10.2%) patients had pre-ablation s-Tg < 1 ng/mL with negative TgAb at the time of ablation. None of the 44 patients showed distant metastasis on post-ablation scintigraphy. At initial assessment after ablation, 93.2% (41/44) of the patients were free of the disease (defined as s-Tg < 1 ng/mL, negative TgAb and neck ultrasound); 2 patients had elevated s-Tg (1.34, and 1.44 ng/mL) and 1 patient had positive TgAb (57.78 IU/ml), but no metastases were detected by the imaging methods, and none of them received additional treatment. During follow-up ranging from 12 to 97 months (me-

dian 48 months), ultrasound detected cervical lymph node metastases in 2 patients who were classified as excellent response in the initial assessment and underwent operation again. The remaining 42 patients without tumor recurrence did not get any additional therapy, including 40 ER(excellent response)and 2 IR (indeterminate response)in the last assessment. Thus, recurrent disease occurred in only 4.5% of patients. **Conclusion:** The presence of undetectable pre-ablation sTg is a common clinical scenario in high risk thyroid cancer patients at the time of remnant ablation. With similar frequency of tumor recurrence compared to low risk patients, high risk patients with undetectable pre-ablation sTg can be reclassified as low-risk. **Conflicts of interest and sources of funding:** Supported by National Natural Science Foundation (Grant No.81471692)

EP-54

e-Poster Area

Clinical -> Therapy study -> Thyroid treatment -> Thyroid treatments, malignant II

EP-0751

Coexistence of chronic lymphocytic thyroiditis and papillary thyroid carcinoma

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Introduction: The association between chronic lymphocytic thyroiditis (CLT) and papillary thyroid carcinoma (PTC) has been investigated for several years from different perspectives. The aim of our study is to evaluate the effect of coexistent CLT on the clinicopathological features of PTC. **Material and Methods:** It was a retrospective study of 60 patients with PTC treated in the years 2015-2017 were divided into two groups according to the presence or absence of concomitant CLT. All our patients underwent total thyroidectomy with a complementary treatment with Iodine 131. **Results:** Patients were divided in 2 groups with clear female predominance (90%). Thyroid nodule was the most revealing mode (68%) of PTC. In group A there were 30 patients affected by PTC alone, the median age was 48 years old [26-73] and in group B there were 30 patients affected with PTC associated with CLT, the median age for this group was 43 years old [16-72]. All our patients had very low to low risk of PTC and have received a first mini-cure of Iodine 131 (30 mCi). The post-irradiation scan revealed no pathological fixation outside the thyroid in all cases. Serum thyroglobulin levels (Tg) was negative (≤ 1 ng/ml) in 40% patients of the group A and 76% of them are declared cured after the 2nd iodine cure. For the group B, 50% of patients had negative Tg levels and 83% of them are declared in remission after the 2nd cure of which 28% patients required only one. **Conclusion:** CLT in patients with a lower grade PTC was associated with less disease persistence and spread, indicated a protective role of CLT, but it does not affect the overall survival of papillary thyroid cancers.

EP-0752

Curative Efficacy and Influencing Factors on ^{131}I Treatment for Pulmonary Metastases from Differentiated Thyroid

Carcinoma

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Objective: To investigate the curative efficacy and influential factors of ^{131}I treatment for pulmonary metastases from differentiated thyroid carcinoma. **Methods:** 119 patients (44 males, 75 females) with pulmonary metastasis who underwent ^{131}I treatment in our department from April, 2012 to March, 2018 were retrospectively analyzed. The efficacy of ^{131}I treatment was assessed using determination of serum Tg level, ^{131}I whole-body scan, and ^{18}F -FDG PET/CT. The possible factors affecting efficacy included patients' gender, age, pathological classification, the diagnostic time of the pulmonary metastasis, the iodine and ^{18}F -FDG uptake of pulmonary lesions, the size and number of lung lesions, extrapulmonary distant metastasis (assign 1 for metastasis, 0 for no metastasis), cumulative treatment dosage. Univariate and multivariate analyses (Student t test, Fisher exact test and logistic regression) were performed to investigate the factors. **Results:** The rate of efficacy and invalid of ^{131}I treatment were 58% (69/119) and 42% (50/119) respectively. Univariate analyses showed that ^{18}F -FDG uptake ($t=-2.243$, $P<0.05$), the size of lung metastasis ($P=0.001$), the number of lung metastases ($P=0.012$), and ^{131}I uptake ($P=0.020$), the diagnostic time of the pulmonary metastasis ($P<0.001$), extrapulmonary distant metastasis ($p<0.036$) were the factors influencing outcome of ^{131}I treatment; Multivariate logistic regression analysis showed that the influential factors included the size and number of lung metastases, the diagnostic time of lung metastasis, and extrapulmonary distant metastasis. The regression equation was as follows: $\text{Logit } P = -4.927 + 2.613 \times \text{the diagnostic time of the pulmonary metastasis} - 1.119 \times \text{the number of lung metastasis} + 1.269 \times \text{extrapulmonary distant metastasis} + 1.087 \times \text{the size of lung metastasis}$. Patients with multiple lung metastasis lesions, lesions greater than 1 cm, extrapulmonary distant metastasis and diagnosed not at the beginning of the ^{131}I treatment indicated a poor prognosis. **Conclusion:** ^{131}I treatment is an effective method for pulmonary metastases from DTC. The patients with the less-than 1 cm and single lung metastasis lesions, no other distant metastasis and diagnosed at the beginning had good response to ^{131}I treatment.

EP-0753

Serum Thyroglobulin Kinetics as the Predictor of Differentiated Thyroid Carcinoma Treatment Outcome

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Objective: To know the role of serum thyroglobulin (Tg) kinetics in predicting the differentiated thyroid carcinoma (DTC) treatment outcome. **Materials and Methods:** Patients with DTC were retrospectively selected from 320 patients underwent total thyroidectomy followed by radioablation from the year 2007–2013 in Hasan Sadikin Hospital, Bandung. Patients without preablation (preTg) and postablation Tg level measurement

were excluded. Clinical and pathological characteristics were assessed. Percentage of serum Tg kinetics (ΔTg) was calculated by subtracting preTg level (preTg) with Tg level at 6 months postablation (Tg-6mos). ΔTg were classified as increased, stable, and decreased ($<-25\%$, -25% to 25% , and $>25\%$, respectively). Disease remission criteria are Tg at 12 months (Tg-12mos) level <3 ng/mL with negative antithyroglobulin antibody (ATA), or if ATA were positive, there were negative wholebody scan and/or ultrasound finding. **Results:** From a total of 320 subjects, only 56 subjects (14 males and 42 females) fulfilled the inclusion criteria. Subjects were histopathologically classified as papillary (60.71%), follicular (21.43%), and follicular variant of papillary thyroid carcinoma (17.86%). Subjects age 14–76 years, mean 45.89 ± 13.86 years. Remission was higher in subjects belongs to decreased ΔTg group (73.53% from 34 subjects), compared with those found in stable ΔTg group (37.50% from 8 subjects), and increased ΔTg group (35.71% from 14 subjects). ΔTg vary between 25%–100% (average 89.50%) in decreased ΔTg group, average with preTg level 5.89 (range 0.10–67.50) ng/mL, and average Tg-6mos level 0.30 (range 0.02–22.00) ng/mL. Average ΔTg in stable and increased ΔTg group were $-8.25\% \pm 6.07\%$ and $-61.75\% \pm 30.52\%$. **Conclusion:** Decreased ΔTg ($>25\%$) is related to better treatment outcome. Further prospective study with more subjects and longer follow up is recommended.

EP-0754

Management and survival of differentiated thyroid carcinoma with distant metastasis at the diagnosis

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Introduction: Differentiated thyroid carcinoma (DTC) is the most common malignant tumor of the endocrine system, with a better prognosis, however few patients present at the diagnosis with distant metastasis. The main of this study is to determine the predisposing factors and the survival of these patients. **Materials and Methods:** We retrospectively reviewed 727 patients diagnosed with DTC, between 1990–2016, who underwent radioactive iodine therapy in our medical center. All patients were treated by total thyroidectomy. 52 patients (7.15%) debuted with metastasis at the diagnosis. 13.46% were poorly differentiated. **Results:** The average age was 59 years (12 and 87 years), 65.4% women. The most common histology was papillary carcinoma (61.5%), followed by follicular carcinoma (23.0%) and poorly differentiated (13.46%). The sites affected by the metastases were lungs (63.0%), bone (30.4%), lungs and bone (6.5%), mediastinum (5.8%), liver (1.9%) and skin. (1.9%). For patients <45 years the survival was 100% at 3 years and 78% at 10 years, whereas for those >45 years it was 75% and 20%, respectively ($P = 0.007$). Survival at 3 and 10 years of papillary carcinoma patients was 88% and 44%, follicular carcinoma 80% and 27% and poorly differentiated carcinoma 61% and 14%, respectively ($P = 0.027$). According to the site of metastasis, it was higher for lung (87%) versus bone (73%) at 3 years and 43% versus 15% at 10 years ($P = 0.238$). **Conclusions:** The most important factors

that determine a longer survival in patients with DTC with distant metastasis at the diagnosis, are the histology and the age of presentation. More than 50% of our patients survived 3 years after the diagnosis.

EP-0755

Prognostic factors and outcome of differentiated thyroid cancer with distant metastases: influence of detection time of distant metastases

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Purpose: Distant metastases (DM) from DTC occur in 5-25% of cases determining lower survival; the prognostic significance of the temporal onset of DM is unclear. Our aim was to retrospectively analyze the prevalence of metastatic disease in DTC patients and to assess the prognostic role of the timing of manifestation of DM regarding the outcome. **Subjects and Methods:** We included 174 patients with DM from DTC (mean age 64 years). According to the time of disease manifestation, DM were divided in two groups: synchronous DM (n=66) defined as metastases present at initial diagnosis and metachronous DM (n=108) as diagnosed during follow-up. SDM were further subgrouped in pre-RAIT SDM when diagnosed during pre-surgery work-up (n=35) and baseline-RAIT SDM when detected by first whole body scan after RAIT (n=73). Disease-specific survival (DSS) was analyzed using the Kaplan-Meier method. Univariate and multivariate analysis including Cox proportional hazards model were performed with a significance level of $p < 0.005$. **Results:** Stimulated Tg level, total RAI activities and number of radiometabolic treatments were significantly higher in SDM, while loss of RAI-avidity was more frequent in MDM. After an average time of 10 years, 44 patients died during follow-up; 41 were DTC-related deaths. The median DSS from the diagnosis of DM was 8 years; 5-year and 10-year DSS were 80% and 56%. On univariate analysis, MDM had significantly shorter DSS than SDM; 5-year and 10-year DSS were 83% and 61% for SDM, and 76% and 51% for MDM. Also histotype and loss of RAI-avidity were significant risk factors of impaired survival. On multivariate analysis, only loss of RAI-avidity remained as independent negative predictor ($p = 0.043$). Considering SDM, in pre-RAIT group follicular carcinoma, bone metastases and loss of RAI avidity were more frequent and stimulated Tg value was significantly higher in comparison with baseline-RAIT group. DSS was significantly shorter in pre-RAIT group than baseline-RAIT ($p = 0.004$). There was no significant difference between pre-RAIT and MDM in survival outcome ($p = 0.875$). **Conclusions:** According to time of onset of DM in DTC patients, no significant difference were found between SDM and MDM despite worse survival rates in the second group. Among SDM, pre-RAIT DM had significantly shorter DSS compared to baseline-RAIT DM. Patients whose metastases avidly concentrated RAI and didn't lost RAI-avidity presented better survival rates than metastases not RAI-avid. This evidence was present in both SDM and MDM. Timing of detection of DM may add an important prognostic feature to risk stratification in DTC.

EP-0756

Dose-dependent hemorheological impairment in patients with differentiated thyroid cancer following I-131 ablation/metastasis treatment

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Aim: Therapy of differential thyroid cancer (DTC) is total thyroidectomy and followed by radioactive iodine therapy with Iodine-131 (RAIT). RAIT is thought to affect blood cells and oxidative stress. The aim of this study was to determine the effects of three different doses of RAIT on hemorheological parameters, serum total oxidant level (TOS) and total antioxidant levels (TAS) in patients with DTC. **Method:** Totally 31 DTC patients (mean age 46.32 ± 11.15 years) and 26 healthy controls (mean age 50.50 ± 6.22 years) were included in our study. Of the 31 patients; 7 (22.6%) were treated with a low (30 mCi) RAIT dose, 19 (61.3%) with ablation (100 mCi) dose and 5 (16.1%) with higher dose (> 100 mCi). Venous blood samples were collected from each patient before and after treatment (7 days, 1 month and 6 months). Red blood cell (RBC) aggregation and deformability were determined by an ektacytometer. TOS and TAS were measured by a commercial kit and the oxidative stress index (OSI) was calculated. Data were analyzed with the SPSS 21.0 program. Analysis of variance in repeated measures was used when parametric test assumptions were provided; and the Friedman test was used when parametric test assumptions were not provided. $p < 0.05$ was considered statistically significant. **Results:** There was no statistically significant difference between erythrocyte deformability values and between TAS, TOS, OSI values in before and after treatment (7th day, 1st month and 6th month) ($p > 0.05$). RBC deformability of the patients determined at 16.87 and 30 Pascal (Pa) were lower than healthy individuals (16.87 Pa; 0.562 ± 0.02 vs 0.585 ± 0.03 ; $p = 0.014$) (30 Pa; 0.582 ± 0.02 vs 0.623 ± 0.03 ; $p = 0.0001$). RBC aggregation index (AI) of the patients was higher (74.16 ± 8.47 vs 67.82 ± 6.87 ; $p = 0.0001$), whereas erythrocyte aggregation half-time ($t_{1/2}$) was lower compared to control (1.30 ± 0.76 vs 1.72 ± 0.74 ; $p = 0.0001$). These alterations indicate increased RBC aggregation in patients. Administration of higher dose of RAIT resulted in a further decrease in RBC deformability at 16.87 and 30 Pa 1 week after treatment compared to lower and ablation dose administrations (16.87 Pa; 0.53 ± 0.05 , 0.57 ± 0.01 , 0.57 ± 0.01 ; $p = 0.017$) (30 Pa; 0.54 ± 0.05 , 0.59 ± 0.02 , 0.58 ± 0.02 ; $p = 0.025$). TOS of ablation dose group measured on the first week following treatment was higher than low dose group (6.78 ± 2.53 vs 3.76 ± 1.02 ; $p = 0.011$). **Conclusion:** Patients were in a worse hemorheological condition compared to healthy individuals. The issue that high dose of RAIT results in further decrement in RBC deformability should be kept in mind especially for patients who are not hemodynamically stable. **Key words:** I-131, radioactive iodine therapy, erythrocyte deformability, erythrocyte aggregation, oxidative stress.

EP-0757**Comparing radioiodine abdominal absorbed dose in differentiated thyroid cancer patients undergone thyroid remnant ablation in either levo-thyroxine withdrawal or after rhTSH stimulation**

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Aim: In differentiated thyroid cancer (DTC) patients, radioactive iodine therapy (RAIT) is an important therapeutic tool for both thyroid remnant ablation (TRA) and adjuvant treatment (AT). Two stimulation strategies can be used to perform RAIT: (I) Levo-Thyroxine (L-T4) withdrawal; (II) rhTSH-stimulation. The use of rhTSH has been proven to be as effective as L-T4 withdrawal in achieving both TRA and AT. Aim of the present work was to compare radioiodine abdominal absorbed dose (AAD) among patients treated after either L-T4 withdrawal or rhTSH-stimulation. **Patients and Methods:** We reviewed the records of 63 patients (F=51, M=12) affected by DTC. All patients underwent TRA within three months from thyroid surgery, after either rhTSH-stimulation (Group A, n=36) or L-T4 withdrawal (Group B, n=27). Thirty-three patients were treated with 2220 MBq (18 after rhTSH-stimulation) while 30 patients were treated with 3700 MBq (18 after rhTSH-stimulation). A post-therapy whole body scan (pT-WBS) was obtained 5 days after RAIT. All patients drank 1.5 liters of water and took laxatives drug two days before pT-WBS. Quantitative analysis was performed writing 7 region-of-interest (ROI) on abdomen in anterior-posterior views, with different shapes, corresponding to liver(L), stomach(S), ascending-colon(AC), transverse-colon(TC), descending-colon(DC), rectum(R), small-intestine(SI). For each region, we evaluated activity incorporated at pT-WBS as geometrical mean of anterior-posterior counts, corrected for background. To estimate the AAD, the effective half-lives of 15.7 and 10.5 hours were used for withdrawal and rhTSH patients, respectively, as already described. The AAD and average activity ratios between A and B Groups were estimated. **Results:** The AAD for L, S, AC, TC, DC, R, SI evaluated in Group B patients were higher than in Group A patients with ratio values of 3.62, 4.16, 4.34, 3.19, 2.93, 3.66 and 3.48, respectively. In addition, the average activities evaluated on L, S, AC, TC, DC, R, SI of Group B patients were significantly higher than in Group A patients with p-values of 0.000, 0.000, 0.001, 0.000, 0.022, 0.007, 0.002, respectively. Finally, the lowest values of both AAD and average activity for each region were observed in Group A patients treated with 2220 MBq. **Conclusion:** As the efficacy of rhTSH-stimulation is equal to L-T4 withdrawal to obtain TRA, our data suggest a preference for rhTSH-stimulation rather than L-T4 withdrawal since the AAD is significantly lower than in patients treated in hypothyroidism. This reduces the risk of both abdominal radio-induced secondary tumors and liver dysfunction.

EP-0758**Predictive factors of radioiodine refractory tumours in patients with metastatic differentiated thyroid cancer**

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Purpose: Radioiodine (RAI) therapy has been used in the treatment of patients with differentiated thyroid carcinoma (DTC). Since patients with RAI refractory DTC can nowadays be treated with several molecular targeted agents, it is important to identify patients with RAI refractory DTC. We evaluated the outcomes of patients undergoing RAI therapy for metastatic DTC and the predictive factors of RAI refractory DTC. **Subjects and Methods:** We retrospectively reviewed the data of 194 patients who underwent RAI therapy for metastatic DTC at our institution between January 2011 and December 2017. Patients who underwent RAI more than once were counted once, and those whose outcome were not confirmed after RAI therapy were excluded; thus, 112 patients were analysed. For RAI therapy, the “per session” dose of I-131 was 3.70-5.55 GBq and the median accumulated dose was 8.51 GBq (range, 3.70-47.7 GBq); the patients underwent a median of 2 cycles of therapy (range, 1-9). RAI refractory patients were defined as those with at least one tumour without uptake in RAI scintigraphy; with at least one tumour showing progression after RAI therapy despite RAI uptake; or whose accumulated dose was ≥ 22.2 GBq. We analysed if age, sex, pathological findings, primary/recurrent disease, metastatic region, and scintigraphy findings during the first RAI therapy were predictive factors of RAI refractory DTC, using the Fisher's test for univariate analysis and the logistic regression for multivariate analysis. Statistical significance was set to $p < 0.05$. **Results:** The median age of the patients (40 men and 72 women) was 66 years (range, 18-85 years). The pathological findings were papillary carcinoma (PTC) (n = 89), follicular carcinoma (n = 12), and ‘others’ (n = 11). Primary metastases were observed in 50 patients, and 62 patients had a recurrence. Metastasis (including overlaps) was localized to the lungs (n = 100), regional lymph nodes (n = 8), bone (n = 14), and liver (n = 1). A total of 66 patients (59.0%) were identified as RAI refractory. Pathological findings (PTC), recurrent disease, and no uptake during the first RAI therapy were significant predictors for RAI refractory DTC in the univariate analysis. Recurrent disease and no uptake during the first RAI therapy were also significant predictors in the multivariate analysis. **Conclusion:** About 60% of patients had refractory DTC after RAI therapy. Knowing the predictive factors of RAI refractory DTC will help us identify these patients early on.

EP-0759**Can Decision Making For Radioiodine Ablation Be Modified By Prophylactic Central Neck Dissection In Patients With Clinically Node-negative Papillary Thyroid Carcinoma?**

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Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy. Despite its extremely favorable prognosis, cervical lymph node metastases are a common feature of PTC and a known independent risk factor for local recurrence. In PTC patients the indications for a radioiodine ablation post surgery is well defined, while the role of prophylactic central neck dissection (PCND) remains a matter of debate in patients with clinically node-negative (cN0) PTC. Moreover the additional information provided by PCND can be used to tailor radioiodine treatment as patients without nodal metastasis after central neck dissection may be able to safely receive lower doses of ^{131}I . Aim of the study is to evaluate the clinical impact of PCND in decision making for radioiodine treatment and in improvement of outcome in patients with cN0-PTC. Between January 2000 and December 2015, 186 consecutive patients with cN0-PTC were included in the study. 74 patients (12 males and 62 females, age range 53 ± 16 years) underwent total thyroidectomy associated with PCND (group A), while 112 patients (29 males and 83 females, age range 57 ± 14 years) underwent total thyroidectomy alone (group B). Radioiodine ablation was performed in 43 patients of group A (58.1%) and in 55 patients of group B (49.1%) ($p=0.23$). 3700 MBq of ^{131}I was administrated in 42 patients (98%) of group A and in 52 patients (95%) of group B; while 1850 MBq of ^{131}I was administrated in 1 patient of both groups (p value not significant). No significant differences in terms of indication to radioiodine ablation treatment and in determining of ^{131}I dose between the two groups were observed ($p=0.50$). Overall survival was not significantly different between the two groups of patients and well exceeded 90% at 10 years (93% in group A and 91% in group B, respectively; $p=1.0$). Tumor-related deaths are reported in 1.3% of cases (1 patient) in group A and 0.9% of cases (1 patient) in group B ($p=1.0$). Recurrence rate is 5.4% (4 patients) in group A and 3.6% (4 patients) in group B, with no significant differences between the two sets ($p=0.71$). Our results after 15 years of follow-up show that in cN0-PTC patients the use of PCND is not able to modify the indication or the dose for radioiodine ablation and there is no clear evidence of reduction in recurrence or added benefit survival.

EP-0760

Risk Factors For Predicting Recurrence In Patients With Papillary Thyroid Carcinoma

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Purpose: Papillary thyroid carcinoma (PTC) is the most common malignancy of thyroid gland. Although PTC has excellent prognosis with slow progress and good therapeutic effect, 5-10% of patients experience recurrence. Various prognostic factors for predicting recurrence have been reported over the past several decades. The aim of this study was to determine prognostic factors of recurrence in PTC patients who underwent thyroid surgery and postoperative radioiodine therapy (RIT). **Method:** To-

tal 294 patients with PTC who underwent total thyroidectomy with central and/or lateral neck dissection and postoperative RIT were included in this retrospective study. We investigated age, gender, clinical and pathologic variables, serum thyroglobulin (Tg) level immediately before postoperative I-131 therapy (Preablation Tg), and lymph node ratio (LNR). Definition of LNR was the ratio of positive lymph nodes out of total removed lymph nodes. The specimens with less than three lymph nodes retrieved during surgery were excluded in order to avoid falsely exaggerating the LNR when only one or two LNs were available. Kaplan-Meier estimates for disease free-survival were classified into 0.1 to 1.0 at 10% interval for LNR and compared by the log-rank test. Multivariate analysis was performed using the Cox proportional hazard model to evaluate independent prognostic factors. **Result:** In univariate analysis, the gender, capsular invasion, multiplicity, bilaterality of tumor, the group with a LNR ≥ 0.4 and preablation Tg 6.5 ng/mL were significantly associated with recurrence of PTC. Multivariate analysis showed that LNR was no longer a significant factor associated with recurrence. Rather, gender ($p=0.002$), multiplicity ($p=0.010$), bilaterality of tumor ($p=0.012$) and preablation Tg (HR 9.21, $p<0.001$, 95% CI 3.80-22.3) were significantly associated with recurrence. In the same analysis without preablation Tg, LNR (HR 2.56, $P=0.033$, 95% CI 1.07-6.09), gender ($p<0.001$), multiplicity ($p=0.002$) and bilaterality of tumor ($p=0.002$) were significant factors. **Conclusion:** Preablation Tg was identified as the stronger prognostic factor of recurrence. However, preablation Tg can be influenced by the level of anti-Tg antibody or procedures for preparation of RIT such as thyroid hormone withdrawal or recombinant thyrotropin injection. Therefore, LNR along with preablation Tg may have a potential to determine early detection and management of recurrence in PTC.

EP-0761

A retrospective evaluation of the timing of distant metastasis occurrence in papillary thyroid cancer

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Aim: The aim of this study is to retrospectively evaluate the timing of distant metastasis occurrence in papillary thyroid cancer (PTC) by the age of initial surgery, and to clarify changes of incidence rate during follow up. **Materials and Methods:** From January 2007 to December 2016, 136 adult cases of initial radioiodine therapy for distant metastasis of PTC were performed in Noguchi Thyroid Clinic. Metastases were discovered at the time of initial disease staging in 53 cases. In the remaining 83 cases, metastases were identified during follow-up. In Japan, there is a shortage of radioiodine treatment facilities. And because of this shortage, it is usual for patients to have initial radioiodine therapy when metastases are discovered. So we assumed that the timing of the development of distant metastasis was when initial radioiodine therapy was performed. The timing of distant metastasis occurrence were evaluated in the 83 cases by dividing into three groups by the age of 21-40, 41-60 and over 61 at the time of initial surgery. Also the follow up was divided by 5 years in order to compare the incidence rates of metastases

during follow up. **Results and Conclusion:** The average timing of distant metastasis occurrence were 17.4 years (209.4 month), 13.8 years (165.3 month) and 6.5 years (78.5 month) in each group. In the youngest age group, only 1 patient (4.0%) developed distant metastasis within 5 years of follow up. 8 patient (28.0%) developed distant metastasis in 6–10 years, 4 (16.0%) in 11–16 and 13 patient (52.0%) developed distant metastasis after 16 years. The middle age group had 4 (13.8%) within 5 years, 5 (17.2%) in 6–10, 10 (34.5%) each in 11–15 and after 16 years. In the eldest group, 13 (44.8%) developed distant metastasis within 5 years, 11 (37.9%) in 6–10 years and 5 (17.2%) in 11–15 years. Even though the average timing of distant metastasis occurrence were slightly latter in the youngest age (21–40) group, incidence rates of distant metastasis did not change between the youngest age group compared to the middle age (41–60) group, when divided by 10 years (within 10 years: 32~33%, after 10 years: 68~69%). Compared to the younger groups, the eldest (over 61) group had a drastic difference in both average timing of distant metastasis occurrence and incidence rates (average timing: 6.5 years, within 10 years: 82.7%, after 10 years: 17.2%).

EP-0762

Clinical Value of Combined Use of Stimulated Serum Thyroglobulin Value, Ultrasonography and Tc99m Pertechnetate Scintigraphy in Detecting Residual Thyroid Tissue after Total Thyroidectomy

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Purpose: The aim of this study was to investigate the rate of detecting postablative residual thyroid tissue on I-131 whole body scan (WBS) in low risk well-differentiated thyroid carcinoma patients in whom no residual thyroid tissue was detected by Tc-99m pertechnetate WBS and ultrasound after total thyroidectomy and before I-131 ablation and with undetectable serum thyroglobulin levels. **Subjects & Methods:** A total of 1987 patients diagnosed with well differentiated thyroid carcinoma after total thyroidectomy were retrospectively evaluated. 56 patients who were candidate for I-131 ablation therapy but with no activity compatible with postoperative residual thyroid tissue on Tc-99m pertechnetate pinhole imaging and with also no residual thyroid tissue or probable metastatic lymph node on ultrasonography were included in the study. All patients included in the study had undetectable stimulated serum thyroglobulin (Tg) levels when TSH > 30 µIU/L after withdrawal of levothyroxine for 4 weeks. Anti-thyroglobulin antibody (TgAb) levels and time period between postoperative imaging studies (Tc-99m pertechnetate and ultrasound) and postablative I-131 WBS were recorded. Statistical significance of differences between groups was determined by Fisher's exact and Mann-Whitney U tests. Value of $P < 0.05$ was considered statistically significant. **Results:** In 43 of 56 (76.8%) patients, residual thyroid tissue was detected on postablative I-131 WBS. TgAb was positive in 15 of 56 (26.8%) patients. Detection of post-ablative residual thyroid tissue was not statistically related with positive TgAb. Interestingly, number of TgAb positive patients founded to be significantly higher in patients without postablative residual tissue than in

the other (Fisher's exact test; $P < 0.05$) in anticipation of general expectancy. Difference of the mean time period from postoperative imaging studies to postablative I-131 WBS between the patients with and without residual thyroid tissue was nonsignificant (Mann-Whitney U test; $P > 0.05$). **Conclusion:** Detection of postablative residual thyroid tissue in patients in whom no residual tissue was detected after thyroidectomy cannot be explained with high TgAb levels or long time period between postoperative imaging studies and I-131 ablation. So, we thought that I-131 ablation therapy should be applied in patients who are candidate for ablation therapy regarding histopathological and clinical features, even if they do not have residual thyroid tissue evidence scintigraphically, ultrasonographically and biochemically before ablation.

EP-0763

Retrospective comparison of thyroid and whole-body residence time of radioiodine in patients with differentiated thyroid carcinoma at initial ablative radioiodine therapy and follow-up whole-body scintigraphy after a short period of hypothyroidism or under rhTSH stimulation.

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Aim: Adjuvant radioiodine therapy (RIT) for differentiated thyroid carcinoma (DTC) can be performed with either endogenous TSH stimulation by thyroid hormone withdrawal or with exogenous stimulation by rhTSH. Existing publications report a lower thyroid and whole-body radiation exposure when using rhTSH. These publications compared rhTSH to a long levothyroxine withdrawal of up to 8 weeks. Our aim was to examine whether there is still a lower radiation exposure when using rhTSH compared to a shorter period of levothyroxine withdrawal. We analyzed the thyroid and whole-body residence time as a dosimetric value whose calculation is not dependent on the thyroid remnant mass. **Methods:** A retrospective study was performed on patients admitted for adjuvant radioiodine ablation for DTC to the University Hospital of Cologne over a five year period starting 2010. Dosimetric data of 366 patients was analyzed. 363 patients returned for a follow-up whole-body scintigraphy (WBS), those who received the scintigraphy in hypothyroidism ($n=27$) had a levothyroxine withdrawal of 5 weeks. **Results:** At RIT the median duration of thyroid hormone withdrawal was 18 days in the hypothyroid group and 25 days in the rhTSH group ($p < 0.01$). The thyroid residence time was 2.1 in hypothyroidism respectively 1.8 hours under rhTSH stimulation with no significant difference ($p=0.26$). The whole-body residence time in hypothyroidism was 11.9h, under rhTSH stimulation 11.8h ($p=0.64$). A subgroup analysis of hypothyroid patients with at least four weeks hypothyroidism showed a higher median TSH of 68.4mU/l compared to 44.1mU/l in all hypothyroid patients, this resulted in a longer thyroid and whole-body residence time of 2.5 hours respectively 21.3 hours and lower p-values of $p=0.10$ and $p=0.27$ but there still were no significant differences. At the WBS hypothyroid patients had a significant longer thyroid residence time of 1.1h compared

to rhTSH with 0.8h ($p<0.01$). The whole-body residence time was also longer in hypothyroidism, 13.6h respectively 11.5h ($p<0.01$). **Conclusion:** With a short period of thyroid hormone withdrawal there are no significant differences in thyroid and whole-body residence time compared to rhTSH stimulation at RIT. A subgroup analysis of patients who received RIT after a longer levothyroxine withdrawal showed a longer thyroid and whole-body residence time. This analysis still didn't show significant differences which might be due to the still shorter period of levothyroxine withdrawal compared to almost all previously reported studies. At the WBS hypothyroid patients had a long levothyroxine withdrawal and a significant longer thyroid and whole-body residence time.

EP-0764

Does T-staging affects Disease Specific Survival in Differentiated Thyroid Cancer?

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Aim: The aim of the study was to analyze the influence of different T-staging (patients with T1- and T2-stage versus T3- and T4-staged patients) on disease-specific survival (DSS) in patients with differentiated thyroid cancer (DTC). **Patients and Methods:** 569 DTC patients were treated with I-131 (RAI) in our institution from January 2001 to December 2010. DSS and its predicting factors were analyzed for the entire group as well as separately for different T-staged patients (Group I: 379 patients staged T1- and T2; Group II: 190 patients staged T3- and T4) by Kaplan-Meier's method. Statistical significance of differences was tested by Log rank test. **Results:** There were 378 (66.43%) T1- and T2-staged patients and 185 (32.51%) T3- and T4-staged patients, while T was not defined in 5 (0.88%) patients; 132 (23.2%) males and 437 (76.8%) females; 237 patients <45 years and 332 patients ≥45 years. Histologically, there were 57 (10%) follicular and 465 (81.7%) papillary carcinomas, while tumor type was not defined in 3 (0.53%) patients. Initial regional metastases were present in 202 (35.5%) patients. DSS was 96.5%; 93.5%; 87%, and 69.6% after 5, 10, 15 and 17 years, respectively influenced by: gender ($p=0.003$), age ($p=0.0001$), T-staging ($p=0.02$), initial metastases ($p=0.0001$), histology ($p=0.039$), type of initial treatment ($p=0.01$), while number of RAI course did not influence the survival ($p=0.087$). In T1-and T2-staged patients, DSS after 5, 10 and 15 years was 97.8%; 96.7% and 87.1%, respectively; it was significantly influenced by presence of initial metastases ($p=0.0001$), age ($p=0.001$), and histology ($p=0.021$), while type of initial therapy, gender and number of RAI courses had no significant influence ($p=0.296$, $p=0.597$, and $p=0.949$, respectively). In T3- and T4-staged patients, DSS after 5, 10 and 15 years was 92.8%; 87.4%; and 83.3%, respectively, influenced by gender ($p=0.001$), age ($p=0.002$), type of initial therapy ($p=0.031$), and number of RAI courses ($p=0.05$), while histology had no influence to DSS ($p=0.457$). **Conclusion:** In general, DTC patients have long DSS, influenced by several prognostic factors. Age is the only strong prognostic factor for survival in all T-staged patients. Gender, type of initial treatment and number

of RAI courses significantly influence DSS in T3- and T4-staged patients while histology and presence of initial metastases are strong predictors in T1- and T2- staged patients.

EP-0765

The Role Of BRAF^{V600E} Mutation In Predicting Clinical Response Of Radioiodine Therapy In Papillary Thyroid Carcinoma

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Purpose: BRAF^{V600E} mutation is the most common and specific oncogenic event in papillary thyroid carcinoma (PTC). Several preliminary studies showed that BRAF^{V600E} mutation was highly prevalent in radioiodine-refractory papillary thyroid cancer, and was associated with the loss of radioiodine uptake due to low expression or no expression of iodine-metabolizing genes. However, in clinical practice, the impact of BRAF^{V600E} mutation on the radioiodine therapy was uncertain. This study aimed to evaluate its impact on the clinical response to radioiodine therapy and establish its role in radioiodine therapy decision-making. **Methods:** This retrospective study included PTC patients without distant metastases who received total thyroidectomy with lymph node dissection, radioiodine therapy and thyroid-stimulating hormone (TSH) suppression between January 2012 to March 2016. Patients with "very low-risk" [T1aN0M0] or with positive serum Tg antibody (TgAb) were excluded from this study. Included patients were divided into two groups based on the BRAF mutation status. The association between clinicopathological characteristics and BRAF^{V600E} mutation was evaluated. After a median follow-up of 37 months, the clinical outcome between these two groups was also compared based on the ongoing risk stratification. **Results:** A total of 512 PTC patients without distant metastases were included, with positive BRAF mutation in 338 patients. No significant association was observed between BRAF mutation and clinicopathological characteristics except gender, tumor size and extrathyroidal extension. In comparison with non-mutation patients, more patients with BRAF mutation were presented with extrathyroidal extension ($p=0.001$) and large size ($p=0.001$). In addition, the proportion of male in positive mutation group was higher than that of negative group ($p=0.001$). In the overall cohort, the response to radioiodine therapy was not significantly associated with BRAF mutation ($p=0.321$), and the majority of patients achieved ER+IR at the end of follow-up (86.4% for positive-mutation group, 89.1% for negative-mutation group). A trend was observed that more patients had BIR+SIR (13.6%) in mutation group than in wild-type group (10.9%). Although for the patients with intermediate or high risk level, a worse outcome was observed with lower rate of ER+IR for positive mutation group compared with negative group; however, no significant difference in clinical outcome was observed between these two groups ($p=0.741$, $p=0.680$). **Conclusions:** The BRAF^{V600E} mutation status may not impact the clinical response to radioiodine therapy for PTC patients without distant metastases. **Financial support:** This study was supported by National Natural Science Foundation of China (Grant No. 81471692).

EP-0766**Red marrow Absorbed Dose in Patients Treated with I-131 for Differentiated Thyroid Cancer**

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Purpose: Red marrow (RM) is the most critical organ in therapies with radiopharmaceuticals, with a dose limiting organ of 200–300 cGy to avoid mielotoxicity. Although RM dosimetry is a complex dosimetry MIRD approach allows to study patient-specific RM dosimetry in patients undergoing I131 therapy for differentiated thyroid cancer (DTC). **Subjects and Methods:** A practical and suitable methodology is developed to assess RM absorbed doses D_{RM} . The results are presented for 13 DCT patients treated with I-131 activities between 2.22 and 6.29 GBq (all with Thyrogen) using a measure of activity in a blood sample taken 48 h after administration of I-131, and of 3 measures of external exposure rate at 1 meter of the patient at 24, 48, 72 h after the administration of I-131. Two source regions are considered: The whole body (TB) for penetrating radiation (p), and RM for non-penetrating radiation (np). The activity/litre of blood in the blood samples $[A_{BL}]$ is measured with NaI(Tl) 2.5"×2.5" well counter Canberra-2M2/2-X. The quotient $[A_{RM}]/[A_{BL}]$ value known as RMBLR allows know $[A_{RM}]$, here RMBLR was set to a fixed value of 0.36. An effective half life of 14.8 h is considered for the kinetics of RM. Exposure to 1 m of each patient is measured with environmental ion-chamber Victoreen-450. Using the conversion factor obtained in a previous calibration of 61 uSv/GBq the accumulated TB activity of each patient is determined. The $S_{np}(RM \downarrow RM)$ value (Gy g GBq⁻¹ d⁻¹) is obtained from current physical data of I-131 and from Eckerman-Stabin phantoms. The $S_p(RM \downarrow TB)$ value (mGy GBq⁻¹ d⁻¹) is obtained from a Coffey and Watson general relation linearly adjusted to the patient mass. **Results:** There is extensive variability in the estimated D_{RM} with a range of 52 to 1299 mGy: Ten patients (75%) have a D_{RM} lower than 279 mGy and only three (25%) have a D_{RM} higher than 279 mGy. The minimum value was 52 mGy and the maximum value was 1299 mGy. The worst excretion and the higher RM uptake and D_{RM} corresponded to a patient with metastases: 56 h, 60 MBq/l and 1299 mGy, respectively. The (p) contribution was 4–10 times the (np) contribution. **Conclusion:** MIRD methodology to assess RM absorbed-dose allows predict hematological toxicity in patients undergoing I131 therapy for DTC. Special considerations must be done for patients with red marrow pathology of bone metastasis.

EP-0767**Successful ablation with 131I in patients with differentiated thyroid cancer: can TNM staging system predict it?**

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Aim: to evaluate in differentiated thyroid cancer (DTC) the ability of TNM staging system to predict the complete response after

ablation with 131I. **Subjects and Methods:** This retrospective study included 47 patients (27 male, with median age of 47 yo) who, in the period 2015–2017, underwent total thyroidectomy and subsequent ablation with oral 3700 MBq of 131I. Patients were classified according to AJCC/TNM staging 7th edition as stage I before ablation (20 patients), II (26) and III (1). All of them underwent I131 whole body scans in 2 time points after ablation : 1) in day-7 and 2) in month-10 (±2) receiving oral 185 MBq of 131I. Stimulated thyroglobuline (ST) levels were obtained before ablation and in month-10 (±2). Incomplete response was considered when radioiodine scan was positive or ST at month-10 >1 ng/ml. **Results:** A successful ablation was seen in 41/47 patients: 17 in stage I and 24 in stage II. An incomplete response was showed by the 6 remaining patients: 3 in stage I, 2 in stage II and 1 in stage III. No statistically significant association was observed between stages and successful ablation ($p>0.05$). On the other hand, an increased ST level (>1 ng/ml) could be associated with a higher risk of no ablation (5 of 7/47 patients). **Conclusion:** In our study TNM staging system was not a good predictor of successful radioiodine ablation but high ST levels could be a risk factor for incomplete response. A larger sample size is required to increase precision when estimating association between successful radioiodine ablation and TNM staging system or baseline ST levels.

EP-0768**Low activity treatment with ¹³¹I in differentiated thyroid cancer**

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Objective: Our aim was to review the therapeutic effectiveness of low activity ablation with ¹³¹I in low-risk differentiated thyroid cancer (DTC) and the relationship between thyroglobulin levels and persistence of thyroid remnants after whole body scintigraphy annual control. **Material and Method:** Retrospective study of 29 patients (20 women), mean age 45.8 years, with low risk DTC treated with low activity. Post-ablation distribution and control diagnosis was performed after stimulation with rhTSH. Thyroglobulin (Tg) and basal anti-thyroglobulin antibodies (AntiTg) were monitored 24 and 72h post-stimulus / after stimulation. **Results:** 29 patients, treated with an average activity of 28.7mCi. The average time between surgery and treatment was 4.24 months, between treatment and scintigraphic control was 12.17 months. All the patients presented thyroid remnants in a post-ablation distribution scan, but only 8/29 associated thyroid remnants in the control. The average baseline Tg before treatment was 1.41 ng/mL (<0.04–8.55) and at 72h post-stimulation 11.52 ng/mL (<0.2–128), presenting only two patient AntiTg positive, who were excluded of the Tgs rates. The average post-ablation baseline Tg was 0.25 ng/mL (<0.04–1.83) and 72h post-stimulation 1.87 ng/mL (<0.04–22.36). In patients with thyroid remnants in the control, the baseline Tg-media pre-ablation was 3.31 ng/mL (0.2–8.55) and 72h from 28.75 ng/mL (0.56–128). In the control the baseline Tg was 0.56 ng/mL (<0.02–1.83) and at 72h 5.7 ng/mL (0.09–22.36). In patients without thyroid rem-

nants in the control, the baseline Tg-media pre-ablation was 0.94 ng/mL (<0.04–5.1) and at 72h it was 6.35 ng/mL (<0.2–35.5). In the control the baseline Tg was 0.15 ng/mL (<0.04–0.97) and at 72h 0.57 ng/mL (<0.04–4.87). The effectiveness of ablation with low activity was 72.4% for elimination of thyroid remains. The mean Tg of patients with thyroid remnants showed statistically significant differences with respect to those who did not (p : 0.003 in Tg-basal preablation). **Conclusion:** In our low risk DTC series we found highly effective ablations with low activity for elimination of thyroid remnants, and that higher Tgs imply a higher probability of persistence of remains. Larger series are needed to calculate the cutoff point of significant Tg.

EP-0769

Differentiated Thyroid Microcarcinoma: Prognostic factors

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Aim: The aim of the present study was to evaluate clinical and histopathological prognostic factors for differentiated thyroid microcarcinoma (DTMC). **Materials and Methods:** We retrospectively analyzed the data of 58 patients with DTMC who were followed up in the Nuclear Medicine department between 2000 and 2011 with a mean follow-up time of 7.7 years ($\pm$ 3.27 years). We evaluated the following histopathological factors and their impact on recurrence/persistence of disease: Sex, histological type, lymph node metastases (LNM), multifocality and presence of distant metastases. **Results:** The mean age at diagnosis was 44 years and the sex ratio was 0.2 with a female predominance. DTMC was revealed by goiter in 43.1% of patients and was incidentally discovered in 3.4% of cases only. All patients received total thyroidectomy followed by iodine-131 therapy. Lymph node dissection was performed in 38 patients (65.5%). Our patients received an average dose of 274 mCi ($\pm$ 153 mCi) of iodine-131, however higher doses up to 800 mCi were required in case of lymph node involvement or distant metastasis. The most common subtype was the classical papillary thyroid carcinoma (82.8%). The other subtypes of papillary thyroid carcinoma found were follicular variant (8.62%), oncocytic variant (3.45%) and trabecular variant (1.72%). No one presented a vascular invasion. Complete remission of the disease was achieved in 84.5% of cases. Lymph node recurrence, locoregional persistence of DTMC and bone metastasis was noted respectively in 1.72%, 12% and 1.72% of patients. The progression free survival (PFS) 76.3% at ten years. The cox regression multivariate analysis showed that presence of LNM (p =0.01) and distant metastases at diagnosis (p =0.01) were predictive of recurrence and persistence of disease. Progression free survival at ten years was respectively 50% and 100% in the presence of LNM and in its absence with a statistically significant difference (p =0.01). **Conclusion:** In our study, we found that lymph node metastases and distant metastases are correlated with less favorable outcomes in patients with DTMC despite maximal surgical and

isotopic treatment. However, sex, histopathological types and multifocality do not seem to have an impact on the prognosis of this disease.

EP-0770

Apatinib therapy of medullary thyroid carcinoma metastasis: one case report

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A 23-years-old male patient with repeated diarrhea, cough, asthma, and left neck mass came to our department for PET-CT imaging. Besides low ^{18}F -FDG uptake in thyroid lesion, enlarged bilateral neck and upper-mediastinal lymph nodes displayed increased ^{18}F -FDG accumulation ($\text{SUV}_{\text{max}}=2.7$) and pulmonary multiple nodes (long diameter ranging from 0.4 to 0.8 cm) demonstrated low ^{18}F -FDG uptake ($\text{SUV}_{\text{max}}=0.9$). Laboratory results revealed increased level of calcitonin (18040 ng/L). Medullary thyroid carcinoma with bilateral neck and upper-mediastinal lymph node metastasis was diagnosed and confirmed by postoperative pathology. Surgery was the first choice for MTC. However, MTC tends to recurrence and metastasis and therapeutic effect of chemotherapy was limited. Chest CT scan was performed during follow-up three months after operation and revealed disease progression. It demonstrated increasing number of pulmonary nodes and enlarged mediastinal lymph node with significant calcitonin increase. It was urgent for systemic regimen determination. Vascular endothelial growth factor (VEGFR-2) was reported to be over expressed in MTC and metastatic lesions. Apatinib, a small molecular vascular endothelial growth factor tyrosine kinase inhibitors, has been proved to be effective in clinical trial in the treatment of stomach cancer in China, and Apatinib therapy was adopted to this patient at dose of 500 mg each day. Chest CT scan was performed regularly at 1, 3, 6, 12 months from the start of Apatinib therapy. Partial response (PR) was reached based on significant decrease and shrinkage of metastatic calcitonin level (from 63040 ng/L to 13410 ng/L). Possible side effects such as Hand Foot Skin Reaction (HFSR) and pulmonary fungal infection with cavity formation were noted. From this case, we found that Apatinib, as one VEGFR-2 targeted pharmaceutical, was potential for the treatment of MTC and metastasis.

EP-0771

Comparison of the effectiveness of radioiodine treatment in patients with differentiated thyroid cancer with low-intermediate risk

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Aim: Radioiodine ablation after thyroidectomy is associated with longer survival in patients with intermediate risk of differentiated thyroid cancer DTC. The objective of this study was to compare the effectiveness of different doses. **Subjects and Methods:** A retrospective observational study was conducted from

January 2014 to December 2016, at Ramón y Cajal University Hospital, of 150 patients with DTC (T1-T3N0NxM0, T1-T3N1M0). The patients were divided in two groups: -The first group without lymph node involvement N0Nx: 91 patients, of which 18 treated with a low dose of 1.1-2.9 GBq of ¹³¹I and 73 with an average dose of 3.7 GBq. -The second group with lymph node involvement N1: 59 patients, of which 37 treated with an average dose of 3.7 GBq of ¹³¹I and 22 with a high dose of 5.5 GBq. All patients underwent a total thyroidectomy with or without lymphatic dissection. The response to treatment was evaluated one year after treatment with ¹³¹I, considering a complete response when TG thyroglobulin was less than 1 ng / ml (after stimulation with recombinant TSHr), antiTG antibody <20 IU and negative total body scan. Patients with thyroglobulin preablation > 100 ng / ml were excluded from the study. **Results:** We studied 44 men (29%) and 106 women (71%), 11 follicular DTC (7%) and 139 papillary DTC (93%), age range from 8 to 77 years. The preablation of TG levels (median) were: 2.58 ng / ml in patients with low doses and N0. 2.07 ng / ml with medium dose and N0. 5.02 ng / ml with medium doses and N1. 1.79 ng / ml with high doses and N1. One year after treatment with ¹³¹I, within the group N0: There was an excellent response in 16/18 (88%) patients with low doses and in 67/73 (94%) of medium doses. In the other group N1: in 35/37 (94%) of the average dose and in 23/25 (94%) of high dose, $p > 0.05$ not significant, for the two groups. Anti-Tg levels of ac are not different in medium and high doses. **Conclusion:** Low and medium doses, in patients with CDT free of metastasis, are sufficient and effective as ablative treatment after thyroidectomy and have less cervical discomfort, sialadenitis or gastritis. Although it requires long-term evolutionary studies, the evaluation of relapses and / or second tumors.

EP-0772

The evolution of dosimetry in the ablation of residuals in Differentiated Thyroid Cancer

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Purpose: We want to analyze follow-up(FU) in patients treated with ¹³¹I for Differentiated Thyroid Cancer in the ablation of the residuals using personalized activity to understand if some approaches could be modernized. **Subjects and Methods:** We consider 334 patients with DTC from January 2009 until December 2012 and FU until April 2018. For 48 we have no FU information. We calculated the administering activity according to the DTC Italian Guidelines : maximum uptake at 24° h and residuals volume by a integrated scintigraphic - ultrasound imaging. After treatment we made Whole Body Scintigraphic (WBS) image to compare the treated volume and to confirm the effective dose to the residuals. We made FU with a WB image in the first 6 months and then ultrasound image and blood tests, considering ablated if Tg and ABTg value are undetectable or decreasing and scintigraphic image are clear. **Results:** In 286 studies we found that 230 submitted to a single treatment (ST)(80%),

meanwhile the restant 56 (20%) submitted multiple treatment (MT) (36 a second one (64%), 20 multiple (36%)). Staging are collected in table 1-2-3-4. In ST, 125 (54%) received less than 300 Gy to the thyroid (mean 148.7 Gy, median 138.13 Gy, range 17-296 Gy). 105 pts (46%) received more (mean 577.3 Gy, median 437.5 Gy, range 301-2624). In MT, in the first one 29 (52%) received less than 300 Gy (mean 157 Gy, median 176.6 Gy, range 10-299 Gy) , meanwhile 27 (48%) received more (mean 701.1 Gy, median 495.9 Gy, range 324-3679 Gy). For those MT with more, we have 17 (68%) with papillary classical variant, 3 (12%) papillary follicular variant, 2 (8%) follicular and 3 (12%) tall cells or Hurtle. These patients had inferior WBS post volume (mean -85%, range -390%-87%). **Conclusion:** we thought that it is not correct to skip dosimetry in case of ablation of residuals in DTC: it is fundamental for evaluating the correct activity to administer. A correct volume evaluation is the first step, by the use of TC or ¹²⁴Pet. The next step is pre and after volume difference between to have best control on patient FU.

EP-0773

Low dose radioiodine activity for ablation after thyroidectomy in patients with differentiated thyroid carcinoma

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Objective: To evaluate the response after one and two years of ablative treatment with low doses of ¹³¹I (30mCi/1110MBq) in Differentiated Thyroid Cancer. **Materials and Methods:** Retrospective observational study between September 2014 and February 2017 of 39 patients (37 women and 2 men), age range 25-72 years old with an average age of 49.6 years. It includes patients who have undergone surgery with total thyroidectomy with or without associated lymph node dissection (23 TT and 16 TT + VC), prior to ablation. Histologically, there were 36 papillary carcinomas, 2 follicular carcinomas and 1 mixed follicular-papillary pattern. Patients were initially classified according to TNM 7th Edition (T1-T3 N0-N1a Mx-M0) and risk of recurrence/persistence ATA 2015 classification (36 patients low and 3 intermediate risk). The response to treatment was assessed according to a dynamic stratification risk of ATA 2015 classification for Total Body Scan (TBS) with ¹³¹I, cervical ultrasound and hormone levels (thyroglobulin and anti-thyroglobulin antibodies). All patients received an ablative dose of 30mCi/1110MBq with a hospital stay of approximately 6.5 hours with dosimetry hospital discharge less than 40mSv/hr at 50cm. **Results:** In the annual/biannual follow-up, 94.87% were found to have excellent response (37 patients), with an undetermined response in 5.13% (2 patients). We evaluated the excellent response as TBS and cervical ultrasound negative, undetectable thyroglobulin and negative or declining anti-thyroglobulin antibodies. The indeterminate response was given, in both patients, by elevated thyroglobulin and anti-thyroglobulin antibodies, but in descent with normal cervical ultrasound, no patient during follow-up required additional doses of ¹³¹I therapy. **Conclusions:** Ablative treatment at low doses of 30 mCi of ¹³¹I of Differentiated Thyroid

Cancer in patients with low and intermediate risk provides a high rate of effectiveness and a high percentage of excellent response. It is essential to carefully select in patients evaluating clinical, radiological, histological, molecular and biochemical data prior to the administration of the treatment.

EP-0774

Occurrence of TENIS syndrome in papillary thyroid carcinomas with tall cell variant

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Introduction: There are several variants of papillary thyroid carcinomas (PTC) with different histological patterns, some believed to be more aggressive than classical PTC. The most common of these aggressive variants is the tall cell variant (TCV). We report two cases of TCV variant of PTC showing high thyroglobulin levels with negative iodine scan after initial therapy. **Subjects**

and Methods: We retrospectively reviewed clinical records of the two patients. We analyzed clinical outcomes and thyroglobulin rate as well as imaging findings after radio-iodine therapy.

Results: Our patients were 33 and 40 years old females, who underwent total thyroidectomy with bilateral neck dissection for malignant thyroid nodules. Histopathology exam revealed a PTC with TCV infiltrating the thyroid parenchyma and the thyroid capsule associated to macroscopic extra thyroid extension and nodal metastases. The two patients were referred for RAI therapy. The initial post therapeutic whole body scan showed cervical uptake with high thyroglobulin levels (36 and 20 ng/ml respectively). A negative iodine scan with persistent elevated thyroglobulin (>10 ng/ml under stimulation) occurred after ablative dose of 200 mCi I131. Morphological exams were negative suggesting biological residual disease. The first case showed progression to RAI refractory lung metastases. She was dead after 4 years of follow-up. The second patient had better prognosis with a remission after cumulative dose of 1400 mCi and under L-thyroxin suppressive therapy. **Conclusion:** TCV is a high-risk PTC that warrants more intensive treatment and close follow-up strategies. Our two cases showed elevated thyroglobulin with negative post therapeutic iodine scan. In such cases, The use of other imaging modalities like FDG-PET scan is needed to detect RAI refractory disease implicating a worse prognosis.

EP-0775

Primary Papillary Thyroid Carcinoma as an Incidental Finding in Branchial Cleft Cyst

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Branchial cleft cysts are commonly occurring congenital anomalies in pediatric otorhinolaryngology, but papillary carcinomas

arising from them are rare. Here we present a case of a 16-year-old girl, which was referred to surgery because of lateral neck mass on the right neck side, palpable in the last three months prior examination. There was no anamnestic history of neck irradiation or trauma. Neck ultrasound revealed a 2.9 cm mixed cystic and solid mass in the right lateral aspect of the neck, and fine needle aspiration cytology was suggestive of a cystic lesion, without neoplastic cells. Preoperatively, papillary carcinoma arising from a branchial cleft cyst was not in the differential diagnoses. After the patient underwent cyst excision, histopathologic examination of the 3.7 cm cystic mass demonstrated the presence of papillary thyroid carcinoma with randomly oriented papillae with ground glass nuclei associated in follicles and psammoma bodies present, and collapsed pseudocystic space partially lined with neoplastic tissue with psammoma bodies. There was no normal thyroid tissue adjacent to the focus of papillary carcinoma in the specimen. The non-neoplastic epithelium of the cyst was typical for branchial cleft cyst. Right to the cyst, a metastatic lymph node was found. Therefore, a total thyroidectomy with region VI neck dissection was followed, which found normal thyroid gland and lymph node tissue. On follow up neck ultrasound, metastatic cervical lymph nodes were found in region II and III on the right neck side, region I and region IIA on the left neck side. The neck dissection was followed by radioiodine treatment. In conclusion, the surgeon must be cautioned by the possibility of finding primary papillary carcinoma in the branchial cleft cyst.

EP-0776

Parathyroid function alteration after thyroidectomy and ¹³¹I treatment: a clinical analysis concerning the influence of radionuclide therapy

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Introduction: Radioiodine ablation of thyroid tissue remains an important treatment for patients with differentiated thyroid carcinoma after thyroidectomy. Some reports have indicated thyroidectomy sometimes may impair parathyroid function and wonder how parathyroid function changes after ¹³¹I therapy. This study is to explore the influence of operation and ¹³¹I therapy on parathyroid function. **Methods:** A retrospective cohort study was undertaken including patients undergoing ¹³¹I therapy between 2016 and 2017 in our department. 950 patients, age from 18 to 80, were assessed for eligibility in the study. The inclusion criteria for this study were: (i) postoperative total thyroidectomy, (ii) pathology were differentiated thyroid cancer and conforming to indications of ¹³¹I therapy. Finally, 78 patients were enrolled. 27 patients were men and 51 were women. The median age was 45.99±12.19 (range, 18-72) years. The main outcome data observed were: (i) pre/postoperative calcium and parathyroid hormone (PTH) levels, (ii) calcium and PTH levels before iodine treatment and 1 month or 4 months later (iii) 24h-thyroid ¹³¹I absorption rate. The range of normal values for PTH was 15 to 65pg/dl. Hypocalcaemia was defined as <2.10mmol/l, hypoparathyroidism as <15pg/ml. The PTH levels and calcium of preoperative were compared with post-

operative and 4 months after the treatment of ^{131}I . Compared the PTH levels and calcium of postoperative with 24h-thyroid ^{131}I absorption rate to explore if they have a connection. In addition, PTH levels of patients with high rate (group 1, 24h-thyroid ^{131}I absorption > 2%) after surgery were compared to low rate patients (group 2, 24h-thyroid ^{131}I absorption ≤ 2%). **Results:** 1. There is a significant statistical differences between the pre- and post-operative groups in both calcium and PTH values (both $p < 0.01$, U-test). No significant difference was found between the calcium and PTH levels before iodine treatment and 1, 4 months later ($p > 0.01$, U-test). The different data show that surgery can cause a transient reduction of PTH with hypocalcemia. 2. Concerning the PTH levels and 24h-thyroid ^{131}I absorption rate there was no statistically significant difference between group 1 and group 2 ($p > 0.01$, U-test). The data show ^{131}I treatment has no significant effect on PTH and calcium. **Conclusions:** Total thyroidectomy can lead to transient hyperparathyroidism, and iodine treatment has no significant effect on parathyroid function.

EP-0777

Pericardial Uptake On Radioactive Iodine Therapy Whole Body Scan- An Unusual Case

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Introduction: We report an unusual case of pericardial uptake on ^{131}I whole body scan following radioactive iodine (RAI) adjuvant therapy. This is a rare finding, the second in our department in the last thirty years. While both cases have been attributed to hypothyroidism, the emphasis on the use of Single-photon emission computed tomography (SPECT/CT) should be stressed to avoid confusion with possible pulmonary metastases. **Subjects and Methods:** We report the case of a 50 year old female who presented post-total thyroidectomy for follicular variant of papillary thyroid cancer. Prior to administration of RAI, thyroid hormone replacement was withdrawn for 4 weeks and biochemistry showed an elevated TSH at 90.97 mIU/L. An initial 2 mCi (74 MBq) RAI diagnostic whole-body diagnostic scan showed uptake in the thyroid bed and a left level III lymph node. **Results:** A month later, 150 mCi (5550 MBq) of RAI was administered for adjuvant therapy. Patient had a whole-body therapy scan 72 hours following therapy administration and prior to discharge. The scan showed the same uptake as the diagnostic pre-therapy scan as well as an unusual mediastinal uptake. Single-photon emission computed tomography (SPECT/CT) localized this unusual mediastinal uptake to the pericardium. A cardiac Echocardiography done two weeks after the adjuvant RAI therapy confirmed the pericardial effusion but patient remained asymptomatic and had no other comorbidities. **Conclusion:** This is the second case in our department in over 30 years of practice that demonstrates the rare possibility of pericardial effusion secondary to thyroxine withdrawal-related hypothyroidism. Tomographic (SPECT/CT) imaging of abnormal uptake in the left lower chest should always be done to minimize the potential for confusing a unilateral and small volume effusion for a pulmonary metastasis.

EP-55

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Preclinical and translational aspects -> Preclinical aspects -> Animal models and in-vitro studies

EP-0778

Engineering and Characterization of a Human Tumour Xenograft Mouse Model Heterogeneous for HER2 and EGFR to Assess Tumour Delivery of Bispecific Radioimmunoconjugates (bsRICs)

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Purpose/Introduction: Patients with HER2-positive breast cancer (BC) may be treated with trastuzumab, pertuzumab, or trastuzumab-emtansine. Despite improvements in survival, resistance to HER2-targeted therapies remains a major problem. One resistance mechanism is loss of HER2 and increased EGFR. We have developed bispecific radioimmunoconjugates (bsRICs) that link trastuzumab Fab (anti-HER2) to EGF through a 24-mer polyethylene glycol (PEG₂₄) spacer. These bsRICs labeled with ^{64}Cu enable PET of tumours displaying HER2 and EGFR and labeled with ^{177}Lu may be used for radioimmunotherapy (RIT). Our aim in this study was to engineer and characterize a novel tumour xenograft mouse model that is heterogeneous for HER2 and EGFR to assess the tumour delivery of these bsRICs. **Subjects and Methods:** Human tumour xenograft mouse models heterogeneous for HER2 or EGFR were established by s.c. inoculation of a mixture (70%/30%) of MDA-MB-468 (EGFR+/HER2-) human BC cells and SK-OV-3 (EGFR-/HER2+) human ovarian cancer cells in NOD-SCID mice. The percentage of each cell line was identified by the cell-doubling times in culture. Homogeneous tumours were generated by inoculation of only MDA-MB-468 or SK-OV-3 cells. At 6 weeks, tumours were excised and stained by immunofluorescence for HER2 using Alexa Fluor 488-trastuzumab or EGFR using Alexa Fluor 647-panitumumab. The presence of each cell type was further identified by flow cytometry. Immunohistochemical staining (IHC) were used to assess the spatial distribution of HER2 and EGFR. MicroPET/CT was performed in NOD-SCID mice with heterogeneous tumours at 24 h p.i. of ^{64}Cu -bsRICs. Tumour and normal tissue uptake were quantified by biodistribution studies. **Results:** Confocal microscopy of heterogeneous tumours showed both red (EGFR-positive) and green (HER2-positive) immunofluorescence while homogeneous MDA-MB-468 and SK-OV-3 tumours contained only red or green cells, respectively. Flow cytometry of heterogeneous tumours showed two distinct peaks associated with HER2-positive or EGFR-positive cells, while homogeneous tumours showed a single peak. IHC staining of heterogeneous tumours revealed that HER2 and EGFR positivity were spatially complementary. MicroPET/CT at 24 h p.i. of ^{64}Cu -bsRICs successfully imaged heterogeneous tumours (tu-

mour uptake = 4.7 ± 1.0 % ID/g; tumour:blood ratio = 2.4 ± 0.2).
Discussion/Conclusion: A tumour xenograft model heterogeneous for HER2 and EGFR was engineered and characterized. To our knowledge, this is the first description of a tumour xenograft model engineered to express both HER2 and EGFR. The model would be very informative to compare the tumour delivery of bsRICs with monospecific agents that bind a single receptor.

EP-0779

Better therapeutic results after fractionated administration of ^{177}Lu -octreotate in mice bearing human neuroblastoma

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Background: Neuroblastoma (NB) is a neuroendocrine tumor and one of the most common cancer types in infants. NB is a heterogeneous cancer form, meaning that it has various characteristics and features, with diverse outcomes. High-risk NB has a 5-year survival rate of only 40-50%, demonstrating the need for new and improved treatment options for this patient group. Since NB overexpresses somatostatin receptors ^{177}Lu -octreotate has the potential to be a treatment option. Our previous in vitro studies indicated high and specific uptake of ^{177}Lu -octreotate in the human NB cell lines CLB-Bar and IMR-32. Furthermore, bio-distribution studies of ^{177}Lu -octreotate in NB-xenografted mice showed high uptake in tumor tissue in comparison with risk organs. These promising results encouraged studies on the anti-tumor effects of ^{177}Lu -octreotate therapy. The aim of this work was to study the anti-tumor effects after fractionated administration of ^{177}Lu -octreotate in nude mice bearing CLB-Bar. **Methods:** Nude BALB/c mice aged 5-6 weeks were injected with 2×10^6 CLB-Bar cells on the flank of the mice. Mice with tumors between 250 and 1100 mm³ were included in the study. Three groups of mice were i.v injected with totally 15 MBq ^{177}Lu -octreotate: given as 15 MBq x1, 7.5 MBq x2 with a 2-h interval or 5 MBq x3 with 1-h interval. The tumor volume was measured with a caliper twice a week after injection and the mice were killed when the tumor mass exceeded 10 % of the body weight. **Results:** The relative tumor volume 7 days post injection was 2.0, 1.7 and 1.3 for the 15 MBq x1, 7.5 MBq x2 and 5 MBq x3 group, respectively, corresponding mean survival time after study start was of 9.6, 14 and 16 days, respectively. **Conclusion:** The fractionated administration of ^{177}Lu -octreotate resulted in a better anti-tumor effect, with the most prominent results from 3x5 MBq. These results might be due to saturation of the somatostatin receptors for the higher amounts of ^{177}Lu -octreotate or upregulation of receptors from previous fractions. Further studies are needed to optimize the fractionation scheme and to evaluate the mechanisms behind the results.

EP-0780

The investigation of the spreading of a novel spontaneous high grade lymphoma from BALB/c mice with CLI and different imaging modalities

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Introduction: The baseline aim of the study was to investigate the spreading of Bc-DLFL.1 lymphoma in vivo and ex vivo with high resolution CLI (Cherenkov Luminescence Imaging) and other imaging modalities. Bc-DLFL.1 is a novel spontaneous high grade lymphoma from BALB/c mice which shows preferentially peritoneal distribution and propagate via the lymphatic vessels towards the mesenteric lymph nodes and the spleen. **Subjects and Methods:** First we compared the FDG uptake of the lymphoma cells and normal lymphocytes in vitro. The lymphoma cells were adjusted to 10^6 /recipients, and were injected intraperitoneally. After several day (1,2,4,5,6,9,11,13) of the injection we administered intravenous and in early stage (24-48 hour after lymphoma inoculation) also intraperitoneal FDG, or Ga-67 citrate to the mice. After the radiotracer injection we performed in vivo PET and SPECT/MRI and ex vivo CLI and autoradiography. For the anti-FITC immunohistochemistry detection CFSE-labeled lymphoma cells were adjusted to the recipients. The abnormal structures were verified histologically with hematoxylin-eosin (HE) staining and immunofluorescence. **Results:** We found that FDG uptake of lymphoma cells are 20-25 times higher than in normal lymphocytes. Most effective imaging method has varied among the different stages of the disease in our lymphoma-modell. In early stages with autoradiography (after the intraperitoneal injection of FDG) and CFSE-based immunohistochemical labeling we found the same: delineation of microscopic lymphoma clusters within the mesentery and along the gut wall. Despite that vivo CLI was not suitable for early detection, at more advanced stages CLI allowed accurate detection of FDG accumulation in tumors. We observed lymphoma foci accumulating FDG in the expected regions of adipose tissue along mesenteric veins, within enlarged mesenteric lymph nodes, in the omentum and also in the splenic hilus. In the late stage tumor-bearing mice (11-13 days after LI) with the combination of SPECT/MRI and ex vivo CLI we could clearly reveal lymphoma accumulation in the parathyroid lymph nodes, which were unnoticeable with MR imaging only. **Conclusion:** The CLI was capable of identifying 200-300 micrometer sized structures at the late stage of disease both with FDG and also with Ga67-citrate, which reveals the importance of CLI both in clinical and preclinical practice, to imaging radionuclides and therefore detect and emphasize tumorous tissues and to guide the surgical resection. Beside CLI with other imaging modalities we can detect the exact intraperitoneal spreading ways which contributes the understanding of tumor cell migration via the lymphatics and peritoneal cavity.

EP-0781

Development of [^{11}C]leucine PET as a tool to measure brain protein synthesis in rats.

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Alzheimer's disease (AD) is characterised by severe alterations of cognitive function and memory. Memory consolidation depends on protein synthesis which promotes neuronal plasticity and new connections and all are altered in AD^{1,2}. [¹¹C]-Leucine is a good tracer to measure protein synthesis rate (PSR) by PET because of its single metabolic pathway. The aim of this study is to model PSR in rats and validate an image-derived input function (IDIF), which should enable the future evaluation of PSR in the TgF344-AD rat model of AD. All experiments were ethically reviewed and performed in accordance with the UK Animals (Scientific Procedures) Act 1986 and the GSK Policy on the Care, Welfare and Treatment of Animals. Male Wistar rats (n=6) were scanned using PET-CT for 60min following [¹¹C]-leucine administration (tail vein i.v, 30–60MBq). Brain and heart-ventricular time-activity curves were extracted from the PET images. Online measurement of blood radioactivity was performed using a Twilite™ detector; blood samples were also taken at 2, 5, 10, 20, 30, 40 and 60min for γ -counting. Brain activity was also evaluated by γ -counting at the end of the scan. The [¹¹C]-leucine time-activity curve (TAC) over the heart ventricle peaked at 22s post-injection (SUV=7.7 $\pm$ 1.61), followed by a rapid wash-out which then plateaued (7–20min, SUV=0.67 $\pm$ 0.11) followed by a slight increase between 20 and 60min (SUV=0.82 $\pm$ 0.06) post-injection. Whole-blood and plasma γ -counting confirmed these observations. The ratio of free/protein-bound [¹¹C]-leucine decreased with time. [¹¹C]-Leucine uptake in various brain regions showed similar pharmacokinetics, displaying a rapid uptake within the first 5 minutes post-injection and reaching a plateau from 10 minutes onwards. PET analysis and γ -counting of different brain regions were in good agreement revealing the highest [¹¹C]-leucine uptake in cerebellum and cortical regions (SUV=0.62 $\pm$ 0.07), intermediate in hippocampus (SUV=0.59 $\pm$ 0.06) and thalamus (SUV=0.54 $\pm$ 0.06) and the lowest in the striatum (SUV=0.51 $\pm$ 0.03). The biodistribution and pharmacokinetics of [¹¹C]-leucine in blood, plasma and brain observed here are similar to those obtained previously in rats³ and young adult men⁴. We observed good agreement between γ -counting and heart-ventricular values as measured by PET, supporting the feasibility of modelling an IDIF for [¹¹C]-leucine, which we are currently performing. We will then proceed with measuring PSR longitudinally in the TgF344-AD transgenic rat model of AD. **1.** Ma T. *et al.* (2013). *Nat Neurosci*.16:1299–1305. **2.** Garcia-Esparcia P. *et al.* (2017). *Am J Neurodegener Dis*.6:15–25. **3.** Lauenstein L. *et al.* (1987). *Neurosurg Rev*.10:147–150. **4.** Bishu S. *et al.* (2008). *J Cereb Blood Flow Metab*.28:1502–1513.

EP-0782

SPECT Imaging of Atherosclerotic Plaques using the SSTR2 Antagonist ¹¹¹In-JR11

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Introduction: Atherosclerosis is a lipid-driven inflammatory

disease leading to fatty plaque formation in the arteries. Early detection of atherosclerosis and plaque monitoring following intervention remains a major challenge. Macrophages are attractive imaging targets for the detection of atherosclerosis, as they are involved in all stages of disease. Somatostatin Subtype Receptor 2 (SSTR2) is expressed on macrophages and has proven a promising imaging target in recent studies using the receptor agonist [DOTA,Tyr³]-octreotate (DOTATATE). [DOTA]-JR11 is a receptor antagonist with a reported ~10x higher tumour binding compared to DOTATATE, and as such holds potential to improve inflammation imaging of plaque as well. The aim of this study was to assess the feasibility of antagonist-mediated SSTR2 imaging of macrophages in atherosclerotic plaques using ¹¹¹In-JR11 Single Photon Emission Computed Tomography/Computed Tomography (SPECT/CT) in a mouse model of atherosclerosis. **Methods:** Atherosclerotic mice (ApoE^{-/-}), fed an atherogenic diet up to 20 weeks (n=8), were imaged by SPECT/CT 2 hours post injection of ¹¹¹In-JR11 (~200 pmol, ~50 MBq). **In vivo** imaging results were validated by **ex vivo** imaging and **ex vivo** autoradiography (ARG) of excised arteries. Oil Red O (ORO) staining of lipids was used to validate plaque presence in the arteries. Presence of macrophages and expression of SSTR2 in excised aortas was evaluated by immunohistochemical analysis of tissue sections. Specific binding of the tracer to the target was assessed via **in vitro** ARG on human Carotid Endarterectomy (CEA) sections. **Results:** **In vivo** SPECT/CT, **ex vivo** SPECT/CT, and **ex vivo** ARG showed high tracer uptake in the aortic arch, and ORO staining confirmed plaque build-up inside the aortic arch of all mice. Tracer uptake in the thymus complicated **in vivo** visualization of arch signal. **In vitro** ARG performed on human CEA sections confirmed specific tracer binding, while immunohistochemistry visualized macrophage and SSTR2 presence inside the plaques. **Conclusion:** Our study shows promising results for plaque imaging using ¹¹¹In-JR11, yet **in vivo** imaging in mice is significantly hampered by thymal uptake of ¹¹¹In-JR11. As the thymus poses no problem for human imaging, current imaging studies are performed on mice in which the thymus is removed before scanning, to underline the high potential of **in vivo** plaque imaging using ¹¹¹In-JR11.

EP-0783

In Vivo Imaging Of Diabetic Retinopathy Using (68)Ga-Labeled Peptides

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Introduction: Angiogenesis is the process of new blood vessel formation. One can be observed physiologically in wound healing and embryogenesis, but it has discovered in several human pathological disorders such as tumors, coronary artery disease or retinopathia diabetica. The asparagine-glycine-arginine (NGR) peptide sequence known as a possible biomarker of

angiogenesis. Previous studies have shown that the NGR peptides are specifically bind to APN/CD13 molecules expressed by tumors. Ga-68 labeled NGR peptides allowed the preclinical PET conducted non-invasive imaging of neo-angiogenic processes.

Methods: The cyclic NGR peptide was prepared successfully by solid phase peptide synthesis. The NGR derivate was conjugated with NOTA macrocyclic chelator. The complete ligand was purified by RP-HPLC and then was lyophilized. The product was characterized by ESI-MS and ¹H-NMR. Left eye of rats (Fischer-344) (n = 10) were ligated surgically using a cannula guided loop. Ischemia can be induced by tightening the noose (90 min.) furthermore it can be terminated by loosening it. The upper mentioned surgical procedure suitable to develop lesions that occur during reperfusion. One day after ischemia-reperfusion (I/R) induction labeled radioligand (15 MBq in 150 µl saline) was injected intravenously (lateral tail vein) to surgical and non-surgical control (n = 5) groups to determine the baseline. After the appropriate incubation time (90 min.) the radiopharmaceutical distribution was determined in vivo using PET (MiniPET-II small animal PET scanner) and CT (Micro-CT). To evaluate the changes of I/R related uptakes, the rats were scanned at 3, 5, 7 and 10 days after the surgery. **Results:** NGR peptides conjugation with NOTA chelator was prepared successfully. ⁶⁸Ga-NOTA-c(NGR) was produced with high specific activity (5.13–5.92 GBq/µmol) and with excellent radiochemical purity (95%<), at all cases. The quantitate labeling range was determined. It was over 10 µmol/dm³. In the left bulbus of the surgical group significantly (p≤0.05) higher tracer uptake was observed (SUV mean) compared to the control (internal control) and non-surgical control group. Kinetic studies showed that compared to the baseline value, the tracer uptake reaching its peak on day 7. Western blot analysis confirmed the presence of neo-angiogenic markers (APN / CD13).

Conclusion: The above outlined application suitable for study in vivo I/R mediated receptor expression in Diabetic Retinopathy rat model. The kinetic analysis performed in this study will be useful for the quantitative evaluation of ⁶⁸Ga-NOTA-c(NGR) binding to (APN / CD13) in angiogenic tissues. Thus, creates an opportunity to develop modern diagnostic methods in various pathological processes.

EP-0784

Radiolabelling And Biodistribution Studies In An Open Wound Animal Model Of Negatively Charged Polystyrene Microspheres

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PolyHeal®Micro, composed by Negatively Charged Microspheres (NCMs), is a device that promotes healing. It is indicated for the treatment of chronic and hard-to-heal wounds^[1]. The aim of this work was to radiolabel NCMs with ^{99m}Tc for biodistribution studies in an open wound animal model to confirm their lack of dermal absorption and demonstrate their safety.

Materials and Methods: NCMs were radiolabeled with Sn-Cl₂-reduced ^{99m}Tc-pertechnetate in an oxygen-free atmosphere.

Colloids and radiolabeling yield were measured by ITLC-SG after centrifugation. Stability experiments were carried out in saline and human plasma for up to 24h; 0.1 mM DTPA was used for competition studies to define the specificity of the radiolabeling. An interescapular surgical wound was made in female Wistar rats (n=22) under anesthesia. ^{99m}Tc-NCMs (0.0175 mg/animal; 6.5±0.5 MBq) or free ^{99m}Tc-pertechnetate (control, 6.1±0.75 MBq) were placed in the wound and covered with a dressing. We analyzed a single dose model treated once (G1) to study dermal absorption; and a multiple dose model, treated daily for 11 days (G2) to analyze the activity of phagocytic system activity on NCMs. SPECT/CT imaging was carried out at 1,2,12 and 24 hours immediately after administration (G1) or starting on day 10 (G2). Quantification was carried out by drawing VOIs over CT images transferred to SPECT. At the end point animals were euthanized, organs/tissues extracted and radioactivity measured in a gamma counter, calculating the percentage of injected dose (%ID/organ). **Results:** NCMs showed a mean size of 5.18 µm and were negatively charged (-93 mV). Radiolabelling yield was >99% after optimization, with no colloids (0.6±0.4%), and stable until 24h in saline (92.2±3.6%) and plasma (97.3±2.5%). After DTPA challenge, 88.9±1.6% yield was obtained. SPECT/CT studies showed that more than 99% of ^{99m}Tc-NCMs remained in the wound area for at least 24h (G1 & G2). Most of the NCM were withdrawn with dressing removal (82.1±6.2%), and some NCM remained in the skin surrounding the wound (2.9±2.4%) on group 2. No activity in lymph nodes was found by *ex vivo* studies suggesting absence of phagocytosis. ^{99m}Tc-pertechnetate was absorbed as expected and found mainly in stomach and intestines. **Conclusions:** NCMs radiolabeling was found to be simple and stable. No systemic absorption was found on the wound as seen in SPECT/CT imaging either after single or multiple administrations of NCMs. There was no evidence of NCM accumulation in any organ, which could be associated with a NCM phagocytosis exerted by macrophages. J. WoundCare. 2013;22(3):144-55

EP-0785

Increased Radioiodine Uptake Induced By Combination Of Dabrafenib And Chidamide In Papillary Thyroid Cancer Harboring BRAF^{V600E} Mutation

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Objective: Accumulating evidence suggested that BRAF^{V600E} mutation significantly correlates with loss of radioiodine uptake and the histone deacetylation (HDAC) at the sodium/iodine symporter (NIS) promoter is an important mechanism in the silencing of NIS gene. Therefore, this manuscript aimed to evaluate whether inhibiting both BRAF^{V600E} mutation and HDAC process would produce strong expression of iodine-handling genes and proteins, further increase iodine uptake in BRAF^{V600E}-positive thyroid cancer cells. **Methods:** Three thyroid cancer cell lines were used in this study with two BRAF^{V600E}-positive cells (BCPAP and K1) and one BRAF^{V600E}-negative cell (FTC-133). The effects of BRAF^{V600E} inhibitor (Dabrafenib) /HDAC inhibitor (Chidamide) alone or in combination on the expression of iodine-handling

genes and proteins were investigated using real-time PCR, western blotting and immunofluorescent analysis. Then, radioiodine uptake of thyroid cells was also examined in vitro and vivo. The specific killing effect of these two inhibitors in combination with ^{131}I was investigated by clonogenic assay in vitro and was assessed by therapeutic experiment in vivo. **Results:** For BCPAP and K1, combination of these two inhibitors induced the most robust expression of iodine-handling genes and proteins including NIS, TSHR, TPOAb and Tg. After additional treatment of TSH, more NIS protein was localized in the cell membrane. Combined treatment induced 4.07-fold higher and 3.69-fold higher radioiodine uptake in BCPAP and K1 cells respectively compared with nontreated cells. With the additional incubation of TSH, iodine uptake was more robustly enhanced with 10.67-fold higher in BCPAP and 7.99-fold higher in K1, respectively. For clonogenic assay, the number of colonies was smallest in the group treated with combination of two inhibitors and ^{131}I , with 66.8% reduction in BCPAP and 61.3% reduction in K1, respectively. In vivo, the iodine uptake of tumor in experiment group was 2.81-fold higher than that in control group at 2 hours after injection. In addition, the combination of inhibitors and radioiodine therapy significantly inhibited the tumor growth and prolonged the median survival time (23 days vs. 34 days, $p < 0.05$). **Conclusions:** Simultaneous inhibition of BRAF^{V600E} mutation and HDAC induced a robust expression of iodine-handling genes and proteins in vitro and vivo in BRAF^{V600E}-positive thyroid cancer cells. Furthermore, the tumor growth was significantly inhibited by the combination of inhibitors and radioiodine therapy.

EP-0786

Nonclinical Evaluation Of [^{18}F]T-401, A Novel Pet Imaging Agent For Monoacylglycerol Lipase

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Introduction: Monoacylglycerol lipase (MAGL) is a cytosolic serine hydrolase that cleaves monoacylglycerols into fatty acids and is believed to be a target for novel treatments of CNS disorders related to the endocannabinoid system and neuroinflammation. We have recently developed (4R)-1-(3-(2-[^{18}F]fluoropyridin-3-yl)phenyl)-4-(4-(1,3-thiazol-2-ylcarbonyl)piperazin-1-yl)pyrrolidin-2-one ([^{18}F]T-401) as a novel, reversible, and selective PET imaging agent for MAGL. The aim of this study was to non-clinically examine the utility of [^{18}F]T-401 for PET measurements of in vivo occupancy of MAGL by a potential therapeutic agent in rat and monkey brains. **Methods:** In vitro binding of [^{18}F]T-401 in rat and monkey brain sections was assessed by autoradiography (ARG) in the absence and presence of JW642, a known MAGL inhibitor. PET imaging of rat and monkey brains was performed with [^{18}F]T-401 at baseline and after treatment with a single dose of unlabeled T-401 and JW642 to determine kinetic models for [^{18}F]T-401. Dose-dependent blockades of [^{18}F]T-401 binding by JW642 were also assayed by in vivo PET imaging of the monkey brains. **Results:** In ARG studies, [^{18}F]T-401 displayed a heterogeneous distribution, which was in agreement with lo-

calization of MAGL, and was blocked by co-incubation with an excess amount of JW642. PET scans of rat and monkey brains showed high uptake rates and fast and reversible kinetics of [^{18}F]T-401. Its distribution was consistent with in vitro ARG data. The radioactivity in the brain significantly decreased to a fairly uniform level among brain regions by pre-treatment with excess unlabeled T-401 (1 mg/kg, i.v.) and JW642 (1 mg/kg, i.v.). Regional time-activity curves over 120 min in monkeys were well described by a 2-tissue compartment model in consideration of radiotracer metabolism in the brain. This yielded reliable estimates of a regional distribution volume (VT). Baseline VT values in monkeys were ranked as high in the frontal cortex, striatum, and occipital cortex; medium in the cerebellum and hippocampus; and low in the pons. Pretreatment of monkeys with JW642 reduced VT values in a dose-dependent manner. **Conclusion:** Pharmacokinetics of [^{18}F]T-401 in rat and monkey brains was robustly described by a reversible binding model, which was also valid in quantifying the blockade of radiotracer binding by a MAGL inhibitor. These observations support the utility of [^{18}F]T-401 for PET assays of MAGL in healthy and diseased conditions and for in vivo evaluations of interactions between MAGL and candidate therapeutics.

EP-0787

Theranostic approach in ovarian cancer using Anti-MISRII radiolabeled antibodies

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Here, we assessed in preclinical models the possibility to use radiolabeled 16F12, a mouse monoclonal antibody (mAb) that targets the MISRII receptor, in a theranostic approach for small-volume ovarian peritoneal carcinomatosis, for instance after cytoreductive surgery. **Methods:** The 16F12 mAb was radiolabeled with beta (^{177}Lu) or alpha (^{213}Bi) particle emitters for therapeutic use, and with ^{89}Zr for positron emission tomography (PET) imaging after conjugation with DOTA-, DTPA- or DFO-conjugated, respectively. At day 13 post-xenograft, mice bearing intraperitoneal MISRII-positive AN3CA endometrial carcinoma cell tumor xenografts were treated by conventional intraperitoneal radioimmunotherapy (IP-RIT) with 10 MBq ^{177}Lu -16F12 or 12.9 MBq ^{213}Bi -16F12, or by brief intraperitoneal radioimmunotherapy (BIP-RIT) using 50 MBq ^{177}Lu -16F12 or 37 MBq ^{213}Bi -16F12. For BIP-RIT, 30 minutes after injection of high activities of radiolabeled mAbs, the peritoneal cavity was washed to remove the unbound radioactivity. The biodistribution of ^{177}Lu - and ^{213}Bi -16F12 mAbs was determined and then used for dose assessment. Hematological toxicity was also monitored. **Results:** Tumors were efficiently monitored and SPECT/CT (after BIP-RIT with ^{177}Lu -16F12) and PET/CT images (after injection of ^{89}Zr -16F12 in the tail vein) showed focal uptake at the tumor

site. IP-RIT with ^{177}Lu -16F12 was shown to be slightly more efficient in delaying tumor growth than IP-RIT with ^{213}Bi -16F12. Conversely, ^{213}Bi -16F12 was more efficient than ^{177}Lu -16F12 in BIP-RIT. The biodistribution analysis showed that the tumor-to-blood uptake ratio was significantly higher with BIP-RIT than with IP-RIT for both ^{213}Bi - and ^{177}Lu -16F12. Hematological toxicity was more pronounced with ^{177}Lu -16F12 than ^{213}Bi -16F12. **Conclusion:** Radiolabeled 16F12 could represent a new theranostic tool for small volume ovarian peritoneal carcinomatosis. Specifically, ^{213}Bi -16F12-based BIP-RIT could be proposed to selected patients as an alternative adjuvant treatment immediately after cytoreductive surgery while ^{177}Lu -16F12 would be more suitable for intravenous RIT. An anti-MISRII mAb is currently being used in a First in Human study, thus making radiolabeled anti-MISRII mAbs a realistic theranostic option for the clinic.

EP-0788

Alpha-Emitting Radiopharmaceutical for IP Therapy of Peritoneal Metastases: In Vitro Evaluation and Therapeutic Effects in a Murine Model

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Purpose: Radium-224 (^{224}Ra) labeled calcium carbonate (CaCO_3) microparticles have been developed with the intent to treat micrometastases located in the abdominal cavity. The microparticles act as carriers for the α -emitter ^{224}Ra and ensure high intraperitoneal (IP) retention of the radioactivity without cellular targeting. This novel α -therapy has a short action range in tissue and is designed to confine the radiation exposure to the IP cavity, treating both linings of the peritoneal surfaces as well as liquid volumes. The retention of radioactivity adsorbed on the surface of CaCO_3 microparticles was examined *in vitro* and *in vivo*. Therapeutic efficacy of the ^{224}Ra -microparticles was evaluated in a murine xenograft of an ascites presenting human cell line. **Materials and Methods:** The retention of ^{224}Ra and its daughter ^{212}Pb adsorbed on different amounts of CaCO_3 microparticles was evaluated over time both *in vitro* and *in vivo*. Immunodeficient athymic nude mice were used for the *in vivo* studies. For investigation of therapeutic effect, mice inoculated IP with human ovarian cancer cells ES-2 were used. The ES-2 cell line causes aggressive development of ascites. Varying amounts of ^{224}Ra -microparticles were administered IP (5–25 mg) with 10–25 kBq total activity per mice. The treatment was injected the day after cell inoculation. Survival was assessed. **Results:** The retention of ^{224}Ra and its daughter ^{212}Pb on CaCO_3 microparticles increased with increasing amounts of microparticles. This was observed both *in vitro* and in biodistribution studies in mice. The survival studies showed that free cationic ^{224}Ra (given as $^{224}\text{RaCl}_2$ solution) had a therapeutic index (ratio of median survival of treated mice versus control) of 1.8, whereas administration of ^{224}Ra -labeled CaCO_3 microparticles gave a therapeutic index (TI) up to 2.8. No strong correlation between microparticle amount and effect on survival in mice with IP xenografts were observed,

at the microparticle amounts tested. The highest amount (25 mg per mice) however, showed inferior survival (TI of 1.7). **Conclusion:** Efficient ^{224}Ra -labeling of CaCO_3 microparticles was achieved, with high retention of the radionuclide on the particles both *in vitro* and *in vivo*. Therapeutic studies showed superior survival when treating with IP injection of ^{224}Ra - CaCO_3 microparticle suspension compared to IP injection of free cationic ^{224}Ra solution. The data also indicate that high concentrations of particles may potentially reduce the antitumor activity of the ^{224}Ra - CaCO_3 -suspensions.

EP-0789

Near-infrared Photoimmunotherapy Targeting Pancreatic Cancer With Tissue Factor Antibody

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Purpose: Tissue Factor (TF) is a transmembrane protein and its overexpression is associated with increased tumor growth, tumor angiogenesis and metastatic potential in many malignancies, including pancreatic cancer. Near infrared photoimmunotherapy (NIR-PIT) is a new target-cell-specific cancer treatment that enables highly selective cell death after systemic administration of a photosensitizer-antibody conjugate followed by subsequent NIR light exposure. In this study, we describe the photoimmunotherapeutic effect induced by a rat IgG_{2b} anti-TF monoclonal antibody (anti-TF mAb), conjugated to the photosensitizer, Indocyanine green (ICG), in a TF-expressing BxPC-3 pancreatic cancer model. **Materials and Methods:** Specific binding of the anti-TF-ICG antibody to the TF-expressing BxPC-3 pancreatic cancer cell line was examined by fluorescence microscopy. NIR-PIT-induced cell death was determined by using cell viability imaging assay after exposure of the cells to NIR light. Anti-TF-ICG antibody accumulation in xenograft tumor was acquired in *in vivo* longitudinal fluorescence imaging. To conduct NIR-PIT, tumor-bearing mice were separated into 5 groups: (1) 100 μg of anti-TF-ICG i.v. administration followed by NIR light exposure (50 J/cm²) for two consecutive days (Day 1 and 2); (2) NIR light exposure (50 J/cm²) only for two consecutive days (Day 1 and 2); (3) 100 μg of anti-TF-ICG i.v. administration; (4) 100 μg of unlabeled anti-TF i.v. administration; (5) the untreated control. Biweekly tumor volume measurements, histopathological and immunohistochemical (IHC) analyses of tumors at 3 days post-administration of anti-TF-ICG antibody were performed to monitor the effect of treatments. **Results:** Dead cells were obviously seen with cell viability imaging assay. Tumor growth was inhibited by NIR-PIT and statistically significant difference of relative tumor volume ($P < 0.05$) were observed for 27 days after the treatment start date when compared with the other control groups. Tumors received NIR-PIT showed the evidence of necrotic cell death associated features on H&E staining and decreased cell proliferation marker Ki-67-positive cells on IHC

examination. **Conclusion:** The anti-TF-ICG antibody is suitable as a photosensitizer-antibody conjugate for NIR-PIT. Furthermore, NIR-PIT with the anti-TF-ICG antibody conjugate promises to open a new avenue for treatment of TF-expressing pancreatic cancer and that could be ultimately applicable in clinical use.

EP-0790

Targeting activated synovial fibroblasts using photodynamic therapy in experimental arthritis

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease affecting synovial joints. In RA activated synovial fibroblasts (SF) are actively contributing to the inflammation. SF are characterized by the expression of Fibroblast Activation Protein (FAP). Here, we investigated the potential of targeted photodynamic therapy (tPDT) using the anti-FAP antibody 28H1 to selectively kill activated synovial fibroblasts. **Methods:** To create our multimodal tPDT tracer, both ITC-DTPA and the photosensitizer IRDye700DX were conjugated to 28H1 (28H1-700DX). For tPDT, this tracer was exposed to 690 nm light to generate cytotoxic ROS. The tracer was tested *in vitro* with 3T3 fibroblasts stably transfected with FAP that were incubated with 6.67 pM 28H1-700DX or an irrelevant antibody-700DX control for 4 hours and exposed to 13.7 J/cm² light. Cell viability was measured using the CellTiter-Glo assay. For *in vivo* biodistribution (expressed as % injected dose per gram tissue (%ID/g)), 5 days after onset of antigen-induced arthritis (AIA) C57Bl6 mice were injected with [¹¹¹In]In-DTPA-28H1 with or without IRDye700DX. tPDT was assessed in arthritic mice injected at day 5 of AIA with 28H1-700DX or PBS and exposed to 50 or 90 J/cm² light 24h post injection. Joints were isolated at day 10 for histological analysis. **Results:** tPDT significantly reduced cell viability (89.27%±2.48% reduction compared to the control (p<0.001)) in 3T3-FAP cells but not in FAP-negative fibroblasts. Conjugating the anti-FAP antibody to 700DX (substitution ratio 3 IRDye700DX molecules per antibody) resulted in higher liver accumulation (27.06±0.95 %ID/g vs. control 6.08±0.42 %ID/g, p<0.001) and lower blood levels (5.32±0.36 %ID/g vs. control 12.72±0.80 %ID/g, p<0.001). 28H1-700DX accumulation in the arthritic joints was not significantly different compared to 28H1 without 700DX. Histological inflammation scores after tPDT were not significantly different in the treated groups compared to the controls. However, relative neutrophil levels correlated positively with inflammation scores and tPDT significantly reduced the slope of this correlation, indicating that tPDT reduces relative neutrophil levels, suggesting early treatment response and faster resolution of inflammation. **Conclusions:** We demonstrated FAP-mediated cell death using tPDT, suggesting FAP-based tPDT as a promising new tool in treating RA. Furthermore, we demonstrated that the addition of 700DX does not affect uptake in the inflamed knee joint. The contribution of neutrophils to the total inflammatory infiltrate decreases after tPDT, indicating changes in the inflammatory

process. Further experiments will further elucidate the potential of FAP-targeted PDT in treating arthritis.

EP-0791

Chronic mild stress does not affect ovariectomy-induced depressive-like behavior or changes in brain metabolism in female rats

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Introduction: The increased incidence of depression among post-menopausal women suggests that fluctuations in estrogen levels may be a risk factor for developing depression. Since not all post-menopausal women develop this psychiatric disorder, it is likely that an additional trigger is needed to induce depression in this population. We therefore investigated the effect of chronic mild stress (CMS) on depressive-like behaviour and alterations in brain metabolism in ovariectomized (OVX) rats, lacking ovarian estrogen production. **Methods:** OVX rats were divided into two treatment groups, placebo (VEH) and estradiol replacement (EST), and further divided into two condition groups, animals with and without exposure to chronic mild stress (CMS) for six weeks. Animals were submitted to the open field test (OFT), forced swim test (FST) and a [¹⁸F]FDG PET scan both at baseline (obtained 13 days after OVX, but before the CMS protocol) and after 6 weeks of CMS. Data collected at baseline and after the CMS protocol were analyzed separately. **Results:** The 13 days of estrogen depletion resulted in both increased (effect size: 2.08) and decreased [¹⁸F]FDG uptake in different subcortical brain regions (effect size: 2.32), but not in behavioral changes. Depressive-like behavior was only present after prolonged estrogen depletion, i.e. 6 weeks later, as was evident from an increase in immobility time in the FST (EST 26.8±10.6 s; VEH 99.2±36.5 s; EST+CMS 25.3±9.8 s; VEH+CMS=63.5±23.8 s; p<0.05). In addition, prolonged estrogen depletion caused a decrease in [¹⁸F]FDG uptake in frontal cortex and hippocampus (p<0.001; effect size: 2.97-4.72), and an increase in [¹⁸F]FDG uptake in temporal cortex, hypothalamus and brainstem (p<0.001; effect size: 2.54-4.17). Anxiety-like behaviour did not differ between groups, neither at baseline nor during follow-up. CMS did not affect body weight, depressive-like behavior and [¹⁸F]FDG uptake. **Conclusion:** Reduced levels of estrogen as a consequence of ovariectomy induced depressive-like behavior and changes in glucose metabolism in brain areas involved in cognition and emotion. CMS did not show any significant contribution to depressive-like symptoms, or to changes in brain metabolism in our study.

EP-0792

Uptake of 18F-Fluorothymidine in Experimental Abdominal Aortic Aneurysms of Small Rodents Detected Using PET/CT

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Purpose/Introduction: Current diagnostic and surveillance approaches for abdominal aortic aneurysm (AAA) disease are limited to anatomical visualisation of size changes. Patients require a significant burden of anatomical imaging surveillance before they are offered surgical intervention. Molecular imaging with novel radiotracers may help stratify patients with early-stage AAA to more 'light-touch' surveillance. Uptake of the gold-standard radiotracer 18F-fluorodeoxyglucose (18F-FDG) has been demonstrated previously in AAA models; however, its non-specific uptake is limited to indicating glucose-dependent activity, which may exclude other key mechanisms. The radiotracer 18F-fluorothymidine (18F-FLT) has been implemented extensively in tumour imaging, as its uptake correlates with cell proliferation. The aim of this study was to investigate the feasibility of using positron emission tomography/computed tomography (PET/CT) with 18F-FLT to visualise AAA in murine models. **Subjects & Methods:** Fourteen-week-old apolipoprotein E-knockout mice were administered either saline or angiotensin II infusions via subcutaneously implanted osmotic mini-pumps for 28 days. Ninety-minute PET/CT under recovery isoflurane and anaesthesia was performed on days 14 and 28 after 18F-FDG (9.79 ± 2.10 MBq) or 18F-FLT (day 14, 7.63 ± 3.02 MBq; day 28, 9.61 ± 1.34 MBq) was injected via the tail vein. Images were reconstructed using three-dimensional (3D) ordered subsets expectation maximisation algorithms, and 3D isocontour regions of interest (ROIs) were manually drawn in all AAA regions. Maximum standardised uptake values (SUVs) were determined for each ROI. **Results:** Uptake of 18F-FDG and 18F-FLT in the inferior vena cava were observed in the first 15 seconds of the respective scans, indicating intravenous tracer delivery. 18F-FDG and 18F-FLT uptake were observed in the myocardium and spleen, respectively, of all control and AAA models, consistent with anticipated uptake regions. The abdominal aorta exhibited significantly greater 18F-FLT uptake in AAA models than in control models on days 14 and 28 (SUV percentage differences: day 14, 4496.80, $p < 0.001$; day 28, 430.35). This enhanced uptake was more consistently demonstrated across different mice with 18F-FLT than with 18F-FDG (standard deviations: 18F-FDG, 0.14; 18F-FLT, 0.04 (day 14), 0.02 (day 28)). As 18F-FLT is a cell proliferation marker, these preliminary results were also validated by greater Ki67 positivity in stained aortic tissue from an independent cohort of mice with AAA than in non-AAA sections (percentage difference: 4669.19, $p < 0.001$). **Discussion/Conclusion:** To our best knowledge, this is the first study to demonstrate the potential utility of 18F-FLT PET/CT in AAA. Quantitative and biological analysis to validate these preliminary results and elucidate the time course and molecular mechanisms of AAA are ongoing.

EP-0793

¹⁸F-Flumazenil PET of GABA_A receptor binding in the Mongolian gerbil - comparison of different approaches for quantification and age dependency of results

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Introduction: Age-dependent hearing loss is characterized by initially pathological and subsequently reactive plastic changes in the central auditory system, involving especially the GABAergic system. Mongolian gerbils are well-suited animal models to study such changes. As a prerequisite to examine the pathophysiology of hearing impairment caused by aging we elaborated for the first-time positron emission tomography (PET) in gerbils, using ¹⁸F-flumazenil (¹⁸F-FMZ) to measure GABA_A receptor binding quantitatively. **Material and Methods:** 13.8 ± 2.3 MBq ¹⁸F-FMZ were injected in the vena femoralis of 6 young and 11 old gerbils (3–6 months young; 36 months old). Simultaneously to tracer injection, a 60min list-mode acquisition was started employing an Inveon PET/CT (Siemens) system. Animals were anesthetized using isoflurane. Data were reconstructed iteratively into 32 time consecutive frames including attenuation-correction. Analyses were performed using PMOD3.7 software. Values of non-displaceable binding potential (BP_{nd}) were calculated based on a previously created VOI atlas for auditory cortex (AC), inferior colliculus (IC), medial geniculate body (MGB), somatosensory cortex (SC) and cerebellum (CB) and pons as a reference region. Both, plasma input (two-tissue compartment model, 2TCM; Logan plot, Logan) and reference tissue models (simplified reference tissue model, SRTM; Logan reference, Logan Ref) were applied. Image derived plasma input was obtained from the vena cava caudalis. Akaike information criterion (AIC) was used as a measure for the goodness of fit. **Results:** Moderate absolute differences in BP_{nd} could be observed between the different models. With respect to means of BP_{nd}, Logan and Logan Ref delivered for all regions significantly ($p < 0.0001$) higher values. Goodness of fit was highest (AIC lowest) for SRTM followed by Logan and 2TCM. With respect to age: in all regions, BP_{nd} obtained with Logan, Logan Ref and SRTM was significantly higher ($p < 0.0001$) in young gerbils compared to old ones. For 2TCM significant difference was seen for young compared to old animals in AC ($p = 0.0107$), MGB ($p = 0.0014$), SC ($p = 0.0018$) and CB ($p = 0.0024$), but not in IC. SPM analysis using both, Logan Ref or SRTM, also revealed significantly ($p < 0.0001$, uncorrected) higher non-displaceable binding potential in young gerbils throughout cortical areas, especially the AC, as well as at the level of the lower midbrain - particularly in the IC. **Conclusion:** Here we successfully implemented quantification of GABA_A receptor binding in gerbils. Comparing quantification models, some perform better like the SRTM providing best fit while detecting decreased GABA_A receptor binding in old animals for all evaluated brain regions and in SPM analysis.

EP-0794**Radiolabeling, cell binding analysis, and NanoSPECT/CT imaging of ^{111}In -DTPA-anti-mesothelin in mice bearing KLM-1 pancreatic cancer xenografts**

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Aim: Mesothelin, an immunogenic membrane glycoprotein of 40 kDa, is overexpressed in many human cancers, such as ovarian cancer, pancreatic cancer, mesothelioma, and lung cancer, and has limited expression in normal tissues. In cancerous cells, mesothelin may be involved in the promotion of cell proliferation, adhesion and migration, chemotherapy resistance, and inhibition of apoptosis. The aim of this study was to perform the radiolabeling and preclinical evaluation of ^{111}In -DTPA-anti-mesothelin.

Materials and Methods: Anti-mesothelin, obtained from Creative Biolabs, was conjugated with p-SCN-Bn-DTPA at a 25-fold molar excess in 0.1 M carbonate-bicarbonate buffer, pH 8.4, at 37°C for 3 h. After conjugation, the average number of DTPA molecules linked to the mAb was determined by MALDI-TOF. Radiolabeling was performed by mixing 200 µg DTPA-mesothelin conjugates and 3.94 mCi $^{111}\text{InCl}_3$ for 30 min at 37°C. Radiochemical purity of the product was determined by High Performance Liquid Chromatography (HPLC) and Instant Thin Layer Chromatography-Silica Gel (ITLC-SG) analysis. For stability study of ^{111}In -DTPA-anti-mesothelin, the radiolabeled antibody was stored at 4°C and aliquots were analyzed at 0, 4, 24, 48 and 72 h by ITLC-SG. Cell binding affinity was analyzed using flow cytometry and gamma counter. **In vivo** biodistribution was evaluated using nanoSPECT/CT imaging in nude mice bearing KLM-1 xenograft tumors (about 240 mm³) at 4, 24, 48 and 72 h after injection of 8 MBq of ^{111}In -DTPA-anti-mesothelin. **Results:** The conjugation reaction produced one DTPA molecules per anti-mesothelin mAb. The radiochemical purity of ^{111}In -DTPA-anti-mesothelin was > 90% after purification and the specific activity was 19.3 mCi / mg of anti-mesothelin. The stability of ^{111}In -DTPA-anti-mesothelin was > 90% after 4 h incubation at 4°C. Flow cytometry data showed that anti-mesothelin strongly bound KLM-1 pancreatic cell line and conjugation of DTPA didn't change the binding affinity. Cell-bound fraction of ^{111}In -DTPA-anti-mesothelin in KLM-1 pancreatic cell line was 36.41±0.39%. NanoSPECT/CT imaging study showed an obviously specific accumulation of ^{111}In -DTPA-anti-mesothelin in tumor region. The tumor/muscle ratio at 4, 24, 48 and 72 h after drug administration were 1.75, 2.52, 4.97 and 6.45, respectively. **Conclusion:** Pancreatic cancer lesions as well as antibody biodistribution could be visualized by ^{111}In -DTPA-anti-mesothelin nanoSPECT/CT imaging, emphasizing the potential applications for personalized medicine.

EP-0795**Zr-89 Labelling of Exosomes for In Vivo Tracking**

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Introduction: To develop Zr-89 labelling methods for exosomes and track the biodistribution of the labelled exosomes by PET/CT in mice. **Materials and Methods:** Zr-89 was produced and purified in house via adaptations of the methods of Walther et al[1],[2]. Human Neural stem cell-derived exosomes and prostate cancer (Du145)-cell derived exosomes were internally labelled with Zr-89 Oxine via an adaptation of the methods of Blower et al[3]. Mice were injected with ~1MBq of Zr-89 labelled exosome either via tail vein or intraperitoneal route. Mice were scanned under anaesthesia on a Mediso nanoscan PET/CT scanner up to 6 times post injection over a 15 day period. **Results:** High purity (95-100%) and high yield (up to 60MBq purified product) exosome labelling was achieved. A marked difference of biodistribution was observed between injection routes with a predominantly liver and spleen signal for tail vein injected mice and a predominantly lymph node associated distribution for intraperitoneally injected mice. **Conclusions:** The Zr-89 cell labelling methods translated extremely well to exosome labelling providing useful information on their biodistribution in vivo. These methodologies will be of benefit in the understanding of exosome biology and the development of exosome based therapies. **References:** 1 Walther M, Gebhardt P, Grosse-Gehling P, *et al.* Implementation of 89Zr production and in vivo imaging of B-cells in mice with 89Zr-labeled anti-B-cell antibodies by small animal PET/CT. *Appl Radiat Isot* 2011;**69**:852-7. doi:10.1016/j.apradiso.2011.02.040 2 Dabkowski AM, Paisey SJ, Talboys M, *et al.* Optimization of Cyclotron Production for Radiometal of Zirconium 89. *Acta Phys Pol A* 2015;**127**:1479-82. 3 Ferris TJ, Charoenphun P, Meszaros LK, *et al.* Synthesis and characterisation of zirconium complexes for cell tracking with Zr-89 by positron emission tomography. *Dalton Trans* 2014;**43**:14851-7. doi:10.1039/C4DT01928H

EP-0796**Neuromodulatory effects of Ginkgo biloba extract EGb761(R) on vestibular compensation in the rat model of chemical unilateral labyrinthectomy**

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Introduction: To investigate whether and how Ginkgo biloba extract EGb761® can improve vestibular imbalance after unilateral labyrinthectomy (UL) in the rat by behavioural analysis and serial [¹⁸F]-FDG-µ-PET. **Material and Methods:** 32 rats were treated with control or EGb761® diet for 6 weeks before and 15 days after UL. Rats were randomized into groups (n=8), which received control/control or EGb761®/EGb761® (735mg/kg feed; 367.5mg/kg feed; 184mg/kg feed) diet. All animals underwent a left-sided UL by transtympanic injection of bupivacaine and arsenilate. Behavioural evaluation (nystagmus, postural asymmetry, locomotion analysis) and sequential [¹⁸F]-FDG-µ-PET imaging was conducted before and on days 1, 3, 7 and 15 post

UL. Measurements of terpene lactone in blood plasma were performed before and 15 days post UL. **Results:** The EGb761*/EGb761* (735mg/kg feed) group showed a significant reduction of nystagmus on day 3 and postural asymmetry on days 1, 3 and 7 post UL compared to the control group ($p < 0.05$). The course of postural and locomotor compensation was displaced forward by about 7 days. The dose-response study revealed a significant improvement of postural imbalance on days 3, 5 and 7 post UL in the EGb761*/EGb761* (367.5mg/kg feed) group compared to controls ($p < 0.05$). Nystagmus was significantly reduced on day 5, postural imbalance on day 2, 3 and 5 post UL in the EGb761*/EGb761* (184mg/kg feed) group versus controls ($p < 0.05$). Regression analysis showed a faster increase in locomotor velocity over time with higher blood levels of Ginkgolide A and B ($r = 0.47/r = 0.46$). Measurements of the regional cerebral glucose metabolism (rCGM) by serial [^{18}F]-FDG- μPET revealed a gradual increase of rCGM in the hippocampal formation and decrease in the cerebellum on days 1 and 3 post UL ($p < 0.005$) in the EGb761*/EGb761* (735mg/kg feed) group $>$ EGb761*/EGb761* (367.5mg/kg feed) group compared to the control group. The EGb761*/EGb761* groups showed no difference to the control group on days 7 and 15 post UL. **Conclusion:** EGb761* improves vestibulo-oculomotor (nystagmus), vestibulo-spinal (postural imbalance) and vestibulo-locomotor symptoms (locomotor velocity) after UL significantly and dose-dependently and thus is a promising compound to modulate vestibular compensation in the clinical context of an acute unilateral peripheral vestibulopathy. Serial [^{18}F]-FDG- μPET imaging indicated that EGb761* appears to modulate hippocampal and cerebellar neuronal circuits during vestibular compensation. Ginkgolide A and B likely are the pharmacologically active substrates in the polyvalent EGb761* extract.

EP-0797

Early prediction of tumor response to radiotherapy: preclinical validation of $^{99\text{m}}\text{Tc}$ -CP3-peptide

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Objective: To establish $^{99\text{m}}\text{Tc}$ -CP3-peptide, a novel $^{99\text{m}}\text{Tc}$ -labeled caspase-3 polypeptide imaging agent, to detect non-invasive early detection of tumor cell apoptosis. **Methods:** The prodrugs were labeled with $^{99\text{m}}\text{Tc}$ by direct labeling. The radiochemical purity of the product was determined by HPLC at 0, 1, 2, and 4 h after labeling. In vitro cell binding assay was performed on human lung squamous cell carcinoma H520 cells treated with radiotherapy (2 Gy or 4 Gy). $^{99\text{m}}\text{Tc}$ -CP3-peptide was mixed with the treated cells. After mixing for 30 min, the radioactivity uptake rate was measured ($\% \text{ID} = \text{cellular radioactivity uptake} / \text{radioactivity activity} \times 100\%$). The cell apoptosis rate was detected by flow cytometry. Imaging of $^{99\text{m}}\text{Tc}$ -CP3-peptide was performed in nude mice bearing H520 tumors. H520 tumors were irradiated with 0, 4 and 8 Gy doses ($n = 6/\text{group}$). After 24 hours, $^{99\text{m}}\text{Tc}$ -CP3-peptide was injected through the tail vein of rats. After 1 hour, SPECT imaging was performed to delineate the ROI and calculate the tumor and muscle tissue (T/NT) radioactivity ratio. The $\% \text{ID/g}$ uptake of $^{99\text{m}}\text{Tc}$ -CP3-peptide by tumors and

muscles was calculated after imaging. Tumor tissue was taken for TUNEL to detect the apoptosis of tumor cells. Data processing using SPSS 19.0 statistical software, measurement data using $\bar{x} \pm s$, comparison between groups using One-Way ANOVA, correlation research uses the Pearson correlation analysis, $p < 0.05$ for the difference was statistically significant. **Result:** The radiochemical purity of $^{99\text{m}}\text{Tc}$ -CP3-peptide at 0, 1, 2, and 4 h after labeling was ($99.33 \pm 0.12\%$), ($99.30 \pm 0.38\%$), ($99.21 \pm 0.13\%$), and ($99.33 \pm 0.12\%$). There was no statistical difference in the time of radiotherapy ($p > 0.05$). H520 cells after radiotherapy increased the uptake rate of $^{99\text{m}}\text{Tc}$ -CP3-peptide in a dose- and time-dependent manner, and the cell uptake rate was correlated well with the apoptosis rate detected by flow cytometry ($p < 0.05$). The SPECT imaging showed that the radiation uptake of tumor tissues in the radiotherapy group was significantly higher than that in the control group ($p < 0.05$). The radiotherapy dose of 8 Gy and 4 Gy group were $2.98 \pm 0.168\% \text{ID/g}$ and $2.56 \pm 0.078\% \text{ID/g}$ measured by γ counter which were significantly higher than the control group ($0.58 \pm 0.026\% \text{ID/g}$, $n = 6$, $p < 0.05$). The uptake of tumor tissue was positively correlated with the apoptosis rate detected by TUNEL ($p < 0.05$). **Conclusion:** $^{99\text{m}}\text{Tc}$ -CP3-peptide has high uptake targeting in tumor cells and tissues after radiotherapy, and has the potential of early non-invasive monitoring of tumor cell apoptosis. [Key words]: Apoptosis; Peptide; SPECT imaging; Tumor; Radiation therapy

EP-0798

A Computational Phantom of the Adult Labrador for Use in Preclinical Nuclear Medicine Dosimetry Studies

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Introduction: With the completion of the canine genome project, dogs have been proven to be an ideal species for pre-clinical investigations of both molecular imaging agents and therapy radiopharmaceuticals. There is thus an expressed need to establish computational anatomic models of dogs of different species to support the associated organ radiation dosimetry for these studies. In this work, we present a comprehensive hybrid computational anatomic and dosimetric model of the adult Labrador. This species - representative of many large breeds - is known to present with high incidence of osteosarcoma that is both genetically and phenotypically similar to human bone cancer. **Methods:** NURBS and polygon mesh models were constructed from high-resolution CT images of a 1.5-year Labrador imaged prior to euthanasia under an approved animal research protocol at the University of Florida. Bone samples from the skeleton were harvested and ex-vivo CT imaged at sub-millimeter resolution to obtain volume fractions of cortical bone, spongiosa, and medullary cavity space. Next, spongiosa bone cores were taken from 30 skeletal sites and subjected to microCT imaging at 30 micrometer resolution. The microCT images were segmented to assess volume fractions of trabecular bone and total marrow space of spongiosa. Voxel retagging procedures were applied to establish bone microstructures at varying marrow cellularities. Paired-image radiation transport was per-

formed to assess values of monogenetic electron specific absorbed fractions across the canine skeletal sites. **Results:** A database of specific absorbed fractions (SAFs) has been assembled for both monoenergetic photons and electrons emitted within 32 different source tissues of the adult male Labrador phantom. Values of energy deposition to active marrow and skeletal endosteum were obtained via energy-dependent integration of the volumetric photon fluence in regions of trabecular spongiosa and newly developed canine-specific fluence-to-dose photon response functions. Canine-specific S values are presented for several key radionuclides used in diagnostic and therapeutic nuclear medicine. **Discussion:** Dosimetric applications of the Labrador model are presented for model osteosarcoma tumors treated with ^{153}Sm -EDTMP or ^{153}Sm -PEI-MP. Based upon the ^{153}Sm S values established in this model, and a six-compartment biokinetic models of each agent (to include blood, urinary bladder content, kidneys, trabecular bone surfaces, cortical bone surfaces, and tumor), model tumor doses ranged from 16 to 50 Gy for ^{153}Sm -PEI-MP and from 8 to 25 Gy for ^{153}Sm -EDTMP.

EP-0799

Whole blood sampling utilizing microextraction by packed sorbents (MEPS) technique for [^{11}C]SMW139 radiometabolite analysis in micro-PET

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Aim: The radiometabolite analysis is a crucial primary step for quantitative analysis of positron emission tomography (PET) measurements. Blood sampling for radiometabolite analysis has been a challenge especially with small animal PET research where low blood volume is a limiting factor. We have previously used protein precipitation technique for radiometabolite analysis but this method is not straightforward and it is time-consuming. To overcome this problem as an alternative we present here microextraction by packed sorbents (MEPS) which is a fast method that needs only a few micro-liter sample volumes. Additionally we have evaluated the capability of MEPS for blood radiometabolite analysis of the P2X7R PET radioligand [^{11}C]SMW139 in small animal. **Materials and Methods:** One female Sprague-Dawley rat was anaesthetized with inhalation of 1.5–2% isoflurane (50/50 air/oxygen). The animal was cannulated on both lateral tail veins. One of the cannula was used for bolus injection of 17.3 MBq [^{11}C]SMW139 while the other was used for blood sampling. Four approximately 0.1 mL blood samples have been collected 4, 16, 30 and 60 minutes after injection of the radioligand. To perform a MEPS 4 mg of C18 sorbent was packed and manually inserted inside a glass syringe and the sorbent material was tightened by two filters. The MEPS was conditioned with optimized amount of methanol and water. The blood sample (0.1 mL) was diluted with 1 mL Water/formic acid (0.1%), 1 mL ACN/formic acid (0.1%) and vortexed and centrifuged. The supernatant was then loaded to the MEPS and washed with 0.1 mL water. The [^{11}C]SMW139 was eluted with 1 mL methanol and 1 mL water. Finally, the eluted sample was injected into a radio-HPLC. **Results:** Based on obtained HPLC chromatograms the unchanged percent of [^{11}C]SMW139 for 4,

16, 30 and 60 minutes blood samples was 100%, 71.18%, 58.69% and 27.07%, respectively. MEPS decreased the [^{11}C]SMW139 sample preparation time with half resulting also in a good recovery in plasma which was in the range of 88–93%. The results demonstrated that each MEPS is quite stable and after each extraction can be regenerated using 2x0.5 mL water/formic acid (0.1%) and it can be used for at least 20 sequential [^{11}C]SMW139 extractions. **Conclusions:** The MEPS technique proved to be useful for radiometabolite analysis of [^{11}C]SMW139 for up to 60 minutes even during conditions of low blood volume and low radioactivity. MEPS could potentially also be useful for mice and non-human primate radiometabolite analysis.

EP-0800

Antioxidant Effects of Vitamin D on Lacrimal Glands against High Dose Radioiodine-Associated Damage in an Animal Model

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Purpose/Introduction: High dose radioiodine (RAI) has been used as an effective treatment agent for hyperthyroidism and especially for differentiated thyroid cancers. However, this valuable treatment comes with some side effects including damage to the lacrimal glands. Iodine is concentrated in the thyroid tissue by an energy-dependent transmembrane protein called sodium-iodide symporter (NIS). A number of extrathyroidal tissues, such as lacrimal glands and nasolacrimal duct of humans, also express NIS. Several ocular complications, such as chronic or recurrent conjunctivitis, dacryostenosis and xerophthalmia have been reported after RAI therapy. The aim of this study was to evaluate antioxidant effects of active vitamin D (calcitriol) against high-dose RAI therapy-associated damage of lacrimal gland. **Subjects & Methods:** Wistar albino rats were used and divided into three groups randomly (n=12/group). Group 1 was appointed as the control group. Group 2 received 3 mCi RAI via gastric gavage while Group 3 received 3 mCi RAI via same method and calcitriol (200 ng/kg/day) via intraperitoneal administration. Seven days after RAI administration, bilateral intraorbital (IG), extraorbital (EG) and Harderian (HG) glands were removed for the evaluations of histopathologic, tissue cytokine, total oxidant status (TOS), and total antioxidant status (TAS). **Results:** RAI led to significant increase in tissue TOS, TNF- α , IL-6 levels, and significant decrease in IL-10 and TAS levels (P <0.05 for each). Addition of adjunctive calcitriol reversed all these parameters significantly (P <0.05 for each). The following histopatholog-

ic parameters were seen more frequently in Group 2 than the other groups: Abnormal lobular pattern, perivascular infiltration, periductal infiltration, lipofuscin-like accumulation, acinar atrophy, periductal and periacinar fibrosis in all lacrimal gland types ($P < 0.05$), acinar fibrosis in EG ($P = 0.049$), periductal fibrosis in EG and HG ($P = 0.049$ and 0.038 respectively), abnormal cell outlines in EG and HG ($P = 0.020$ and 0.011 respectively) and variation in cell size in the IG and the HG ($P = 0.003$ and 0.049 respectively). **Discussion/Conclusions:** RAI caused significant oxidative stress and inflammation in lacrimal glands. Vitamin D demonstrated potent anti-inflammatory, antioxidant and radio-protective effects on lacrimal glands in histopathologic, tissue cytokine and oxidant/antioxidant level evaluations.

EP-0801

Evaluation of ^{99m}Tc -(V)-DMSA in vascular calcification process based on A7r5 vascular smooth muscle cells model

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Aim: Vascular calcification is an established feature of atherosclerosis in which vascular smooth muscle cells (VSMC) undergoing osteochondrogenic differentiation. Several pathways contribute to vascular calcification. One of them implies sodium/phosphate transporter Pit-1 which acts as biosensor in vascular calcification of VSMC. Strategies are needed to be developed to target early stages of vascular calcification, which reflects a vulnerable phase in the evolution of atheroma plaque, and predict cardiovascular events. We previously reported that ^{99m}Tc -(V)-DMSA uptake was mediated by Pit-1 transporter in tumoral cell. The goal of this *in vitro* study is to determine whether ^{99m}Tc -(V)-DMSA can evaluate the vascular calcification process in Vascular Smooth Muscle Cells (VSMCs) based on Pit-1 expression. **Material and Methods:** From rat aortic VSMC (A7r5 cell line), we set up a model of calcification within 7 days using a calcifying medium containing high inorganic phosphate concentrations (5mmol/L). Phosphocalcic deposits were monitored with Alizarin-red and Von-Kossa staining and with phase-contrast microscopy. Pit-1 expression was evaluated with immunofluorescence assay. Osteoblastic-like differentiation was assay by OPN expression, realized with whole cell ELISA. ^{99m}Tc -(V)-DMSA uptake was compared in control and calcifying conditions. Phosphonoformic acid, a Pit-1 inhibitor, was used as negative control. **Results:** Under hyperphosphatemia conditions cells overexpressed osteopontin and synthesized mineralized matrix with phospho-calcic deposition. Calcified cells overexpressed Pit-1 transporter at cell membrane. The use of phosphonoformic acid inhibits the calcification process. ^{99m}Tc -(V)-DMSA uptake was to $2.8 \pm 2.08\%$ DA/mg-protein in control cells and $42 \pm 24\%$ DA/mg-protein in calcified cells ($p < 0.001$). Pit-1 inhibition with phosphonoformic acid decrease ^{99m}Tc -(V)-DMSA uptake to

$2.2 \pm 0.6\%$ DA/mg-protein that prove Pit-1 involvement in ^{99m}Tc -(V)-DMSA uptake. **Conclusion:** These results demonstrated that ^{99m}Tc -(V)-DMSA *in vitro* uptake is mediated by Pit-1 transporter during VSMC's calcification. This radiopharmaceutical may have some potential to study changes of VSMC metabolism occurring in the atherosclerosis process.

EP-0802

Pharmacokinetic Analysis of Monoamine Oxidase-B Tracer [^{11}C]-Deprenyl in Rats

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Introduction: The MAO-B inhibitor [^{11}C]-deuterium-L-deprenyl ([^{11}C]-DED) has been used previously as a marker of astrocytosis in patients. While [^{11}C]-DED is potentially useful for studying astrocytosis in a preclinical setting, this PET tracer has not been fully validated for use in rodents. The goal of this study is therefore to elucidate the pharmacokinetic parameters of [^{11}C]-DED in rats for further use in preclinical studies of astrocytes. **Subjects and Methods:** Healthy male Wistar rats were submitted to a 90 minute [^{11}C]-DED PET scan with arterial blood sampling (rate of injection: 1 mL/min). Radioactivity in blood and plasma (16 samples) was measured using a gamma counter. At five time points after injection blood was taken for metabolite analysis. Kinetic analysis (one (1TCM) and two (2TCM) tissue compartment models) was performed with a metabolite corrected plasma curve for 14 predefined volumes of interest. **Results:** The brain, blood and plasma time-activity curves of [^{11}C]-DED showed a high uptake during the injection time, with a rapid wash-out after 10 minutes. [^{11}C]-DED was rapidly metabolized in the first 15 minutes, with a percentage of metabolites of 70% at 5 min and 53% at 15 min, relatively steady until the end of the scan. Based on the Akaike information criteria, the 1TCM described the data best. The 2TCM showed a similarly good fit, however, a higher variability of V_T was found when compared to 1TCM (coefficient of variation (CoV) V_T 2TCM = 24%; CoV V_T 1TCM = 16% for the whole brain). Additionally, the rate constants k_3 and k_4 were estimated with a large margin of error (>50% std. error), which turns the 2TCM fit significantly less reliable. Using the 1TCM, the highest V_T values were found in the thalamus (3.23 ± 0.5 mL/cm³) and striatum (3.02 ± 0.49 mL/cm³), and the lowest V_T values in the olfactory nucleus (2.23 ± 0.39 mL/cm³). **Conclusion:** The highest tracer binding in the thalamus, is consistent with findings in human studies. Although in the human brain [^{11}C]-DED showed irreversible binding to MAO-B, we found that the 1TCM fitted the kinetics of [^{11}C]-DED best. This suggests that the binding of [^{11}C]-DED to astrocytes in rats is differently from what is found in humans.

EP-0803

The effect of timing and sequence of gemcitabine administration and radiation for the treatment of medullary thyroid carcinoma.

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Background: Medullary thyroid carcinoma (MTC) is a neuroendocrine tumour with sometimes high expression of somatostatin receptors. MTC originates from the thyroid C cell and occurs either sporadically (75%) or is caused by germline mutation of the RET proto-oncogene. At diagnosis, about 50% of the MTC patients have metastases, and low 10-year survival rate for metastatic disease has been reported, about 20%. We recently investigated the effect of gemcitabine, a nucleoside analogue, which inhibits DNA synthesis and repair, in combination with ¹⁷⁷Lu-octreotate or external beam radiotherapy (EBRT) in a patient-derived MTC (GOT2) animal model and our results suggested additive and even synergistic cytotoxic effects. However, the ideal timing of gemcitabine administration with irradiation has not been studied. The aim of this study is 1) to investigate whether the time course and sequence between gemcitabine administration and irradiation is essential for achieving high anti-tumor effect, and 2) to study the molecular mechanisms involved in the interaction between gemcitabine and radiation in GOT2. EBRT was used instead of ¹⁷⁷Lu-octreotate to enable studies of timing. **Materials and Methods:** Balb/C-nu mice with GOT2 tumours were divided into groups with a similar mean tumor volume at the start of treatment. The mice were injected with 60 mg/kg gemcitabine, either 72h before (group 1), 0.25h before (group 2) or 72h after (group 3) irradiation with 3Gy. Tumor size was measured twice a week, using a digital caliper. **Results:** For all groups, tumor regression was observed during the first 11 days with a mean relative volume reduction related to the volume before treatment of 21%, 40% and 46% for groups 1, 2 and 3, respectively. A statistically significant difference was observed between group 1 and groups 2 or 3 ($P=0.029$ and 0.030 , respectively). The lower tumour reduction in group 1 could be due to accumulation of cells in S-phase, which are relatively more resistant to radiation. The higher tumour volume reduction when gemcitabine was given concurrently with or after EBRT, suggests increased delivery of gemcitabine to the MTC tumours and/or enhanced effect of the combination. **Conclusions:** Our findings suggest that the combined effect of gemcitabine and EBRT is higher when gemcitabine is administered simultaneously with or after EBRT. The optimal time schedule of the combined modalities is further investigated, together with translation of results to ¹⁷⁷Lu-octreotate therapy.

EP-0804

Computational Study Of Necrotic Radius In Photodynamic Therapy And Monitoring With PET/CT

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Introduction: Primary and secondary liver malignancies are among the leading death causes in patients worldwide. Con-

cerning the various treatment approaches, radioembolization and other loco-regional tumor therapies (e.g. photodynamic therapy - PDT) are potentially useful palliative approaches. PDT is based on the concept of selective absorption of monochromatic light by photosensitizers, selectively localized in neoplastic tissue, in the presence of oxygen. PDT therapeutic outcome is limited in some cases by the limited tissue penetration of the necessary light for photosensitizer activation, as well as the heterogeneous distribution of tissue oxygen within hypoxic areas. In this work we perform computational modeling of PDT dosimetric parameters in malignant and healthy rat liver tissues, and calculate the necrotic radius after PDT. Pre-therapeutic and post-therapeutic PET/CT imaging for tumor hypoxia could provide a map for a more realistic prediction of the necrotic radius. **Subjects and Methods:** Light and oxygen species dosimetry are assessed using Monte Carlo simulations and photochemical equations, respectively. The malignant liver surface of the virtual samples is assumed to be in contact with a 652 nm laser source, delivering light by a flat, cylindrical beam. 5,10,15,20-Tetrakis(3-hydroxyphenyl)chlorine (mTHPC) is used as photosensitizer. Fluence rate spatial profiles are obtained by a Monte Carlo algorithm and spatial distributions of photosensitizer (S_0), molecular oxygen (3O_2) and apparent reacted oxygen ($[O_{2,rx}]$) concentrations are simulated as a function of depth in tissue (z axis) and distance from light source (r axis) through MATLAB scripts. **Results:** Spatial distributions of $[S_0]$, $[^3O_2]$ and $[O_{2,rx}]$ are obtained allowing estimation of necrotic radius profile and necrotic area ($n_a\%$). Whether increasing $[S_0]$ or light power by 50%, $n_a\%$ increases by 8 to 10%, with small differentiations, although higher light power values offer a wider area coverage in the r axis. Their simultaneous 50% increase leads to 19.8% $n_a\%$ increase, corresponding to $n_a=74.31\%$. **Discussion:** Pre-therapeutic imaging with PET radiopharmaceuticals for tumor hypoxia, such as [¹⁸F]F-MISO could provide a map for a more realistic prediction of the necrotic radius. Moreover, post-therapeutic radionuclide imaging of tumor hypoxia differentiates areas of complete necrosis from areas of PDT-induced hypoxia, which is an undesired phenomenon that can lead to reduced method efficacy. Definitely, further studies are necessary for the optimization of the malignant cells necrosis. **Acknowledgments:** We gratefully acknowledge funding by the “ELI-LASERLAB Europe Synergy, HiPER & IPERION-CH.gr (HELLAS-CH)” MIS 5002735 (Co-financed by Greece and the European Union - European Regional Development Fund).

EP-0805

Development of Human Sodium/Iodide Symporter (hNIS) Transgenic Mouse as Resource of Stem Cells for in vivo Cell Tracking

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Purpose/Introduction: A human sodium/iodide symporter (hNIS), a transmembrane glycoprotein of thyroid follicular cells,

mediates uptake of iodine into the cells. Thus, hNIS gene has been used as a reporter gene combined with radioiodine or $^{99m}\text{TcO}_4^-$ as its reporter probe; cell lines stably expressing hNIS gene have been reported to be tracked *in vivo* in mice. However, stable cell lines cannot be made with stem cells, because they differentiate during the procedure. In the current study, to obtain stem cells that innately uptake $^{99m}\text{TcO}_4^-$ and radioiodine, we developed a transgenic mouse systemically expressing hNIS gene. **Methods:** hNIS genes driven by a CAG promoter were transferred into fertilized ova of C57BL/6N mice by the microinjection method. All animal experimental studies had prior Ethics Approval from institutional authorities. **Results:** Three founder lines were established from 5 founder mice. Bio-distribution studies of $^{99m}\text{TcO}_4^-$ in the transgenic mice showed increased $^{99m}\text{TcO}_4^-$ uptake into the bone marrows and the skeletal muscles and decreased $^{99m}\text{TcO}_4^-$ uptake in the thyroid glands and the stomach compared with the wild-type mice. Fluorescence *in situ* hybridization (FISH) and real-time polymerase chain reaction (PCR) confirmed physical mapping and copy numbers of the hNIS gene in each line of the transgenic mice. Small-animal SPECT imaging using $^{99m}\text{TcO}_4^-$ and small animal PET imaging using $^{124}\text{I}^-$ could detect *in vivo* the hNIS expressing stem cells (1×10^6 and 1×10^5 cells, respectively) derived from the transgenic mice and transplanted subcutaneously into nude mice. **Discussion/Conclusion:** We successfully developed a transgenic mouse systemically expressing a hNIS gene. This transgenic mouse must contribute to regeneration medicine researches as a resource of stem cells enabling *in vivo* cell tracking in mice.

EP-0806

Protective Effect of Coenzyme Q10 Against I131 Toxicity in Rat Livers

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Introduction: Radioactive iodine-131 (RAI) is commonly used both for diagnostic and therapeutic purposes in the treatment of hyperthyroidism and thyroid cancer. However, RAI-related damage is well known. The present study was conducted to evaluate the radioprotective effects of coenzyme Q10, a distinguished anti-oxidant, against RAI-related liver damage. **Subjects and Methods:** Thirty-six rats were divided into three groups. Group 1 was the control group, Group 2 was administered 111 MBq/kg of RAI and Group 3 was administered coenzyme Q10 together with RAI. In the third group, intraperitoneal 10 mg/kg coenzyme Q10 administration was started 1 week before and continued for one week after RAI administration. Twenty-four hours after the administration of the last dose of coenzyme Q10, the animals were decapitated and liver tissue samples were evaluated by histopathology and also for oxidative stress parameters. **Results:** Group 2 rats showed significantly elevated values of malondialdehyde (MDA) and fluorescent oxidation products (FOP) in liver tissues; however, the total sulphhydryl (total-SH) level was decreased compared to Group 1 and Group 3. In addition, the histopathological damage scores, consisting of hyperemia, inflammation, capsule

thickening, fibrosis, cellular changes, bile duct proliferation, perivascular fibrosis, and granuloma formation in Group 2 were significantly higher compared to other groups ($p < 0.05$ for all histopathological parameters). The total tissue MDA, and FOP levels of Group 3 were lower than Group 2 ($p < 0.05$) and total-SH level was higher than Group 2 ($p < 0.05$). Liver MDA and FOP levels of Group 3 were higher than Group 1. However, the difference was not statistically significant ($p > 0.05$). The histopathological damage in Group 3 was significantly less than the damage in Group 2 ($p < 0.05$ for all pathological parameters). **Conclusion:** We have demonstrated that depletion of total-SH levels and increased levels of FOP and liver MDA are the results of RAI-related liver damage. Moreover, Oxidative stress parameters verified the radioprotective effect of coenzyme Q10 treatment on the liver by decreasing the tissue MDA and FOP, and increasing the total-SH levels when compared to RAI group. These results show that antioxidant activities are likely to be involved in the mechanism underlying the radioprotective effects of coenzyme Q10. Further studies might warrant showing that coenzyme Q10 might be used as a hepatoprotective treatment before RAI therapy, particularly in patients with hepatic disease.

EP-0807

Striatal VMAT2 expression correlates with glucose level in rat model of hyperglycemia by ^{18}F -FP-(+)-DTBZ-PET/CT

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Introduction: Hyperglycemia is a high risk factor for various of diseases, including neurodegeneration. ^{18}F -FP-(+)-DTBZ is a ligand targeting Vesicular Monoamine Transporter type 2 (VMAT2), which is a useful imaging marker for quantification of dopaminergic integrity, and apply to evaluate clinical severity of PD. The aim of this study was to examine how does hyperglycemia infect the expression of VMAT2 in striatal of hyperglycemic rat model. **Methods:** Intraperitoneal injection of Streptozotocin (65 mg/kg body weight) and saline in male Wistar rats (200–250 g, $n = 6$) were applied in establishment of hyperglycemic rat model and control rats. PET/CT scans were conducted at 60 min post intravenous injection of ^{18}F -FP-(+)-DTBZ and brain imaging were collected. Brain regions were analyzed by PMOD 3.4 software, SUVs were obtained and specific uptake ratio (SUR) was calculated as [uptake in striatum / uptake in cerebellum-1]. **Results:** Glucose level increased from 5.32 ± 0.83 mmol/L to 24.4 ± 5.18 mmol/L in 1 week after intraperitoneal injection of Streptozotocin, and then return to 7.32 ± 0.33 mmol/L at 6 month post injection of Streptozotocin. Accordingly, striatal uptake in hyperglycemic rats (SUR: 1.42 ± 0.21) was significant lower than control rats (SUR: 2.52 ± 0.16). Accompany with the recovery of glucose level, striatal uptake in hyperglycemic rats (SUR: 2.20 ± 0.47) return to relative normal level at 6-month post injection of Streptozotocin. **Conclusion:** Hyperglycemia infects the expression of VMAT2 in brain, significant decreased ^{18}F -FP-(+)-DTBZ uptake in the striatum of hyperglycemic rats with high level of glucose, and increased expression of VMAT2 was observed when glucose level return to normal level.

EP-0808

In vitro and in vivo evaluation of ^{99m}Tc -polymyxin B for targeting Gram negative bacteria

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Purpose/Introduction: Several radiopharmaceuticals, including antibiotics, have been proposed for in vivo detection of bacteria, but none can be considered highly specific. From clinical point of view, it could be highly relevant to be able to differentiate between Gram+ and Gram- bacteria once the diagnosis of infection has been performed by other tools. Aim of our study was to radiolabel polymyxin B (PMB) with ^{99m}Tc and evaluate its specificity for imaging Gram-negative bacteria only. **Subjects and Methods:** Labelling was performed with indirect method and labelling efficiency and stability in serum and 0.9% NaCl were evaluated by iTLC and HPLC. Laboratory strains *E. coli* (ATCC 25922), *P. aeruginosa* (ATCC 27853), *A. baumannii* (ATCC 19606) gram- and *S. aureus* (ATCC 25923) and *E. faecalis* (ATCC 29212) gram+, as control, were used. In vitro binding studies included viable and non-viable bacteria and in the presence or absence of a 10- and 100-fold of unlabelled PMB. Biodistribution of ^{99m}Tc -PMB was determined in C57/BL6 mice (9 female mice, 5 weeks old), injecting 1.85 MBq of labelled PMB i.v. High resolution images were acquired at 1, 3 and 6h. In other experiments, at each time point, 3 mice were sacrificed and blood samples and major organs were collected, weighted and counted for radioactivity. Targeting studies were performed in mice (n=3 for each group) infected with different amounts (10^7 , 10^8 , 10^9 CFU) of *P. aeruginosa*, *E. coli* or *A. baumannii* in right thigh and Matrigel®, as control, in left thigh. **Results:** The LE was 97% and ^{99m}Tc -PMB was stable up to 24h in serum and 0.9% NaCl. Binding tests showed different results in relation to bacterial strain, being higher in viable *E. coli* and *A. baumannii* than *E. faecalis* and *S. aureus* ($p=0.04$, $p=0.02$ and $p=0.02$ at 30 minutes at 37°C, respectively). Temperature did not influence the binding that was displaced by unlabelled PMB. Ethanol and heat killed bacteria had significantly less binding than viable ones. Biodistribution showed rapid and high uptake by kidneys. In targeting studies, T/B ratios proportionally increased with the number of each Gram- bacteria. The highest ex-vivo T/B ratios were 3.2 ± 2.0 , 2.6 ± 0.3 and 2.6 ± 0.6 at 6h, for 10^9 CFU of *E. coli*, *P. aeruginosa* and *A. baumannii*, respectively. **Conclusions:** ^{99m}Tc -PMB showed excellent in vivo biodistribution and specific uptake in the infected Gram- thighs. Further studies are ongoing in order to evaluate the sensitivity of this new radiopharmaceutical in different infection models.

EP-0809

Comparison and dual isotope imaging of ^{67}Ga and ^{68}Ga on a novel preclinical multi-modality SPECT/PET/CT/OI system.

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Aim: ^{68}Ga is well established for targeted PET imaging in nuclear medicine. In preclinical imaging studies the spatial res-

olution is severely limited by the ^{68}Ga positron range (mean 2.9mm). In preclinical imaging ^{67}Ga SPECT might be an interesting alternative for ^{68}Ga PET; we therefore investigated the performance of ^{67}Ga and ^{68}Ga imaging in a phantom study.

Methods: A SPECT-IQ phantom was filled with 92MBq ^{67}Ga -Citrate and 161MBq ^{68}Ga -DTPA. The phantom was scanned for 16 consecutive frames of 30 minutes in a MILabs VECTOr5 SPECT/PET/CT/OI system (Utrecht, the Netherlands) with a High Energy Mouse collimator with 148 pinholes (HE-UHR-M). Three ^{67}Ga peaks (92keV/22%, 185keV/20%, 300keV/20%) and one ^{68}Ga peak (511keV,20%) were used in Similarity Regulated OSEM reconstruction with 9 iterations. Images were corrected for scatter and for attenuation. Uniformity (%STD) and spill over ratio (SOR) in water and air were determined following NEMA standard NU4-2008. Recovery of the rods was assessed visually and quantitatively by determining the FWHM. Quantitative accuracy and SORs were also determined for ^{67}Ga in every single frame to investigate the influence of ^{68}Ga in the ^{67}Ga channel. Quantitative accuracy is defined as measured activity in SPECT images divided by dose calibrator measurement. The first two frames were added to determine the image quality of ^{68}Ga , the last two frames to determine the image quality of ^{67}Ga . **Results:** Quantitative accuracy for ^{67}Ga was 1.00 ± 0.05 for all frames. SOR in the ^{67}Ga channel slightly increased when the amount of ^{68}Ga was 0.34 times (air) or 0.18 times (water) the amount of ^{67}Ga . SOR further increased with an increasing $^{68}\text{Ga}/^{67}\text{Ga}$ ratio. Uniformity for ^{68}Ga was 13%, for ^{67}Ga 22%. SOR_{air} was comparable (0.053 for ^{67}Ga , 0.063 for ^{68}Ga). $\text{SOR}_{\text{water}}$ however was 11 fold higher with ^{68}Ga (0.20) compared to ^{67}Ga (0.018). Rods down to 0.5mm were resolved for ^{67}Ga in contrast to ^{68}Ga where only the two largest rods (1.0, 1.5mm) were resolved. FWHM improved 1.8 times on average for ^{67}Ga compared to ^{68}Ga . In the ^{68}Ga images there was noticeable higher background activity between the rods. **Conclusion:** Quantitatively accurate dual isotope $^{67}\text{Ga}/^{68}\text{Ga}$ studies were shown to be feasible, enabling to study the biodistribution of a compound labeled with ^{67}Ga and ^{68}Ga in e.g. the same animal in-vivo to investigate the biological equivalence. Recovery of the rods and the SOR in water were significantly better with ^{67}Ga compared to ^{68}Ga , making ^{67}Ga a better alternative for ^{68}Ga in preclinical studies.

EP-0810

Molecular imaging as a quantitative tool during malaria vaccine development

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Introduction: An effective malaria vaccine for *Plasmodium falciparum* (Pf) has the potential to prevent around half a million deaths each year. Live attenuated malaria parasites are the most promising vaccine candidates nowadays. They can offer full protection but this effect is dependent on the ability of the vaccine parasites to migrate through the human host. Little is known about the migration patterns and the interaction of the vaccine malaria parasites within the skin. Using fluores-

cence molecular imaging we tracked malaria parasites (sporozoites; spz) and characterized their movement *in vitro* and in human skin explants. Subsequently we quantified the motility of wild-type (spz_{wt}) and live radiation-attenuated vaccine spz (spz_{vaccine}). **Methods:** Fluorescence confocal microscopy movies were obtained of migrating spz *in vitro* (n=100) and following syringe-based administration in human skin explants (n=702). To analyse the full migrational complexity of spz and to quantify key motility parameters (velocity, movement pattern and track tortuosity), we have developed the image analysis software SMOOT. Using this custom analysis tool we compared the movement of spz_{wt} *in vitro* with the movement of spz_{wt} and spz_{vaccine} in human skin. **Results:** Image analysis revealed that spz_{wt} motility is highly dependent on the environment. *In vitro* spz_{wt} displayed primarily counter clockwise (CCW) circular movement (95% CCW, straightness index (SI) 0.05, angular dispersion (AD) 0.69). This pattern starkly contrasts spz_{wt} movement in skin where the physical constraints asserted by the tissue morphology yield more complex directional migration patterns. Here spz_{wt} movement alternated between turning and linear patterns (63% turning, 37% linear, SI 0.77, AD 0.51), spz_{wt} turns were equally CW (49%) and CCW (51%) and spz_{wt} exhibited a start-stop behaviour or even reverse movement. In skin, spz_{wt} moved significantly slower than *in vitro* (mean 0.64 vs 1.55 $\mu\text{m/s}$, $p=0.000$). In addition, spz_{vaccine} were less directional than the spz_{wt}: the SI was 8% lower and the AD was more similar to the AD found *in vitro* (82% turning, 18% linear, SI 0.71, AD 0.73). **Conclusion:** Using our out-of-the-box molecular imaging approach we created a quantitative tool which enabled us to characterize spz migration patterns in human skin. More importantly, we revealed migrational deficits in spz_{vaccine} which could help explain the reduced vaccine efficacy observed in human trials. This to improve malaria vaccine development.

EP-0811

Is intranasal radio tracer delivery feasible for brain PET imaging?

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Background: The development of clinically useful tracers for PET imaging is enormously challenging and expensive. If the intranasal (IN) pathway presents a viable option, it extends the PET imaging field by increasing the number of tracers available for human use. **Aim:** This study was designed to evaluate the pharmacokinetics and the radiation exposure expected using two different ¹⁸F-labelled radiotracers, [¹⁸F]FDG and [¹⁸F]fallypride via the IN route in order to establish whether or not the IN route is a viable option for radiotracer delivery in PET imaging. We hypothesised that [brain region]:[plasma] ratios would be higher via the IN route as there are two inputs, one directly from the nose to the brain, and another from the peripheral circulation. **Methods:** Male, Sprague-Dawley rats were anaesthetised, and arterial and venous cannulas were surgically placed in the femoral artery and vein, respectively. Rats were dosed with either [¹⁸F]FDG

or [¹⁸F]fallypride via the IN or the intravenous (IV) route. Arterial blood samples were collected at different time intervals, centrifuged to extract plasma and gamma counted. In case of [¹⁸F]fallypride, the plasma samples were processed to separate the parent fraction from metabolites. Image acquisition was carried out using a BioScan nanoPET-CT^{Plus} scanner and images were analysed using VivoQuant 2.0 software and PMOD version 3.7. Standardised uptake values (SUV) (g/cc) was calculated by dividing the image derived concentration with the ratio of the injected dose to the body weight. **Results:** In case of both tracers, the only region that showed higher fractional uptake after IN administration was the olfactory bulb ($p<0.0001$ for [¹⁸F]FDG and $p=0.0073$ for [¹⁸F]fallypride). No other significant differences were observed between any other brain regions. It appears that in both cases, [¹⁸F]FDG and [¹⁸F]fallypride the radiotracer moves into the olfactory bulb region, but then does not progress further into other brain regions. Additionally, as the nasal cavity has a small surface area, extrapolated dosimetry calculations showed that even administering a relatively low dose of 35 MBq into the human nose will have a cumulative skin dose of 500 mSv, which is unacceptably high. **Conclusion:** Therefore, based on the results, we conclude that the IN route of administration for radiotracers is not a viable route for brain PET imaging.

EP-0812

Preclinical studies of ⁶⁸Ga-Labeled PSMA-inhibitors as molecular imaging biomarker for renal cancer

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Introduction: Today ⁶⁸Ga-PSMA (PSMA-11/617/I&T) is the one of most intensively studied and used ⁶⁸Ga-based radiopharmaceutical with significant clinical application. Prostate-specific membrane antigen (PSMA) is expressed by prostate cancer cells as well as endothelial cells within the neovasculature of several malignancies including renal cell carcinoma. To date, a number of clinical cases with kidney tumors visualization by ⁶⁸Ga-PSMA-PET/CT had been reported. At the same time, as we know, there are no systematic preclinical studies for ⁶⁸Ga-PSMA in the case of kidney tumors. **Aim:** In this study, we evaluate the diagnostic potential of ⁶⁸Ga-labeled PSMA-inhibitors (PSMA-617 and one new derivative - NODAGA-PSMA-A) as PET radiotracers for renal cancer. **Materials and Methods:** All chemicals and solvents were of high-purity or pharmaceutical grade and were purchased from Sigma-Aldrich or Panreac. Quality control was carried out with TLC chromatography (ITLC-SG strips, PET-MiniGita radio-TLC scanner). ⁶⁸Ge/⁶⁸Ga generator (Cyclotron Ltd) was used. ModularLab PharmTracer module was used for ⁶⁸Ga post-processing and labeling. In vitro binding and cell internalization of radiotracers was investigated in human renal cell adenocarcinoma ACHN (ATCC® CRL-1611™). Prior to performing the experiments the ACHN cells were plated 24h to achieve a density of approximately 500000 cells/vial (in triplicate) in RPMI-1640 medium with 10% fetal bovine serum. Cells were incubated for 1h with 0.5-0.4 MBq of radiotracers in serum-free medium. Internalization was determined using the standard method. Biodistribu-

tion was studied in BALB/c nude mice. The direct radiometry of dissected organs was made in 1h post injections of 3.6 MBq of DOTA-PSMA and NODAGA-PSMA-A. The retention in tumor and nontarget tissues was expressed as a percentage of the injected dose localized per gram of tissue (%ID/g). Gamma counter Wizard-2480 and G4-microPET (Sofie) were used for in vivo and in vitro experiments. **Results:** Experimental data showed that accumulation of ^{68}Ga -DOTA-PSMA-617 and ^{68}Ga -NODAGA-PSMA-A in ACHN-cells *in vitro* was $1.14 \pm 0.06\%$ and $0.90 \pm 0.03\%$, respectively, with internalization ratios about 72.8% and 62.6%. In vivo experiments showed that accumulation in tumor foci was 2–4 times higher than in healthy tissue. The accumulation of both tracers in orthotopic xenographs was about 2 times higher than in heterotopic. In heterotopic xenographs, the accumulation of ^{68}Ga -DOTA-PSMA-617 was 1.7 times higher than that of ^{68}Ga -NODAGA-PSMA-A. **Conclusion:** Some advantages were found for ^{68}Ga -DOTA-PSMA-617 as a potential radiotracer for PET-imaging of renal cell adenocarcinoma. The research is in progress. *The work was financially supported by Ministry of Education and Science of the Russian Federation - State Contract №14.N08.11.0165.*

EP-56

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Preclinical and translational aspects
-> Preclinical aspects -> Biology, benign disease

EP-0813

Clinical Implications Of PET Image Reconstruction Parameters On Quantitative Assessment Of Epileptogenic Sites In 18F-FDG Brain PET Study

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Purpose/Introduction: PET is a widespread functional imaging tool in the pre-surgical evaluation of patients suffering from epilepsy disorders. In PET, epileptogenic regions show a decreased glucose metabolism, however, precise detection of hypo-metabolic spots depends on SNR and image quality. Over or under iterations can create noise and artifacts. Pointing to the significance of optimal iteration cut off. In this study, We evaluate the influence of PET reconstruction parameters on quantitative results by means of variations in Z-score and SUVmax values. **Methods:** We apply 234 different combinations of iterations (i), subsets (s) and smoothing filter (G) with/without resolution recovery (HD/i-3D) on PET image data acquired by SIEMENS Biograph6 PET/CT scanner. Furthermore, PET images were attenuation corrected using low dose CT images (80–130 kV, 50–80 mAs). The reconstructed PET images were normalized

to Talairach stereotactic atlas of human brain and variations in z-scores were reported as functional deficit cerebral zones, using Scenium software [1]. As compared to FBP, iterative reconstruction methods provide images with better spatial resolution and improved SNR and image quality [2–5]. **Results:** The outcomes showed that reconstruction parameters can affect Z-scores and SUVmax up to 20% in comparison to reconstruction settings provided by software normal database. Also, it is defined that resolution recovery can influence the quantitative assessment. Variations up to 28% and 22% in SUVmax values in i-3D and HD reconstructions were seen respectively. Moreover, Variations up to 20% in z-score values in i-3D and HD reconstructions were seen resulting in many false positive epileptogenic sites. **Conclusion:** As quantitative and semi-quantitative information derived from 18F-FDG brain PET images can be strongly affected by noise, optimized reconstruction settings should be implemented. Various reconstruction settings can affect z-score and SUVmax differently. Thus, accurate use of reconstruction parameters has a vital role in diagnosis, characterization and treatment response.

EP-0814

Impact of long term supplement with artificial sweeteners on insulin dependent glucose uptake

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Aim: The consumption of non-caloric sweeteners (NCS) such as sucralose and acesulfame K has increased throughout the world. Unfortunately, their consumption produces counterintuitive effects including increased risk of metabolic syndrome (Azad et al, 2017). Part of these effects could be the consequence of enhanced glucose absorption via increased intestinal SGLT1 expression. However, the impact of NCS on glucose uptake has never been investigated. We aimed to investigate comprehensively the impact of NCS addition to an obesogenic diet on whole body and selective glucose uptake using a large animal model of morbid obesity. **Materials and Methods:** Twenty 3 years old miniature pigs were made obese by supplying them with high-fat, high sucrose diet during 5 months resulting in about doubling their weight (75.3 ± 6.01 vs 32.7 ± 2.90 kg). Once obese, half of the animals have their diet supplemented with a mixture of sucralose (92 mg daily) and acesulfameK (52 mg daily, sweetener group). This corresponds to the amount supplied by the daily ingestion of 1.5 L of sweetened beverage in humans. The control group received the same diet but without artificial sweeteners. Glucose uptake rates were obtained for the brain, the liver, the duodenum, the skeletal muscle and the adipose tissue using dynamic PET 18FDG scanning in the condition of hyperinsulinemia ($120 \text{ mU.kg}^{-1}.\text{h}^{-1}$) in euglycemia. Regional glucose uptake rates were obtained using Pmod through model analysis of PET images together with direct measurement of arterial input function using an external arterio-venous shunt. Clamp data were used to calculate whole body glucose uptake. **Results:** Whole-body glucose uptake was not significantly different between groups ($p > 0.05$) as a consequence of un-

changed skeletal muscle glucose uptake (3.2 ± 0.43 vs 3.1 ± 0.32 $\mu\text{moles}\cdot\text{min}^{-1}\cdot 100\text{g}^{-1}$). Glucose uptake was also unchanged by NCS for the subcutaneous fat. On the contrary, brain, liver, duodenal and visceral fat glucose uptake were all increased in sweetener vs control group; 29, 66, 57 and 40% for brain, liver, duodenal and visceral fat glucose uptake respectively. This was the consequence of an increased inward flux (K1). In the duodenum only, Phosphorylation rate (k3) was doubled. **Conclusion:** The unaltered whole body sensitivity does not preclude an unchanged glucose metabolism revealed by quantitative PET analysis. Several organs exhibited an increased glucose uptake in the NCS group that might play an important role in the negative health outcomes associated with chronic consumption of artificial sweeteners.

EP-0815

Altered brain processing after long-term artificial sweetener use

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Aim: Sugar-sweetened soft drinks have become extremely popular but fMRI data suggest that brain processing of sweet taste might be altered by long-lasting consumption of non-caloric sweeteners (NCS). Recently, long-term AceK intake has been found to affect cognitive function in mice through reduction of cortical glucose level (Ibi et al, 2018). Unfortunately, the glucose metabolism was obtained indirectly using glucose transporter expression. We aimed at evaluating the impact of NCS long-term consumption on resting brain activity and brain glucose metabolism in a large animal model using quantitative PET FDG imaging. **Materials and Methods:** Twenty 3 years old miniature pigs were made obese by supplying them with high-fat, high sucrose diet during 5 months resulting in about doubling their weight (75.3 ± 6.01 vs 32.7 ± 2.90 kg). Once obese, half of the animals have their diet supplemented with a mixture of sucralose (92 mg daily) and acesulfame-K (52 mg daily, sweetener group). The control group received the same diet but without artificial sweeteners. Glucose uptake rate was obtained for the brain using dynamic PET 18FDG scanning. Quantitative brain glucose uptake maps were reconstructed using Pmod with PET images and direct measurement of arterial input function using an external arterio-venous shunt. These maps were analyzed with SPM12 adapted to the particularities of the porcine brain. ROI based analysis was also performed with the help of our porcine brain atlas. **Results:** Brain glucose uptake was increased in NCS compared to control group (16.1 ± 0.96 vs 10.1 ± 0.97 , $p < 0.01$). This was a direct consequence of a parallel change in the dorsolateral prefrontal cortex that was the sole brain structure with a differential activation between the two groups (p FDR corrected 0.0001). ROI based analysis confirm the SPM analysis and demonstrated that the local change in glucose uptake was the direct consequence of an increased inward flux (K1) within the dorsolateral prefrontal cortex (0.113 ± 0.014 vs 0.082 ± 0.007 $\text{mL}\cdot\text{min}^{-1}$). Small volume correction performed on dopaminergic areas was not able to identify changes in brain activity between

groups. **Conclusion:** Long-term consumption of NCS increased the resting metabolism of the dorsolateral prefrontal cortex. No alteration of the activity of dopaminergic areas was observed unlike in humans with a paradigm integrating an oral caloric sweet tasting. The selective impact on K1 only confirms the probable modification of glucose transporter induced by NCS.

EP-0816

A possible link between reduced metabolic activity of Waldeyer's tonsillar ring and thoracic aortic wall inflammation in smoking status

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Purpose: Waldeyer's tonsillar ring contributes significantly to the immune system acting as the first line of defence. Smoking affects immune system lessening its response, while it has been considered as an important factor for atheroma generation in aortic wall and therefore vessel inflammation. Aim of our study is to investigate the correlation of Waldeyer's tonsillar ring and aortic activity in regards to smoking. **Material and Methods:** 222 adult patients (pts) (138 men, median age 65years; age range 26-87years) were identified having undergone clinical 18F-FDG PET/CT examinations at our centre. None of the 302 pts had any known history of head and neck carcinoma or lymphoma, neck lymph nodes or disease, tonsillectomy, recent upper respiratory tract infection, liver metastases, recent antibiotic medication intake and previous radiotherapy in the head and neck area. Metabolic activity (SUVmax) was measured in the thoracic aortic wall at the level of the aortic arch, liver parenchyma and Waldeyer's ring (a. Right palatine tonsil, b. Left palatine tonsil, c. Lingual tonsil, d. Nasopharyngeal tonsil). Pts have been categorized based on their smoking status as non-smokers (group 1), smokers (group 2), ex-smokers (group 3). **Results:** Sixty (27%, 36 men) out of 222 pts were no smokers, 59 pts (26.6%, 37men) were smokers and 103 pts (46.4%, 65men) were ex-smokers. Using ANOVA there was a significant statistical difference of the mean average SUVmax among the three groups in the Waldeyer's tonsillar ring with the lowest for the group 2, followed by group 3: a. Right palatine tonsil (Group 1: 4.62, Group 2: 3.82, Group 3: 4.1, $p < .006$) b. Left palatine tonsil (Group 1: 4.65, Group 2: 3.86, Group 3: 4.11, $p < .007$) c. Lingual tonsil (Group 1: 4.62, Group 2: 3.82, Group 3: 4.1, $p < .017$) d. Nasopharyngeal tonsil (Group 1: 4.61, Group 2: 3.81, Group 3: 4.1, $p < .037$). Multivariate analysis of the other demographic variables confirmed that smoking acts as an independent factor predicting lower SUVmax for Waldeyer's tonsillar ring. The mean average metabolic activity of thoracic aortic walls at the level of aortic arch for the smoking group was higher (SUVmax: 2.9) compared to the non-smoking group (SUVmax: 2.57) ($p = .001$). The latter interestingly was similar with the ex-smoking group (SUVmax: 2.55). **Conclusion:** Smokers have lower levels of 18F-FDG activity in Waldeyer's ring compared to non-smokers probably reflecting the suppressive effect of smoking on tonsillar immunity. We also found higher metabolic activity of thoracic aortic walls in smokers compared to non-smokers.

EP-0817**Increased VMAT2 expression in brain from birth to adulthood: A Longitudinal Study in Rodent from PET/CT**

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Introduction: Vesicular Monoamine Transporter type-2 (VMAT2) mainly located at nerve endings and reflected the density of dopaminergic neurons, its expression was strongly correlated dopaminergic neurons in striatum. The objective of this study is to evaluate the development of dopaminergic neurons in brains from birth to adulthood in rats. **Subjects and Methods:** A longitudinal study of Wistar rats ($n = 6$) was conducted to measure age-dependent changes of ^{18}F -PF-(+)-DTBZ in different brain regions with PET/CT. PET/CT acquisition was performed at different ages of rats at 40 min post intravenous injection of ^{18}F -PF-(+)-DTBZ. Imaging data were analyzed using PMOD 3.4 software and different brain regions, such as striatum, cerebellum, hippocampus, were collected. Specific uptake value (SUV) was collected, and striatal specific uptake ratio (SUR) were calculated as: (uptake in striatum - uptake in cerebellum) / uptake in cerebellum. **Results:** ^{18}F -PF-(+)-DTBZ uptake in striatum increased significantly from age of 2 month (SUV: 1.36 ± 0.21) to age of 8 month (SUV: 1.97 ± 0.32 , $P < 0.01$), and didn't vary until 12 month (SUV: 1.93 ± 0.18). However, SUR did not alter at these ages (SUR: 2.58 ± 0.38 , 2.45 ± 0.62 , 2.28 ± 0.18 , respectively). Besides increased uptake of ^{18}F -PF-(+)-DTBZ in striatum, ^{18}F -PF-(+)-DTBZ uptake in other brain regions, such as thalamus, hippocampus, did not change significantly. **Conclusion:** Age-dependent changes of ^{18}F -PF-(+)-DTBZ uptake were detected in striatum of rats, which reflect the increased density of dopaminergic neurons from birth to adulthood. ^{18}F -PF-(+)-DTBZ could be a tool to evaluate brain growth.

EP-0818**TSH and thyroglobulin Antibodies association with risk of malignancy of thyroid nodules**

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Background: Thyroid stimulating hormone (TSH) is traditionally considered as a principal stimulator of growth, differentiation and maturation of follicular thyroid cells. Objectives of the study-To evaluate the relation between TSH and thyroid anti bodies [(thyroglobulin Antibodies (Tg Ab) and thyro Peroxidase antibodies (TPO Ab)] before surgery, and differentiated thyroid cancer (DTC). **Methods:** Prospective study of 200 operated patients with nodular goiter (NG), between April 2009 and April 2013. All patients underwent surgery after euthyroid confirmation by TSH evaluation, Tg Ab and TPO Ab titration, echography and fine needle aspiration biopsy (fnab) of thyroid nodules more than 10mm or equal. **Results:** 14% of patients (28/200) have DTC. DTC frequency increase with TSH rising from 2.4% when TSH level is comprised in the interval $[0.25-0.99 \mu\text{UI/ml}]$ to 50% when TSH level is more than $4 \mu\text{UI/ml}$ or equal. This prevalence is much higher in patients group with TSH level comprised in the interval $[2 - 4.25 \mu\text{UI/ml}]$ than in patients group with TSH level comprised

in the interval $] 0.25 - 1.99 \mu\text{UI/ml}]$ 66% (21/32) vs 4.2% (7/168) ($p < 0.001$) respectively. Moreover, the mean TSH is significantly higher in patients with DTC than in patients with benign goiter ($2.45 \pm 1.01 \mu\text{UI/ml}$) vs ($1.03 \pm 0.81 \mu\text{UI/ml}$) ($p < 0.001$). Also, Malignancy prevalence was significantly higher in patients group with positive Tg Ab ($> 70 \text{ UI/ml}$) vs patients group with negative or indeterminate Tg Ab 55.5% (15/28), 6.4% (10/28) and 2% (3/28) respectively ($p < 0.001$). While, in the patients group with TPO Ab positive negative or indeterminate, there's no difference. **Conclusions:** The probability of cancer increase with TSH rising. Just as, positive Tg Ab increase significantly the risk of malignancy. Our results suggest that TSH and Tg Ab may give us complementary information in malignancy prediction, in association with clinical features, in particular in front of indeterminate cytology.

EP-0819**Thoracic duct scintigraphy by orally administered I-123 labeled long fatty acid analogue enclosed in gelatin capsule: A pilot study**

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Purpose/introduction: To validate the thoracic duct scintigraphy by orally administered iodine-123 labeled long fatty acid analogue, 15-(4-iodophenyl)-3(R,S)-methyl-pentadecanoic acid (I-123 BMIPP), enclosed in gelatin capsule. **Subjects & methods:** This study was approved by Institutional Review Board. I-123 BMIPP enclosed in gelatin capsule was administered with milk in 6 healthy subjects under fasting condition. Subsequently dynamic and serial static images were scanned to trace the passage of radiotracer. Finally SPECT/CT was scanned from neck to pelvis. **Results:** No adverse event was observed in all subjects. The capsules immediately burst in stomach after the administration and no residual radioactivity was observed in mouth and esophagus in all subjects. Subsequently I-123 BMIPP was absorbed from the intestine and reached the venous circulation through the thoracic duct. The thoracic ducts appeared at 80 - 160 minutes after the administration and visualized with maximum distinctness at 100 - 200 minutes after the administration. Bilateral thoracic duct (normal variant) was observed in 2 of 6 subjects. SPECT/CT demonstrated 3D-course of thoracic duct in the mediastinum. **Discussion/Conclusion:** Thoracic duct scintigraphy by orally administered I-123 BMIPP enclosed in gelatin capsule is a simple method to visualize thoracic duct. It will be useful for the detection of lymphatic leakage site in the patients with chylothorax.

EP-57**e-Poster Area**

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Preclinical and translational aspects -> Preclinical aspects -> Tumor biology

EP-0820**Analysis of Pulmonary Lymphangitic Carcinomatosis (PLC) in Non-Small Cell Lung Cancer (NSCLC): Applying Radiomics to PET/CT**

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Purpose: Pulmonary lymphangitic carcinomatosis (PLC) is defined as the spread of cancer through the lymphatic system into lung interstitium. The aim of this study was to correlate the outcome of PET/CT texture analysis features (Radiomics) to the histopathologic diagnosis of PLC in NSCLC. **Materials and Methods:** Sixty-five patients addressed for initial staging of NSCLC were retrospectively included. ^{18}F -FDG (FDG) PET/CT texture analysis was extracted using the QuantImage platform (<https://radiomics.hevs.ch/>) in a volume of interest $\geq 1\text{ cm}^3$ in the peritumoral suspected area of PLC within a range of 3 cm. Radiomics outcomes were correlated to the presence or absence of PLC on histopathology of the resected tumors using a logistic regression and multivariate stepwise regression for statistically significant features on univariate analysis with $p < 0.005$. **Results:** Among 65 included patients, 71% (46/65) had histologically confirmed PLC. Logistic regression analysis of 112 elements of the PET/CT-derived Radiomics features showed significant correlations ($p < 0.005$) with PLC for the following intensity-based elements: SUVmax, SUVmean (30% to 70% of SUVmax), SUVpeak (30% to 70% of SUVmax), SUVkurtosis (50% of SUVmax), TLG (50 to 70% of SUVmax), texture based-elements: GLCMsContrast_PET, GLCMsdiffVariance_PET, InnerLog_PET (sigma=75 to 325), MarginLog_PET (for sigma=75 to 275), MarginRieszN1_PET_X_scale and MarginRieszN1_PET_Z_scale. Multivariate stepwise analysis with $p < 0.05$ confirmed a significant positive regression for SUVmean (30% of SUVmax) ($R^2 = 0.28$). Allowing statistically significant CT-derived Radiomics added InnerLog_CT_sigma75 to the multivariate regression model and increased R^2 to 0.35, which was a statistically significant increase ($p = 0.025$). The sensitivity, specificity and AUC using a cutoff of 0.889 for SUVmean (30% of SUVmax) and 37 for InnerLog_CT_sigma75 predicting PLC were 89%, 90% and 0.893 and 76%, 79% and 0.775, respectively. **Conclusion:** FDG-PET/CT texture analysis of the peritumoral NSCLC space can help predict PLC using both PET- and CT-derived extracted texture features, in particular SUVmean (30% of SUVmax) and Log in the VOI with sigma of 75 for the CT. Thus, applying PET/CT texture analysis to the peritumoral space could be a powerful tool to investigate the peritumoral environment.

EP-0821

Analyzing Tumor Necrosis in NSCLC: Radiomics applied to FDG PET/CT Imaging

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Purpose: Radiomics consists of an image-based personalized tumor phenotyping process through mining of quantitative image features from standard-of-care medical imaging and can be used for instance in the quantitative characterization of tumor phenotypes or other physiological or pathological processes. The aim of this study was to correlate the outcome of PET/CT texture analysis features (Radiomics) to the histopathologic

presence of tumor necrosis in NSCLC. **Materials and Methods:** We retrospectively assessed 47 patients (mean age 65 ± 9 years) with histologically confirmed NSCLC and sampled surgical tumor specimens analyzed for the presence or absence of TN by histopathology. After delineation of the tumoral volume of interest, FDG PET/CT texture analysis was extracted using the QuantImage platform (<https://radiomics.hevs.ch/>), in addition to the quantification of minimum tumoral SUV (SUVmin). Featured outcomes were correlated to the presence or absence of TN on histopathology of the resected tumors using a logistic regression and multivariate stepwise regression for statistically significant features on univariate analysis with $p < 0.05$. **Results:** Among 47 included patients, 55% (26/47) had histologically confirmed TN. Logistic regression analysis of 251 elements of the PET/CT-derived Radiomics features showed significant or borderline correlations with TN for the following intensity-based elements: SUVmin ($p = 0.007$), HUMean_3abs -or Mean Hounsfield Unite (HU) of the main tumor voxels with $\text{SUV} > 3$ ($p = 0.045$), int_HUMean_42rel -or Mean HU of the main tumor voxels with $\text{SUV} > 42\%$ of the SUVmax- ($p = 0.030$) and texture based-element: GLCMsDiffEntropy_PET_1_8 -or Difference entropy measure of the GLCMs computed with distance d and number of gray levels n for CT or PET- ($p = 0.054$). All the resultant variables showed statistically significant difference of means between the two groups ($p = 0.001$, $p = 0.023$, $p = 0.021$ and $p = 0.044$, respectively). Multivariate stepwise analysis confirmed a significant positive correlation for the model combining SUVmin and int_HUMean_42rel with a global $R^2 = 0.52$. **Conclusion:** FDG-PET/CT texture analysis of the tumoral volume of NSCLC can help predict TN using both PET- and CT-derived extracted texture features, in particular SUVmin and Mean HU of the main tumor voxels with $\text{SUV} > 42\%$ of the SUVmax. Thus, PET/CT texture analysis could be an effective tool to detect necrotic changes in tumors.

EP-0822

Pretargeted radioimmunotherapy of colorectal cancer through bioorthogonal chemistry

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Introduction: The last decades, pretargeting radioimmunotherapy (PRIT) systems dissociating the injection of mAbs from the one of the radiolabelled probe were developed. Bioorthogonal chemistry, the most recent PRIT approach, is based on the covalent interaction between two chemical entities, a *trans*-cyclooctene (TCO) and a tetrazine (TZ). Using fluorescent TZ, we had identified the best candidate for PRIT in two models of colorectal cancer (CRC), *i.e.* mAb-PEG₆-TCO (Rondon A., Ty N. et al., 2017). Subsequently, we wanted to evaluate biodistributions of pretargeting components in these models and PRIT efficiency on CRC disseminated tumors. **Material and Methods:** Experiments were performed on two models of CRC, one subcutaneously implanted (HT29 cells; Ts29.2 mAb) and one disseminated in the peritoneal cavity (A431-CEA-Luc cells; 35A7 mAb).

In HT29 model, 50 or 200 µg of Ts29.2-TCO were intravenously (i.v.) injected in Nude mice followed 24h later by i.v. administration of 10 MBq of TZ-PEG₄-DOTA-¹⁷⁷Lu. In the A431-CEA-Luc model, 50 µg of 35A7-TCO were injected either i.v. or intraperitoneally (i.p.), followed 24h later by i.p. injection of 10 MBq of TZ-PEG₄-DOTA-¹⁷⁷Lu. At selected times, mice were imaged using SPECT-CT then sacrificed and organs counted in a γ-counter. For therapy study, mice were i.p. injected with 50 µg of 35A7-TCO followed 24h later by i.p. injection of 10, 20 or 40 MBq of TZ-PEG₄-DOTA-¹⁷⁷Lu. Taking into account disease activity index, tumor growth was blindly monitored using bioluminescence imaging or survival analysis. **Results:** In both models, SPECT-CT imaging and biodistribution studies showed a rapid clearance of TZ-PEG₄-DOTA-¹⁷⁷Lu independently of its injection route (< 3h). In HT29, the %ID/g was under 1% in tumor and the tumor/blood ratio reached a maximum of 4.5 at 144h post i.v. injection. The tumor/blood ratio ranged from 10 to 70 in A431-CEA-Luc when both mAbs and TZ-PEG₄-DOTA-¹⁷⁷Lu were i.p. injected. The %ID/g in A431-tumors increased from 1 to 7% respectively 24 to 72h after i.p. injection. PRIT carried on A431-CEA-Luc showed neither significant improvement of survival nor slow-down of tumor growth compared to control groups suggesting a lack of TZ interaction with mAbs-TCO. **Conclusion:** Despite a high tumor/blood ratio in A431 model, disappointing therapy results highlight the complexity of such approaches and the importance to optimize pretargeting components to obtain the best TCO/TZ interaction. For this purpose, different TZ probes will be assessed to determine the best configuration to use for an efficient PRIT on CRC.

EP-0823

Potential protection of renal function in ¹⁷⁷Lu-octreotate treatment using alpha-1-microglobulin

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Background: Peptide receptor radionuclide therapy (PRRT) with ¹⁷⁷Lu-octreotate is used to treat patients with inoperable neuroendocrine tumours (NETs). Clinical results show prolonged survival and improved quality of life, but the cure rate is low. The kidney is one of the major risk organs that limits the treatment. Increased tumour control could therefore be achieved if more effective renal protection were used. A recombinant form of alpha-1-microglobulin (rA1M), a human radical scavenging protein, has been proposed as kidney protector in PRRT with ¹⁷⁷Lu-octreotate. Preclinical studies have shown that rA1M has the ability to protect normal tissues from oxidative stress and its biodistribution is similar to the somatostatin analogues used in PRRT. Here, for the first time, we investigate if rA1M affects therapeutic response in tumour tissue during PRRT with ¹⁷⁷Lu-octreotate. **Aim:** To study if co-administration of rA1M with ¹⁷⁷Lu-octreotate affects the biodistribution of ¹⁷⁷Lu and tumour volume response compared with a single injection

with ¹⁷⁷Lu-octreotate. **Methods:** The biodistribution of ¹⁷⁷Lu was studied in female BALB/c nude mice with xenografts of human medullary thyroid carcinoma, GOT2. The animals were injected with either ¹⁷⁷Lu-octreotate or ¹⁷⁷Lu-octreotate and rA1M. The animals were terminated at different time points, up to a week after injection. Activity concentration in tissues and organs were measured ex vivo and compared between the groups. The potential effects of rA1M on the tumour response after ¹⁷⁷Lu-octreotate treatment were investigated in female BALB/c nude mice, transplanted with human small intestine NET, GOT1. Three groups of mice were treated with either rA1M, ¹⁷⁷Lu-octreotate or ¹⁷⁷Lu-octreotate and rA1M. Volume of the tumours were measured and followed after treatment and compared between the groups. **Results:** Analysis of ¹⁷⁷Lu biodistribution showed no statistical significant difference in the investigated organs and tissues between ¹⁷⁷Lu-octreotate or ¹⁷⁷Lu-octreotate and rA1M. Tumour volume evaluation showed a decrease in mean tumour volume during the first two weeks for both ¹⁷⁷Lu-octreotate and ¹⁷⁷Lu-octreotate + rA1M. Thereafter, the mean volume increased again in a similar way in both groups. In the rA1M only treated group, 9 out of 10 mice displayed no decrease in tumour volume. **Conclusions:** No negative effects in biodistribution of ¹⁷⁷Lu or tumour volume response were observed when co-administering rA1M to ¹⁷⁷Lu-octreotate injection in mice. These findings suggest that rA1M is a potential kidney protector and that the combination treatment of ¹⁷⁷Lu-octreotate and rA1M should be further studied.

EP-0824

Characterization Of Sub-regional Heterogeneity Of Hypoxia With ¹⁸F-MISO PET/CT, Bold fMRI And Immunohistochemistry In Human Breast Tumor Xenograft: Initial Study

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Objective: To demonstrate that both 18F-fluoromisonidazole positron emission tomography computed tomography (¹⁸F-MISO PET/CT) and function magnetic resonance imaging blood oxygenation level dependent (fMRI BOLD) can map intratumoral sub-region of hypoxia consistently. **Materials and Methods:** Both ¹⁸F-MISO PET/CT and BOLD fMRI were performed successively in nude mice bearing human breast cancer MCF-7 cell xenograft. Using tumor to background ratio (TBR) >1.40 and hypoxia sub-volume (HSV) /tumor volume(TV) ≥ 50% as threshold, chronic hypoxia was divided into three sub-types: non-hypoxia(NH), diffused-hypoxia(DH) and localized-hypoxia(LH). For NH and DH tumors, unselective ROIs were delineated to calculate ΔT2*. For LH tumor, MIM software was used to integrate PET/CT/MRI and to locate hottest foci and distinguish hypoxia and non-hypoxia sub-regions inside tumor. The selective ROIs were delineated to calculate ΔT2* in LH subtype. Finally, xenografts were assayed immunohistochemically to obtain the expression level of hypoxia-inducible factor(HIF)-1α. **Results:** 62 xenografts were divided into 23 NHs, 11 DHs and 28 LHs. There was a weak correlation between TBRs and TV values ($r = 0.30$, $P = 0.018 < 0.05$) when all 62 xenografts were considered as a whole

set. However, no significant correlations existed in NH ($r=0.20$, $P=0.055$) or DH ($r=-0.35$, $P=0.280$) or LH ($r=0.31$, $P=0.108$) subtype separately. The ΔT_2^* values of NH xenografts ($62.80\% \pm 21.60\%$) were significantly different to the ΔT_2^* values of DH ($15.10\% \pm 5.30\%$) and ΔT_2^* values of hypoxic sub-regions in LH xenografts ($16.60\% \pm 10.10\%$), with P value < 0.001 for both. In LH xenografts, ΔT_2^* values of nonhypoxic and hypoxic sub-regions were $50.07\% \pm 16.60\%$ and $16.60\% \pm 10.10\%$ respectively, which represented a significant difference ($t = 13.00$, $P < 0.001$). A correlation also existed between entire TBRs and HIF-1 α scores ($r = 0.43$, $P = 0.016 < 0.05$). There were significant correlations between TBRs and HIF-1 α scores in NH group ($r=0.52$, $P=0.024$) and DH group ($r=0.47$, $P=0.045$), but not in LH group ($r=-0.22$, $P=0.262$), when these three subtypes were analyzed individually. Between each sub-group, there was a significant difference between NH vs DH ($t = 31.97$, $P < 0.001$) group or NH vs LH ($t = 4.44$, $P < 0.001$) or DH vs LH ($t = 3.09$, $P = 0.011$). **Conclusions:** Combining with TBR and HSV, hypoxic sub-region inside xenograft could be described more particularly and could be demonstrated by animal ^{18}F -MISO PET/CT, animal BOLD fMRI and immunohistochemically analysis consistently.

EP-0825

Radiolabelled PLGA nanoparticles for cancer imaging

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Purpose/Introduction: Poly-lactic-co-glycolic-acid nanoparticles (PLGA-NPs) have been approved by FDA to deliver encapsulated anticancer drugs but they could also be used for nuclear medicine theranostic approach. Aim of our study was to radiolabel fluorescent PLGA-NPs with $^{99\text{m}}\text{Tc}$ and test them in animal models of cancer to study their biodistribution and accumulation in tumors. **Subjects and Methods:** PLGA-NPs were radiolabelled with $^{99\text{m}}\text{Tc}$ using succinimidyl-6-hydrazinonicotinate hydrochloride (Hynic) as bifunctional chelator. Labelling efficiency (LE) was calculated by thin-layer chromatography (iTLC) and HPLC. To find the most suitable stationary and mobile phases, several solutions with different chemical characteristics were tested. For tumor targeting studies, a syngeneic mouse model was obtained by subcutaneous injection in the right thigh of 10^6 J774a.1 cells (reticulum sarcoma cell line) in Matrigel: Medium (50:50). Pharmacokinetics of fluorescent PLGA-NPs was determined in vivo at 2, 6, 24, 48, 72, 96, 168 and 240h, by optical imaging with a Kodak FX station. At the end of acquisition, animals were sacrificed and organs collected for ex-vivo imaging. Regions of interest (ROIs) were drawn to calculate target-to-background ratios. Biodistribution of $^{99\text{m}}\text{Tc}$ -PLGA-NPs was determined by injecting 5.5 MBq of radiopharmaceutical in the lateral tail vein. Static planar posterior images were acquired using a high-resolution portable mini γ -camera at 6 and 24h. After scan, animals were sacrificed and major organs collected and counted in a single-well γ -counter. Time-activity curves in organs were obtained for both in vitro and ex vivo data. **Results:** Both iTLC and HPLC quality controls revealed a LE of $77\% \pm 5\%$. After purification by size-exclusion chromatography, the radiochemical purity was $>90\%$. Optical imaging studies showed

mainly liver excretion and high uptake in tumors starting from 6h with peak at 72h, confirmed by ex-vivo analysis. Scintigraphic studies of radiolabelled NPs showed that the uptake of $^{99\text{m}}\text{Tc}$ -PLGA-NPs increases from 6 to 24h. The highest tumor-to-muscle ratios (>3) were obtained at 24h. **Conclusions:** Radioactive PLGA-NPs showed a good accumulation in aggressive and high proliferative tumor, starting at 6h and increasing at 24h p.i. $^{99\text{m}}\text{Tc}$ -PLGA can be considered a promising radiopharmaceutical for the diagnosis of malignant tumours. In the future NPs could be radiolabelled with different isotopes for theranostic approach.

EP-0826

Stereotactic radiotherapy boost after definite chemoradiation for non-responding locally advanced NSCLC based on early response monitoring ^{18}F -FDG-PET/CT

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Purpose: The prognosis of locally advanced non-small cell lung cancer (NSCLC) remains poor despite intensive treatment with chemoradiation. To improve local tumor control, this planning study evaluated a stereotactic boost after concurrent chemoradiotherapy (30x2 Gy) aiming to plan a biologically effective dose (BED) of at least 100 Gy that is known to be required for acceptable tumor control probability. The maximum achievable boost directed to radioresistant primary tumor subvolumes based on pre-treatment fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG-PET/CT) (pre-treatment-PET) and on early response monitoring ^{18}F -FDG-PET/CT (ERM-PET) was compared. **Subjects and Methods:** For ten patients with stage III NSCLC that showed a poor response to treatment (total lesion glycolysis decrease $<45\%$) on the ERM-PET, a stereotactic boost (using a volumetric-modulated arc radiotherapy technique) was planned on both the ERM-PET ($\text{PTV}_{\text{boost,ERM}}$) and the pre-treatment-PET ($\text{PTV}_{\text{boost,pre-treatment}}$). A 70% SUV_{max} threshold with a 7 mm margin was used to segmentate the radioresistant subvolumes towards which the boost dose was directed. The dose was escalated till organ at risk (OAR) constraints were met, aiming to plan a minimal dose of 18 Gy in 3 fractions resulting in a minimum total equivalent uniform dose in 2 Gy fractions (EQD_2) of 84 Gy (BED 100.8 Gy). **Results:** In five patients, $\text{PTV}_{\text{boost,ERM}}$ was 9–40% smaller relative to $\text{PTV}_{\text{boost,pre-treatment}}$. Overlap of $\text{PTV}_{\text{boost,ERM}}$ with organs at risk (OARs) decreased also compared to overlap of $\text{PTV}_{\text{boost,pre-treatment}}$ with OARs. However, any overlap with OARs remained in 4/5 patients resulting in minimal differences between planned dose before and during treatment. Median dose (EQD_2) covering 99% and 95% of $\text{PTV}_{\text{boost,ERM}}$ were 15 Gy (range 3–30) and 18 Gy (range 6–32), respectively. The median boost volume receiving a physical dose of ≥ 18 Gy (V18; which equals a total EQD_2 of 84 Gy) was 88%. V18 was $\geq 80\%$ for $\text{PTV}_{\text{boost}}$ in six patients. **Conclusion:** A clinically relevant stereotactic boost, resulting in an $\text{EQD}_2 \geq 84$ Gy, to volumes with high initial or persistent ^{18}F -FDG-uptake could

be planned in addition to 60 Gy conventional radiotherapy. Differences between planned dose before and during treatment were minimal. However, as an ERM-PET also monitors changes in tumor position, we recommend to plan the boost on the ERM-PET.

EP-0827

Fluorescence labeled HSA as an imaging agent for a SPARC (secreted protein acidic and rich in cysteine) expressing glioblastoma

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Purpose: Human serum albumin(HSA) is used as a drug carrier or radioisotope labeled theranostic agent for clinical application. Though the mechanism of HSA uptake in tumor is still unclear, it has been known that albumin targets tumor based on the leaky blood vessel-related enhanced permeability and retention (EPR) effect, indicating that albumin accumulates in tumor by simple infiltration, not by specific uptake. However, it has been suggested that secreted protein acidic and rich in cysteine (SPARC) could sequester albumin in tumor stroma and partly relate to the tumor specific uptake of albumin. We investigated the role of SPARC for HSA uptake in glioblastoma. **Methods:** Fluorescence dye FNR648-N3 and Cy5-N3 were bound to label HSA by click chemistry reaction. Human glioblastoma cell line U87MG was used for evaluating SPARC-dependant HSA uptake. SPARC expression was down-regulated with shSPARC in U87MG cells (SPARC KD). After treatment with FNR648 or Cy5-HSA in U87MG and SPARC KD U87MG, fluorescent signals were measured with confocal microscopy. U87MG and SPARC KD U87MG cells were subcutaneously injected to generate xenograft model. After intravenous injection of FNR648-HSA in tumor-xenografted mouse, fluorescent signals were detected with IVIS Lumina II. Immuno-fluorescence staining with tumor frozen section was proceeded. Blood vessel was stained by CD31 antibody, and cell nucleus was stained with DAPI. **Results:** SPARC mRNAs and proteins were highly expressed in U87MG, but not in SPARC KD U87MG. In vitro HSA uptake test showed that more Cy5-HSA was accumulated in U87MG than SPARC KD cells. SPARC treatment successfully recovers the uptake of fluorescent HSA in SPARC KD cells. In xenograft model, more FNR648-HSA was accumulated in U87MG than SPARC KD U87MG tumor. HSA accumulation in U87MG tumor region was maximized at 4 hour after injection in U87MG tumor, showing 4 times higher uptake than SPARC KD U87MG. FITC-dextran was used for vessel permeability test, and U87MG tumor showed relatively more permeable to vessel than SPARC KD. Though FITC-dextran was gradually excreted from both tumors, FNR648-HSA was accumulated in U87MG tumor. In confocal imaging of tumor section, albumin was more

infiltrated into tumor stroma in U87MG tumor than SPARC KD U87MG. On the other hand, SPARC KD U87MG tumor showed retained albumin in blood vessel. **Conclusion:** We visualized SPARC-dependent tumor targeting of fluorescence labeled HSA in glioblastoma. Our results demonstrate that fluorescence labeled HSA is an efficient imaging agent to target SPARC over expressing glioblastoma with enormous potential.

EP-0828

Preclinical characterization of EGFR-expression-targeting hexapods nanogold particles for photo-thermal evaluation uses

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Introduction: Nanogold particles (AuNP) in past studies can absorb specific radio-frequency and convert it into heat energy, leading to rise the temperature around particles significantly and achieve photo-thermal effect; however, they are not widely approved in clinical uses. In this study, we have synthesized novel hexapods nanogold particles (HAuNP) conjugated with EGFR-expression-targeting C225 antibody and evaluated their potential therapeutic effect in vitro and in vivo. **Materials and Methods:** Sphere nanogold (20 nm), gold chloride trihydrate (HAuCl₄) and Polyvinylpyrrolidone (PVP) were purchased from Sigma-Aldrich. HAuNPs were synthesized by reductive reaction of HAuCl₄ in DMF and ddH₂O. HAuNPs were then analyzed by TEM. The C225 antibody conjugated HAuNPs (C225-HAuNPs) were synthesized and labeled with Ga-67 by a bi-functional chelator NODA. The radiochemical purity (R.C.P.) was determined by ITLC system. After injection with C225-HAuNPs on U87-MG tumor-bearing nude mice, the photo-thermal effect was evaluated by Laser (808 nm) and ThermoThron-RF8. The animal SPECT imaging and bio-distribution was also performed. **Results:** The photo-thermal convert efficacy of HAuNPs was analyzed (>65%); it is better than that of sphere AuNPs in both Laser and ThermoThron-RF8 groups. The R.C.P. of ⁶⁷Ga-C225-HAuNPs was over 90% after purification and showed stable results for 6 hours in room temperature and HEPES buffer. Both in vitro and in vivo study showed significant photo-thermal convert efficient of HAuNPs; the inhibition results of tumor volume of mice were determined after treatment started. SPECT imaging and bio-distribution results showed specific collection of ⁶⁷Ga-C225-HAuNPs in U87-MG tumors. **Discussions:** In this study, ⁶⁷Ga-C225-HAuNPs were successfully developed. Our preclinical characterization of HAuNPs exhibited superior photo-thermal conversion efficiency compared to that of sphere AuNPs. The potential therapeutic effect of C225-HAuNPs was determined in both in vitro and in vivo. We suggested that novel EGFR-expression-targeting hexapods nanogold particles can be useful in photo-thermal evaluation uses in the future.

EP-0829

Ra223 induced clustered DNA damage reduces cell survival independently of androgen receptor variant 7 expression

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Background: Late stage prostate cancer metastasize to distant organs and can be found in liver, lungs and bones and at this stage disease challenging to cure. Usually the treatment involves surgery, radiation therapy, immunotherapy or chemotherapy. In case of castration therapy the treatment success is dependent on androgen signaling and androgen receptor variant 7 (ARv7) expression in cells results in abiraterone acetate and enzalutamide resistance. This receptor variant is missing the ligand binding domain resulting in constitutive activity of the receptor. To manage bone metastasis patients can receive Ra-223 treatment which elevates pain and reduces the extent of the disease. The Ra-223 alpha emitter is a calcium analog that associates with hydroxyapatite found in bones. Even though Ra-223 treatment in clinics is highly successful the molecular mechanisms and its ability to induced DNA damage is poorly documented. Therefore the aim of the study is to understand how Ra-223 induces cell death and how ARv7 expression affects the cell survival in case of Ra-223 treatment. **Results:** In vitro Ra-223 treatment results in similar survival in ARv7 expressing cells and ARv7 negative cells. Furthermore, Ra-223 was able to induce 53BP1 and gammaH2AX foci that was consistent with track like structures. The co-localization of 53BP1 and gammaH2AX was detectable after 1, 4 and 24 hours post exposure to Ra-223. Ra-223 treatment was consistent with DNA fragmentation pattern that are similar to ones found in high-LET irradiated cells. This suggests that Ra-223 treatment induces clustered DNA damage, a form of complex DNA lesions within short stretch of DNA. Furthermore, we show kinetics of double-strand break repair by analyzing phosphorylated DNA-PKcs status after Ra-223 using flow cytometry. **Conclusions:** Ra-223 treatment reduces cell survival independently of ARv7 expression in cells due to induction of clustered DNA damage.

EP-0830

MicroRNA-494 is a potential biomarker of bone metastatic for prostate cancer and via targeting of CXCR4 in PC-3

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Objectives: Early and accurate diagnosis of bone metastases is important for clinical staging and treatment of prostate cancer patients (PCa). Bone metastases of PCa is dependent on a complex microenvironment that includes the osteoblasts, the osteoclasts. Recent researches showed that osteoblastic differentiation and activation are essential parts of bone metastases and also involved the osteolytic. However, the sensitivity of bone scan for lytic metastatic lesions is low, because lytic bone lesions showed not too much uptake of the Tc-MDP in most cases. The expression of miRNAs profiles was significant difference in different bone metastatic patients and it may be helpful for diagnose bone metastasis of prostate cancer. **Methods:** In the present study, the differentially expressed miRNAs were identified

between the primary PCa and different bone metastatic PCa samples by comparing their expression profiling using miRNA microarray. MiR494 levels were also examined in serum samples by using real-time quantitative reverse transcription polymerase chain reactions to confirm the ectopic expression. Then we used the Rt-PCR and Western blot to find the target gene of miR-494-3p in vitro; then we use the co-culture system to clarify the molecular mechanism for bone metastasis of prostate cancer in our project. **Results:** Microarray data revealed that 45 miRNAs were upregulated and 25 miRNAs were downregulated by 2 times compared between lytic and osteoblast bone metastatic of PCa, and miR-494 was one of the miRNAs being most significantly downregulated in lytic bone metastatic of PCa; it is just the reverse in the osteoblast bone metastatic. We found the target gene of miR-494-3p might be CXCR4 via Rt-PCR and Western blot in PC-3; then we found miR-494 can reduce osteoclast genesis when co-culture PC3 and RAW264.7 cells. In addition, we found that the expression of miR-494 influence the osteoclast genesis in RAW264.7 cells, likely via a c-Fos/NFATc1-mediated mechanism. **Conclusions:** These findings indicated that microRNA-494 is a potential biomarker of bone metastatic for prostate cancer and maybe via targeting the CXCR4 to have a tumor suppressive effect on lytic bone metastatic PCa.

EP-0831

SPECT/CT imaging of tumor apoptosis induced by chemotherapy using ^{99m}Tc-labeled dendrimer-entrapped gold nanoparticles

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Purpose: Noninvasive imaging of apoptosis induced by chemotherapy in tumors is of great value in the evaluation of treatment effect. In this study, we report the synthesis, characterization and utilization of ^{99m}Tc-labeled dendrimer-entrapped gold nanoparticles (Au DENPs) for targeted SPECT/CT imaging of tumor apoptosis induced by chemotherapy. **Methods:** Generation 5 (G5) poly(amidoamine) (PAMAM) dendrimers (G5-NH₂) were sequentially conjugated with 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) and duramycin as a targeting ligand for apoptotic tumor cells, and then were used as a template to entrap gold nanoparticles. Followed by acetylation of the remaining dendrimer surface amines and radiolabeling of ^{99m}Tc, the SPECT/CT dual mode nanoprobes were formed. The developed multifunctional Au DENPs before and after ^{99m}Tc radiolabeling were well-characterized. **Results:** The multifunctional Au DENPs display favorable water solubility, colloidal stability under different conditions, cytocompatible in a given concentration range and can be effectively labeled by ^{99m}Tc with high radiochemical stability. Furthermore, the multifunctional nanoprobes are able to be used for targeted SPECT/CT imaging of apoptotic cancer cells *in vitro* and tumor apoptosis after doxorubicin treatment in the established subcutaneous tumor model *in vivo*. **Conclusion:** The designed duramycin-functionalized Au DENPs might have the potential to be employed as a nanoplatform for the detection of apoptosis and early tumor response to chemotherapy.

EP-58

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Preclinical and translational aspects
-> Translational aspects -> Cardiology

EP-0832

Absolute myocardial perfusion and flow reserve with ^{99m}Tc -teboroxime dynamic SPECT in a porcine model

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Aim: Absolute myocardial blood flow (MBF) and myocardial flow reserve (MFR) provide incremental diagnostic and prognostic information compared to relative perfusion. The introduction of dedicated cardiac cadmium-zinc-telluride (CZT) SPECT cameras makes dynamic imaging feasible but currently used ^{99m}Tc -based tracers suffer from non-linear extraction at higher flow rates. Here, we aim to assess MBF and MFR in a pig model using ^{99m}Tc -teboroxime, a radiotracer with high myocardial uptake and rapid myocardial clearance. **Materials and Methods:** Healthy pigs (n=5) underwent a two-day rest-adenosine stress imaging protocol. A 30-min dynamic SPECT scan (Discovery NM530c) was performed after administration of 370 MBq ^{99m}Tc -teboroxime. Colored microspheres, serving as gold standard for MBF assessment, were injected simultaneously with the tracer. Images were reconstructed with CT-based attenuation correction (AC). Since no kinetic model for ^{99m}Tc -teboroxime is available, absolute perfusion quantification was performed using commercially available kinetic models (4DM software, 1-tissue compartment (1CM) and net-retention for either ^{99m}Tc , ^{201}Tl or ^{13}N -ammonia). Perfusion measurements (segmental and vascular territory) were correlated with microsphere-derived MBF and MFR. **Results:** ^{99m}Tc -teboroxime demonstrated a fast wash-out from the myocardium with a half-life of 502 ± 167 sec. 8 AC scans were obtained but only two animals completed the full rest-stress protocol of which one animal did not respond to adenosine. Regional and segmental SPECT- and microsphere-derived perfusion at rest and stress demonstrated a relatively homogenous tracer distribution. Despite differences in absolute values between SPECT and microsphere derived MBF, the correlation for MBF and MFR were $r \geq 0.56$ ($p \leq 0.03$) and $r \geq 0.94$ ($p < 0.001$), respectively. Bland-Altman plots showed the best agreement between SPECT and microsphere-derived MBF for the ^{99m}Tc 1CM kinetic model (per vascular territory: bias -0.21 ml/g/min (limits of agreement (LOA): -0.01 - 1.7 ml/g/min) and per segment bias -0.32 ml/g/min (LOA: -0.30 - 1.95 ml/g/min) while the ^{201}Tl 1CM kinetic model was best suited for the assessment of MFR (bias -1.4,

LOA: 0.36 - 3.16 per vascular territory). However, none of the kinetic models used in this study perfectly reflected the kinetics of ^{99m}Tc -teboroxime. **Conclusion:** Non-invasive imaging and assessment of absolute MBF and MFR with ^{99m}Tc -teboroxime is feasible using a dedicated cardiac SPECT camera. Our study demonstrated the fast myocardial wash-out that could enable rapid serial studies but further optimization of kinetic models specifically developed for ^{99m}Tc -teboroxime and comparison to routinely used ^{99m}Tc -tracers is warranted to evaluate possible clinical applications.

EP-0833

Characterization of a ^{68}Ga -labeled Angiotensin peptide coupled to Rhodamine for diagnostic imaging of heart.

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Objectives: Rhodamine (Rh) is a lipophilic cation, similar to ^{99m}Tc -MIBI that specifically accumulates in the myocardium. In an effort to formulate a PET-based cardiac agent with enhanced cardiac targeting efficiency, we linked Rh to angiotensin II (Ang II), an 8 amino acid peptide that has been known to play an important role in cardiovascular function. In this study we investigate the ^{68}Ga -labeled Rh-Ang II conjugate for its potential as a cardiac imaging agent. **Methods:** Rh-Lys(DOTA)-Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-CONH₂ was prepared conveniently and successfully by standard solid-phase peptide synthesis according to Fmoc/HBTU chemistry. Rh-NHS ester was coupled to the Ang II peptide through the amino group of Lys residue and radiolabeled with ^{68}Ga via DOTA chelator. Metabolic stability of the radiotracer was examined in human plasma and in vivo biodistribution and pharmacokinetics was performed on Balb/c mice and Sprague Dawley rats. **Results:** The Rh-Ang II conjugate was radiolabeled efficiently with ^{68}Ga (>75%) as determined by radio-HPLC analysis and showed sufficient metabolic stability in human plasma. In mice, the radiotracer displayed efficient clearance from the blood and excreted from the body mainly through the renal route with some elimination by the hepatobiliary system. The radiotracer uptake in the heart was found to be $1.85 \pm 0.59\%$ ID/g as early as 30 min post-injection. The accumulation in other major organs including liver, lungs, stomach, intestines and kidneys was below 8% ID/g. A high uptake by these organs may interfere with the efficient visualization of the heart. In case of rats, the radiotracer showed better pharmacokinetic characteristics, with low uptake of radioactivity in the major body organs/tissues (<4.0% ID/g). The uptake of ^{68}Ga -Rh-Ang II in the heart, $1.91 \pm 0.65\%$ ID/g, was higher than the uptake found in the blood and muscle resulting in good heart-to-blood and heart-to-muscle ratios. Additionally the radiotracer exhibited cardiac extraction values comparable to ^{99m}Tc -MIBI in rat hearts. **Conclusions:** Our initial findings suggest that the combination of two cardiac specific biomolecules is an attractive approach to enhance targeting efficiency and for rapid and efficient diagnostic imaging of heart. Further studies are in progress to determine the full potential of this cardiac imaging agent.

EP-0834

Feasibility of ^{99m}Tc -PYP SPECT/CT for quantitative evaluation of ATTR cardiac amyloidosis

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Introduction/Purpose: Planar scintigraphy with pyrophosphate (^{99m}Tc -PYP) is often used in the differentiation of ATTR cardiac amyloidosis. However, hybrid SPECT/CT imaging also allows similar precise anatomical localization and superior characterization of foci of increased tracer uptake when compared to planar imaging. This study evaluated the ability of SPECT/CT with ^{99m}Tc -PYP to distinguish ATTR cardiac amyloidosis from other causes of heart failure. **Materials and Methods:** Fifty patients (25 with ATTR, and 25 with other causes of heart failure) underwent myocardial imaging using ^{99m}Tc -PYP. Planar and SPECT/CT images of all cases were assessed. The degree of tracer accumulation to the left ventricular myocardium was calculated using both semi-quantitative and quantitative analyses. Semi-quantitative scores were set as follows: 0=no cardiac uptake; 1=cardiac uptake<bone; 2=cardiac uptake=bone, and 3=cardiac uptake>bone in planar images and 0=LV wall<LV lumen, 1=LV wall=LV lumen, 2= a part of LV wall>LV lumen, and 3=diffuse LV wall>LV lumen in SPECT/CT. In quantitative analysis using planar images, regions of interest (ROIs) were drawn circularly over the heart as targets and the contralateral chest for background, and the heart-to-contralateral chest ratio (H/CL) was calculated. In quantitative analysis using SPECT/CT, the ROIs were drawn over the maximum LV wall as a target and the LV lumen for background, and the maximum LV wall thickness-to-LV lumen ratio (LV-W/L) was calculated. **Results:** Both score from semi-quantitative analysis and index from quantitative analysis from planar images in the ATTR cardiac amyloidosis group were significantly higher than those of other groups (ATTR; 2.8 ± 0.7 vs. others; 1.1 ± 0.8 using semi-quantitative analysis and ATTR; 1.9 ± 0.4 vs. others; 1.2 ± 0.1 using quantitative analysis). Both values from SPECT/CT imaging in the ATTR cardiac amyloidosis group were also significantly higher than those of other groups (ATTR; 2.3 ± 0.7 vs. others; 0.6 ± 0.2 using semi-quantitative analysis and ATTR; 2.3 ± 0.7 vs. others; 0.6 ± 0.2 using quantitative analysis). Sensitivity, specificity, and accuracy using both semi-quantitative and quantitative analysis of planar images were 90%, 100%, and 93% and in SPECT/CT imaging were 100%, 100%, and 100%, respectively. The AUC values using both semi-quantitative and quantitative analysis in SPECT/CT imaging were higher than those in planar images (1.00 vs. 0.93 using semi-quantitative analysis and 1.00 vs. 0.95 using quantitative analysis). **Conclusion:** This study suggested that the relatively simple semi-quantitative and quantitative protocols using ^{99m}Tc -PYP SPECT/CT might be more useful to distinguish ATTR cardiac amyloidosis from other causes of heart

failure than the conventional methods and should be further validated through larger prospective studies.

EP-59

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Preclinical and translational aspects -> Translational aspects -> Neurology

EP-0835

In vitro and in vivo imaging of inflamed carotid atherosclerotic plaque in patient with a recent ischemic stroke using the TSPO ligand ^{18}F -PBR06

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Aim: Inflamed plaques induce stenosis in the carotids and are symptomatic in ischemic stroke. Thus, imaging inflammation may allow selecting patients who would benefit from carotid endarterectomy. ^{18}F -FDG uptake correlates to the level of inflammation in the atheromatous plaque, but both signal-to-noise (SNR) ratio and specificity are low. The aim of this study was to assess the utility of ^{18}F -PBR06, a high-affinity translocator protein (TSPO, 18kDa) radioligand, to image inflamed symptomatic plaques. **Materials and Methods:** High resolution micro-imaging (HRMI) was performed on 5 paraffin-embedded, formalin-fixed atherosclerosis plaques after carotid endarterectomy of patients affected by ischemic stroke. TSPO genotyping was available for 2 patients (1 high- and 1 mixed-affinity binder). After dewaxing, rehydration and unmasking, binding assay was performed by incubating 1MBq/300 μL of ^{18}F -PBR06 or ^{18}F -FDG during 1h. Non-specific binding was assessed on adjacent slices using 1 μM of reference compounds $^{\text{nat}}\text{F}$ -PBR06 or $^{\text{nat}}\text{F}$ -FDG. Image acquisition was performed for 1h with a Beta-Imager2000 and a Micro-Imager (BiospaceLab). M3Vision software was used for data analysis and quantification. Then, SNR and Delta were calculated (Delta = (SNR Radioligand-SNR Reference Compound)/SNR Radioligand). One patient (high-affinity binder) with recent IS was imaged before surgery using ^{18}F -PBR06 PET/CT. Statistical analysis was performed using Wilcoxon test. **Results:** In all samples, ^{18}F -PBR06 accumulated in the carotid plaque and displayed a SNR equivalent to that of ^{18}F -FDG: 9.8 ± 7.7 vs 4.9 ± 2.8 ($p = 0.16$) respectively. The Delta of ^{18}F -PBR06 was larger than that of ^{18}F -FDG: $29.4 \pm 2.2\%$ vs $2.4 \pm 3.4\%$ ($p = 0.06$). The *in vivo* ^{18}F -PBR06 PET/

CT scan was negative. Notably, the carotid plaque of this patient showed calcification, which is associated with a low level of inflammation. **Conclusion:** ^{18}F -PBR06 showed high uptake in the inflamed carotid plaque. The high uptake was evident not only by visual analysis, but also by the objective criteria of SNR and Delta. These criteria were not statistically different from those obtained with ^{18}F -FDG (the number of samples in this preliminary study is however still small). The only *in vivo* imaging done so far was negative.

EP-0836

Toxicological and dosimetric assessment of a ^{18}F -Sulforhodamine 101 derivative as a novel radiotracer for PET imaging of astrocytosis

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The SR101 N-(3-[^{18}F]Fluoropropyl) sulfonamide (^{18}F SRF101) is a Sulforhodamine 101 (SR101) derivative previously synthesized by our group. The fluorescent dye SR101 has been reported as a specific marker of astroglia in the neocortex of rodents *in vivo*. The aim of this study was to perform preclinical toxicological evaluation of ^{18}F SRF101 and to extrapolate preclinical results of this tracer to humans. A single dose toxicity study was carried out using the guideline on toxicology studies applicable to radiopharmaceuticals. Based on the concept of microdosing, the toxicological limit chosen in this case was lower than 100 μg . This study was carried out with a dose set by an allometric scaling with a safety factor of 100. On day 1, thirty Swiss mice (15 males and 15 females) received a single iv bolus dose of SRF101 formulation. Twenty animals were sacrificed by cervical dislocation on day 2 (10 males and 10 females), while the rest on day 14 (5 males and 5 females). All animals were observed once daily to determine mortality, moribundity, injury, and availability of food and water. Body weight was recorded for each animal on day 1, 2, 7 and 14. Blood samples for hematologic and clinical chemistry analysis were obtained by intracardial puncture, immediately after sacrifice. Postmortem examination was carried out on all animals, including gross examination of brain and principal organs, followed by microscopic examination of hematoxylin-eosin stained sections. Dosimetry studies were based on biokinetic data obtained in small animals and considering activity retained into the intestines contents. Data was extrapolated to human. Effective and absorbed doses were estimated using male and female ICRP-89-derived NURBS models implemented in OLINDA/EXM_V2.0. All animals survived until the end of the study with no systemic signs of toxicity throughout the entire observation period. No drug related changes were noted in the parameters examined during the 14-day study, including body weight, food consumption, eyes changes, clinical pathology parameters, gross necropsy findings, absolute and relative organ weights, histopathology findings, or microscopic lesions. The effective dose for male and female dosimetric models was

4.03 E-03 mSv/MBq and 5.08 E-03 mSv/MBq, respectively. For an administrated activity of 350 MBq this would correspond to 1.41 mSv and 1.78 mSv for the same dosimetric models. The results obtained through the toxicology and dosimetry studies enables to conduct further clinical evaluation in patients of ^{18}F -Sulforhodamine 101 derivative as a novel radiotracer for astrocytosis imaging.

EP-0837

Does Pioglitazone Penetrate into the Brain to Activate the Peroxisome Proliferator Activated Receptor γ (PPAR γ) after Focal Cerebral Ischemia ?

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Aim: The beneficial effects of the peroxisome proliferator activated receptor γ (PPAR γ) agonist, pioglitazone (Pio) may depend on its penetration into the brain and activation of cerebral PPAR γ . We investigated in the rat the effects of brain PPAR γ activation on the neurological outcome and infarction volume after middle cerebral artery occlusion (MCAO) and the pharmacokinetics and distribution of intracerebroventricularly (ICV)-injected ^{123}I labelled Pio in various organs and its penetration into the brain after MCAO by SPECT. **Materials and Methods:** Pio was infused ICV over a 5-day period before, during and 2 days after MCAO (90 min). To synthesize the ^{123}I -Pio, Pio (1 mM) was incubated with 100 MBq Na- ^{123}I in acetic condition at room temperature for 10 min. The efficacy of ^{123}I -labelled Pio (1 to 10 μM) to bind to the PPAR γ was studied in vitro in 3T3-L1 adipocytes. In vivo experiments, male Wistar rats were injected intravenously (IV) with 10 MBq ^{123}I -Pio and blood samples were collected at 0 (control), 1, 2, 5, 10 and 45 min, and at 1, 2, 4 and 24 h thereafter. In vivo ^{123}I -Pio uptake was quantified using a SPECT system. After intracardial perfusion with ice-cold saline, various organs and the brain were isolated, weighted, and the radioactivity was measured in a γ -counter. **Results and Conclusion:** Activation of cerebral PPAR γ reduced the infarct volume and improved the neurological outcome after MCAO. Non-labelled Pio and ^{123}I -Pio showed equal binding activity of to the PPAR γ in 3T3-L1 cells. The blood levels of IV injected ^{123}I -Pio dramatically dropped during the first 2 min followed by a slow decline reaching 0.07% of the initial value after 24 h. ^{123}I -Pio highly accumulated in the thyroid gland (47.4 ± 1.48 ; expressed as a specific organ radioactivity in %/g tissue $\pm$ SEM) and the stomach (1.03 ± 0.37). Low accumulation of ^{123}I -Pio was detected in the lung, spleen, colon, testes and the pancreas; very low values were recorded in the liver and muscles. The ^{123}I -Pio uptake in the brain revealed an equal and low accumulation of the tracer in the normal and infarcted tissue. Our data provide evidence that the activation of cerebral PPAR γ improves the recovery of ischemic stroke. The present results also demonstrate that ^{123}I -Pio is a suitable tracer to study the

accumulation of Pio in organs and suggest that ^{123}I -Pio can also be successfully used for studying the penetration of Pio into the brain after cerebral ischemia.

EP-60

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Preclinical and translational aspects -> Translational aspects -> Therapy

EP-0838

Combination Of Chemotherapy With PRRT Prolongs Overall Survival And Response In Patients With Metastatic Pancreatic Neuroendo-Crine Tumours (NETs)

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Introduction: NETs are a complex and heterogeneous group of tumors, and the choice of an appropriate treatment option is limited. In a NET cohort the aim of this study was to compare the survival duration using dedicated chemotherapy schemes with those receiving additionally Peptide Receptor Radionuclide Therapy (PRRT). **Subjects and Methods:** We retrospectively studied a consecutive cohort of 39 patients: 15 of them underwent chemotherapy (Group A) whereas the remaining 24 of them proceeded to PRRT sessions (Group B) with intra-arterial infusions of ^{111}In -DTPA-D-Phe octreotide (5.4 ± 1.7 GBq) followed by non-carrier-added ^{177}Lu -DOTATATE (7.3 ± 2.3 GBq) with 4-8 weeks intervals between sessions. All patients were receiving long-acting somatostatin analog treatment. The response assessment was evaluated after comparison of the final results with those obtained at the baseline including clinical assessment, biochemical (CgA) investigations and imaging (RECIST, US, CT and MRI). The overall mean survival time was calculated for each group using the Kaplan-Meier analysis method. Results were correlated additionally with the Ki-67 proliferation index.

Results: The estimated overall survival time for Group A, which received traditional chemotherapy was 56 months compared to 116 months in Group B which received PRRT with ^{111}In -DTPA-D-Phe octreotide / non-carrier-added ^{177}Lu -DOTATATE. According to RECIST criteria none of the patients had complete response; 5 patients from Group A underwent PD, 2 patients stopped their therapy, and the rest are still alive to date. One patient from Group A survived 124 months since the beginning of chemotherapy, possibly explained by a low Ki-67 index (<2%). In Group B, 8 patients responded as PD, 2 stopped their radionuclide therapy, and 13 expressed as SD. It is worth mentioning that, 3 patients survived from 107 up to 138 months probably due to

their low Ki-67 index (<2%). **Conclusion:** Although somatostatin analogs seemed to prolong survival in patients with stable disease, their effect on desired tumor control is not enough. On the other hand, chemotherapy in advanced and progressive disease showed a remarkable therapeutic potency. Notably PRRT as first line / adjuvant therapeutic tool for tumor offers efficacy and prolongs patient survival time.

EP-0839

PET/MRI with ^{89}Zr -Df-Bz-NCS-Df-DS-5573a as a theranostic approach

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Purpose/Introduction: Members of the B7-CD28 family regulate T cell activation and tolerance. B7-H3 is a B7 family protein, widely expressed in a variety of cancers. DS-5573a is an anti-B7-H3 humanised afucosylated IgG1 antibody that binds specifically to human B7-H3. The aim of this study was to characterize ^{89}Zr -Df-Bz-NCS-Df-DS-5573a as a theranostic that could aid patient and dose selection in patients receiving DS-5573a therapy. **Subjects and Methods:** DS-5573a (Daiichi Sankyo) was radiolabelled with in-house produced zirconium-89 (^{89}Zr) using the chelator *p*-isothiocyanatobenzyl-desferrioxamine (Df). Imaging and biodistribution studies were performed in MDA-MB-231 tumour-bearing SCID mice in the absence and presence of therapeutic DS-5573a antibody dose (3 mg/kg DS-5573a). Tumour-bearing SCID mice with established tumours (83.37 ± 13.13 mm³, $n = 12$) were randomized in two groups of six mice. One group received weekly intravenous injection of DS-5573a (3 mg/kg) and the second group received vehicle control (PBS, pH 7.4). After four weeks of treatment, groups of three treated and untreated mice were injected with $5\mu\text{g}$ ^{89}Zr -DS-5573a (13.3 μCi) with or without the addition of 70 μg of unlabelled DS-5573 (3mg/kg). PET/MR imaging was performed on day 3 and 7 post injection. After the final scan, mice were humanely sacrificed and organs were collected and radioactivity was counted in a dual-channel γ -scintillation counter. **Results:** The percentage tumour growth inhibition after four weeks of therapy with DS-5573a was 89.8%. Tumour uptake was significantly lower in the groups of mice receiving therapeutic doses of antibody (3 mg/kg) demonstrating saturation of the B7-H3

binding sites at that dose level. All other organs did not show significant differences in ^{89}Zr -DS-5573a uptake, with the exception of the spleen. **Discussion/Conclusion:** These results show the ability of ^{89}Zr -DS-5573a to measure receptor occupancy *in vivo*, and that receptor saturation can be observed at doses required for therapeutic effects.

EP-0840

Radio-embolization Of ^{131}I Labeled Microspheres For Primary Hepatocellular Carcinoma Radiotherapy

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Objective: Radionuclide-labeled microspheres, such as Y-90 and P-32 labeled glass microspheres have already been used for radioembolization for hepatocellular carcinoma (HCC); however, limited treatment effect after complete decay of radionuclides and incapable multiple embolizations are still great challenge because of the non-biodegradable component of microspheres. Thus, radionuclide-labeled microspheres with proper biodegradable period matches radionuclide decay time could be a better choice. This study developed a novel iodine-131-labeled microsphere with ideal biodegradable time, and its radioembolization effect in orthotopic primary hepatocellular carcinoma rat was evaluated. **Methods:** The composited microspheres were prepared with collagen and chitosan. The characteristics of collagen-chitosan microspheres (CCMs) were determined by scanning electron microscope (SEM). The stability of ^{131}I -CCMs was evaluated in saline and human blood serum for up to 30 days, and its biodegradation in those solutions were measured. ^{131}I -radiolabelled microspheres were interventionally injected into hepatocellular livers through hepatic artery in rats. The *in vivo* stability of ^{131}I -CCMs was assessed by histological analysis and SPECT. The anti-tumor effects of microspheres were assessed by liver MRI, post operation survival (POS) and histological analysis from tissue specimen. **Results:** Composited microspheres were successfully obtained with desirable shapes and particle size of 10–20 μm by SEM measurement. Every 1mg of microspheres was able to carry about 50mCi of iodine-131 and radiolabeling efficiency of 92.82% was achieved by TLC analysis. SPECT indicated consistent stability of CCMs in liver through 28 days until iodine-131 was biologically metabolized while other organs are barely rose. Furthermore, the radioembolization by ^{131}I -microspheres significantly prolonged POS from 19 ± 7 d to 28 ± 15 d, and less focuses were observed by MRI and histological analysis. **Conclusion:** The biodegradable ^{131}I -labeled CCMs were successfully prepared and exhibited high radiolabeling efficiency and ideal stability *in vitro* and *in vivo*. Favorable prolonged survival time against primary HCC in rats was observed by radioembolization of ^{131}I -CCMs, suggesting this might be a potential drug for interventional radionuclide cancer therapy. **Key words:** ^{131}I ; Hepatocellular Carcinoma; Microsphere; Collagen; Chitosan; Radioembolization. **Research Support:** This project was partly supported by Sichuan Provincial Department of Science and Technology Support Program (20135Y0009 to Li L and 2016HH0065 to Cai H) and National Science Fund of China (81301250 to Cai H).

EP-0841

Development of a bone-seeker radiopharmaceutical by Scandium-47 and estimation of human absorbed dose

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Recently, ^{47}Sc ($T_{1/2} = 3.35$ d; $\beta_{\text{max}} = 600.1$ keV (%31.6) & 440.72 keV (%68.4); $E\gamma = 159.38$ keV (%68.3)) has attracted attentions because of its favorable radiation and chemical characteristics. In this work, a last generation bisphosphonate risedronate (2-(3-pyridinyl)-1-hydroxyethane diphosphonic acid) was labeled with radio-Scandium and investigated further for reduce the pain due bone metastases by application of ^{47}Sc . Labeling was performed at 95°C for 30 min. The stability of radioconjugate was checked in human serum at 37°C and biodistribution was studied in balb/c mice. Labeling yield was $\geq 90\%$ corresponding to a specific activity of 277MBq/mg. The radioconjugate showed good stability in human serum. Biological evaluation of radiolabeled ligand was performed in balb/c mice. The results showed that radio-scandium-Risedronate had maximum affinity for bone after 48h, that was $6.75 \pm 0.707\%$ ID/g. The maximum uptake for kidney and spleen were, 3.43 ± 0.268 and $2.23 \pm 1.286\%$ ID/g. Our main achievement was high bone uptake (% ID/g at 48h post injection) which may therapeutically be beneficial for the palliation of painful bone metastasis. The human organs' percentage of injected activities (%ID) estimated by extrapolation of animal data. Vital organs uptake for radio-Scandium-Risedronate were evaluated up to 96h (4 days). After estimation of the residence times, they were applied to MIRDose software. The estimated absorbed dose in bone, liver, spleen, kidney and red marrow were 1.35, 0.066, 0.077, 0.306 and 0.385 mGy/MBq respectively. The residence time (τ) in bone was 31.04 (Bq-h/Bq) and the effective dose equivalent was 0.194 mSv/MBq. The absorbed dose for other vital organs were negligible. **Keywords:** ^{47}Sc -Risedronate; Bisphosphonate; pain palliation; MIRDose software

EP-0842

Targeting activated synovial fibroblasts using photodynamic therapy in human rheumatoid arthritis synovial tissue

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Background: Activated synovial fibroblasts play an important role in the pathogenesis of rheumatoid arthritis (RA). They contribute to the pro-inflammatory environment in the joint and the degradation of cartilage and bone. Depleting the synovial fibroblasts could ameliorate both these symptoms in RA. Synovial fibroblasts are characterized by the expression of Fibroblast

Activation Protein (FAP). Here, we investigated the potential of FAP-targeted photodynamic therapy (tPDT) to selectively kill these cells. **Methods:** To create our multimodal tPDT tracer, both ITC-DTPA and the photosensitizer IRDye700DX were conjugated to the antibody 28H1 (28H1-700DX). For tPDT, this tracer was exposed to 690 nm light to generate cytotoxic reactive oxygen species. To demonstrate the proof-of-concept of FAP-based tPDT in ex vivo human tissue, RA synovial tissue obtained during joint replacement surgery was processed into standardized 6mm biopsies and used for FAP-based tPDT. The synovial biopsies were incubated with 28H1-700DX for 4 hours, were washed in PBS, subjected to treatment by 52 J/cm² light exposure, and fixed in formalin after 1h. Tissue was then embedded in paraffin and 5µm slices were stained for the localization of FAP expression. This was then compared to the presence of γH2AX and caspase-3 for DNA double-strand breaks and early apoptosis respectively. **Results:** In the tPDT study on human RA synovial tissue all biopsies did contain FAP expressing fibroblasts. Only those biopsies incubated with 28H1-700DX and subsequently exposed to 690 nm light showed apparent cell death in the tissue as evidenced by the positive staining of both the γH2AX and caspase-3 markers. This staining co-localized with areas of FAP-positive staining predominantly in the synovial lining. No cell death was observed in the FAP-positive areas in the control samples that were not exposed to either 28H1-700DX or light, indicating that tPDT-induced cell death was only achieved when the biopsies were exposed to a combination of the antibody-construct and light. **Conclusions:** Here, we demonstrated that tPDT induces cell death of FAP-positive cells in synovial tissue from RA patients, suggesting that FAP-targeted PDT can be a promising new tool in treating RA.

EP-0843

Correlation Between c-Fos Expression and Radioiodine Radiation Effect in Breast Cancer Cell Lines

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Ionizing radiation hits water molecules in the cell will produce free radicals. The numbers of free radicals are depending on a total dose radiation. Free radicals inhibit of switch from c-Fos to Fra1 in chromatin. The inhibition will lead cells fail to express cyclin D1 and it will follow by cell cycle arrest. The aim of this study is to investigate the correlation between c-Fos with radioiodine effect in breast cancer cell lines. Two breast cancer cell lines (MCF7 and SKBR3), and keratinocyte cell line (HaCaT) were used in this study. To induce c-Fos expression, cells were treated with epidermal growth factor (EGF) 50ng/ml, Adenosine tri-phosphate (ATP) 100µM, and a combination of both. Radioiodine effect was measured by reproductive ability of the cells after treatment of 74.10⁴ Becquerel/well of NaI-131/well. A Quantitative Real-time reverse transcriptase polymerase chain reaction

(qRT-PCR) was used to quantify c-Fos mRNA expression and c-Fos protein was assessed by Immunocytofluorescence. C-Fos mRNA is found only in MCF-7 cell line. A combination of ATP and EGF potentiate to induce c-Fos mRNA 22.74 ± 3.67 fold change (*p* < 0.05). The expression of c-Fos protein is detected in MCF7 cells and it increases by induction with ATP, EGF and combination of both (*p* < 0.05). Reproductive ability of breast cancer cells after of radioiodine exposure reduces significantly compare to HaCaT cells *p* < 0.05. Reproductive ability of MCF7, SKBR3 and HaCaT cells after radioiodine exposure are 22.58% ± 4.82%, 42.06% ± 3.60%, and 99.60% ± 5.38% respectively. Induction with EGF and combination ATP and EGF prior radioiodine exposure reduce reproductive ability of cells until 100% in MCF and SKBR3 cells. Moreover, reproductive ability reduces significantly by the inductions prior radioiodine exposure in all cell lines (*p* < 0.05). Correlation between c-Fos mRNA and protein expressions with radioiodine effect are *r* = - 0.90 and *r* = - 0.97 (*p* < 0.05) respectively. Radioiodine reduces reproductive ability of breast cancer cell lines and considerable potential for breast cancers treatment. ATP and EGF enhance radiation effects of radioiodine. C-Fos plays pivotal role in cell death pathways by radioiodine exposure in MCF7 cells, and other genes may correspond to cell death in SKBR3 cells. Further investigations are needed to cover radioiodine effect in different breast cancer sub-types.

EP-61

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Drug development -> New biological targets and ligands

EP-0844

A Novel PET Tracer For GD2-positive Neuroblastoma

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Introduction: Neuroblastoma is a malignant tumour that develops from autonomous nerves. 7-8 % of all diagnosed malignant tumours in childhood are neuroblastoma. In Germany, 150 children per year get diagnosed with this disease. In the clinic, sonography and MRI as well as SPECT scans with ¹²³I-metaiodobenzylguanidine (mIBG) are standardly used for the diagnosis. Unfortunately, 5 % of the cases are mIBG negative. **Subjects & Methods:** Here, we report on the synthesis and preliminary *in vitro* and *in vivo* results of bifunctional PET tracers that partly consist of dinutuximab beta. Dinutuximab beta is standardly used as therapeutic for GD2 positive neuroblastoma. **Results:** Two radio-

tracers (DOTA-Dinutuximab beta and DTPA-Dinutuximab beta) were successfully synthesized and radiolabelled with gallium-68 and lutetium-177 for imaging or therapy, respectively. Both tracers show labeling efficiencies >90 % with a marked stability in human serum *in vitro*. IMR-2 cells, that are GD2 positive, were used in a CAM assay *in vivo* to prove the functionality of our tracer. **Conclusion:** To conclude, two bifunctional chelators were successfully linked to dinutuximab beta and they show promising results *in vitro* and *in vivo*. In the future, *in vivo* experiments with GD2-positive tumor bearing mice are planned.

EP-0845

Feasibility of MicroSPECT/CT Imaging of RNF-43 Mutant Pancreatic Cancer Xenografts Overexpressing Frizzled-5 with Technetium-99m-Labeled Anti-Frizzled 5/8 Fab Fragments

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Aim: New therapeutic strategies are needed for pancreatic cancer (PnCa). A genome-wide CRISPR-Cas9 screen revealed that Frizzled-5 (FZD5) in the Wnt signaling pathway is a potentially druggable target. FZD5 is overexpressed in some PnCa due to mutation in RNF-43, an ubiquitin ligase that degrades FZD5 in normal cells. Potent growth inhibitory effects of anti-FZD5/8 antibodies were found in RNF-43 mutant PnCa cells *in vitro* and on PnCa tumour xenografts in mice *in vivo*. Imaging FZD5 would be useful to select patients for anti-FZD5 treatment since not all PnCa have RNF-43 mutation. However, it is not known if FZD5 is sufficiently expressed for imaging. Our aim was to develop a ^{99m}Tc-labeled FZD5 probe and assess its feasibility to detect FZD5-positive PnCa tumours in mice by microSPECT/CT. **Methods:** Anti-Frizzled 5/8 Fab (Fab 2919) were labeled to >90% radiochemical purity (RCP) with technetium-99m (^{99m}Tc) using a ^{99m}Tc (I)- tricarbonyl complex ([^{99m}Tc (H₂O)₃(CO)₃]⁺). The immunoreactivity of ^{99m}Tc-Fab 2919 to FZD5 and FZD8 was evaluated in a competition binding assay with Chinese hamster ovary (CHO) cells transfected to express FZD5 and FZD8, respectively, or non-transfected CHO cells (control). MicroSPECT/CT was carried out at 4 and 24 h p.i. of ^{99m}Tc-Fab 2919 or non-specific ^{99m}Tc-Fab 3913 (control) in NOD/SCID mice with s.c. RNF-43 mutant human AsPC-1 human PnCa xenografts. Biodistribution studies were performed following imaging. **Results:** ^{99m}Tc-Fab 2919 were labeled to >90% RCP. Binding of ^{99m}Tc-Fab 2919 to CHO-FZD5, CHO-FZD8 and non-transfected CHO cells was displaced by 95.4 ± 0.02%, 61.8 ± 0.8% and 13.8 ± 8.7%, respectively, demonstrating specific binding to FZD5 or FZD8. AsPC-1 tumours were modestly imaged with ^{99m}Tc-Fab 2919 at 4 h p.i. by microSPECT/CT in comparison to control ^{99m}Tc-Fab 3913, which did not visualize tumors at 4 or 24 h p.i. Biodistribution studies at 24 h p.i. revealed tumour uptake of 0.70 ± 0.12 %ID/g with a T/B ratio of 5.8 for ^{99m}Tc-Fab 2919 in comparison to control ^{99m}Tc-

Fab 3913 (0.31 ± 0.04 %ID/g, T/B = 0.4, p<0.01). **Conclusion:** Fab 2919 were labeled with ^{99m}Tc to high RCP and with preserved immunoreactivity for FZD5 and FZD8. Suboptimal visualization of AsPC-1 tumours by microSPECT/CT suggests low expression of FZD5 or FZD8. Tumor uptake of ^{99m}Tc-Fab 2919 was low but the T/B ratio was higher than control ^{99m}Tc-Fab 3913. Nonetheless, FZD5 expression appears insufficient for tumour imaging in PnCa. **Research Support:** Supported by the Canadian Cancer Society Research Institute.

EP-0846

Evaluation of tumor microenvironment (FAP alpha) targeted SPECT (^{99m}Tc) and therapeutic agent (Tubulysin B hydrazide).

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Aim: Fibroblast activation protein alpha (FAPα) has emerged as a biomarker for cancer-associated fibroblasts (CAFs) cells. CAFs are one of the major cell types present in the solid tumor microenvironment (TME). Restricted expression of FAPα in myofibroblasts and sites of wound healing/chronic inflammation and its expression in 90% of epithelial solid tumors has led to the development of FAPα-targeted therapeutic agents. To date, however, no FAPα targeting ligand has been used to develop SPECT imaging agent and deliver microtubule inhibitor, tubulysin B hydrazide (TubBH) for cancer. Herein we report *in vitro* and *in vivo* (mice tumor xenograft) SPECT imaging and therapy with a FAPα specific small molecule ligand (FL) linked to ^{99m}Tc (FL-L1-^{99m}Tc) and TubBH (FL-L1-TubBH) respectively. The FAPα-targeted SPECT agent will be useful for whole-body imaging of TME. Since the untargeted TubBH cannot differentiate between healthy and cancer cells therefore by targeting it to FAPα the cytotoxic drug can be selectively delivered to the tumor mass. Thus, by selectively killing CAF cells, which play a vital role in tumor progression can be detrimental for tumor growth. **Methods:** FL-L1-^{99m}Tc and FL-L1-TubBH were synthesized by conjugating FL to ^{99m}Tc chelator and TubBH via a non-releasable and a self-immolative disulfide linker respectively. *In vitro* binding of the conjugates was determined by using FAPα-transfected HEK-293 cells (HEK-FAPα). *In vivo* SPECT imaging was performed in MDA-MB-231 xenografts. The efficacy of FL-L1-TubBH was examined in MDA-MB-231 and 4T1 xenografts. **Results:** *In vitro*, the FL-L1-^{99m}Tc exhibited a high binding affinity (K_d=10.5 nM) and *in vivo*, it showed FAPα mediated uptake in tumor in which the cancer cells itself were FAPα negative. The uptake of FL-L1-^{99m}Tc was blocked in the presence of an excess of FL. The biodistribution study suggested that other than tumors there was minimal or no uptake in other tissues except kidneys which were due to the excretion of the conjugate via renal route. *In vivo*, the FL-L1-TubBH demonstrated a near-complete eradication of MDA-MB231 tumors whereas a partial response was observed in 4T1 xenografts. This variation in tumor response due to the different therapeutic doses used in both studies. Furthermore, the *in vivo* blocking study confirmed that the therapeutic response was FAPα mediated. **Conclusion:** Results from *in vitro* and *in vivo* study demonstrated that FAPα targeting small molecule ligand can be successfully used to develop SPECT imaging

agent and deliver TubBH selectively to tumor mass without causing damage to healthy tissues.

EP-0847

[¹⁸F]Tetrazine-trans-cyclooctene mediated labelling of antibodies for PET imaging of amyloid-beta

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Purpose/Introduction: Biomolecules such as monoclonal antibodies and engineered derivatives are increasingly used in therapy and diagnostics owing to their high specificity and high-affinity binding properties. PET tracers based on large proteins are typically labelled with radioisotopes with long half-lives, e.g. zirconium-89, copper-64 or iodine-124 due to slow equilibrium biodistribution and clearance from blood. If these limitations could be overcome, labelling with fluorine-18 would potentially simplify logistics surrounding the PET examination, reduce radiation dose, modify excretion patterns and improve PET data by the shorter positron emission range. In an on-going effort to develop antibody-based imaging of cerebral amyloid-beta, structural modifications are investigated towards enhanced kinetics and brain uptake of labelled antibody constructs, e.g. reduction of the molecular weight and introduction of active BBB transport by transferrin receptor (TfR) binders [1]. **Subjects & Methods:** The work on antibody constructs has been paralleled with a concurrent development towards practical methods for fluorine-18 labelling of biomolecules based on a three step procedure; fluorine-18 incorporation via [¹⁸F]F-Py-TFP [2] activated ester, amide coupling with tetrazine compound and conjugation with trans-cyclooctene-modified antibody. The labelled amyloid-beta antibody constructs were evaluated in Alzheimer's disease mouse models and wild type controls using micro-PET. **Results:** Two different fluorine-18 labelled bispecific antibodies showed approximately 10 and 50-fold increased brain concentrations at 2 h post injection compared to antibodies without TfR binders. PET imaging at 12 h post injection with the antibody construct based on a full-sized anti amyloid-beta IgG fused with single chain variable fragments of TfR antibody 8D3, [¹⁸F]mAb-scFv8D3, displayed a 2-fold higher brain concentration in animals with expression of amyloid-beta compared to wild-type mouse lacking amyloid-beta. The difference was also visually apparent in the PET images. Skull uptake was minimal and decreased over time indicating very limited defluorination. **Conclusion:** Fluorine-18 labelling has been developed and successfully applied in the benchmarking of antibody based PET imaging of cerebral amyloid-beta with the aim to facilitate clinical applications. References: 1. G. Hultqvist, S. Syvänen, X. T. Fang, L. Lannfelt, D. Sehlin *Theranostics* 2017; 7(2):308–318. 2. D.E. Olberg, J.M. Arukwe, D. Grace, O.K. Hjelstuen, M. Solbakken, G.M. Kindberg and A. Cuthbertson *J. Med. Chem.*, 2010; 53 (4):1732–1740

EP-0848

Diagnostic perspectives of the new ^{99m}Tc-labeled CCK2R-antagonist DGA1 in CCK₂R-positive human cancer

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Aim: Radiolabeled gastrin analogs have been proposed for diagnosis and therapy of cholecystokinin subtype 2 receptor (CCK₂R)-positive human tumors. Previous studies have shown the superior pharmacokinetics and higher safety of radiolabeled receptor-antagonists for human use compared to agonists. In the present study, we present the new peptidomimetic CCK₂R-antagonist DGA1, coupled to an acyclic tetraamine for labeling with the SPECT radionuclide ^{99m}Tc. Preclinical comparison of [^{99m}Tc]DGA1 with [^{99m}Tc]DG2 ([^{99m}Tc]Demogastrin 2, a CCK₂R-agonist reference) was conducted in HEK293-CCK2i4svR cells and mouse models. **Materials and Methods:** DGA1 was labeled with ^{99m}Tc in alkaline medium using SnCl₂ as reductant in the presence of citrate. The cell-association of [^{99m}Tc]DGA1 and [^{99m}Tc]DG2 was studied over time at 37°C in HEK293-CCK2i4svR and in HEK293T cells (negative controls devoid of CCK₂R expression). Biodistribution of [^{99m}Tc]DGA1 and [^{99m}Tc]DG2 was carried out in SCID mice bearing subcutaneous twin HEK293-CCK2i4svR and HEK293T xenografts at 4 h post-injection (pi); additional groups of animals were coinjected with gelofusine. **Results:** During incubation at 37°C [^{99m}Tc]DGA1 was found distributed equally between the cell membrane and within HEK-CCK2i4svR cells (10.0% vs 10.8%, respectively at 1 h), whereas [^{99m}Tc]DG2 internalized at high rates (42.8±% at 1 h); no cell uptake was evident for either [^{99m}Tc]DGA1 or [^{99m}Tc]DG2 in HEK293T cells. After injection in mice, [^{99m}Tc]DGA1 displayed markedly higher uptake in the HEK293-CCK2i4svR xenografts (29.8±2.5%ID/g) compared to [^{99m}Tc]DG2 (16.4±3.2%ID/g) at 4 h pi with no radioactive uptake shown for either radiotracer in the HEK293T xenografts. High kidney uptake was displayed by both [^{99m}Tc]DGA1 (94.5±13.2%ID/g) and [^{99m}Tc]DG2 (51.7±8.9%ID/g), but was drastically reduced by co-administration of the plasma expander gelofusine (33.6±2.7%ID/g vs 9.5±0.8%ID/g, respectively) that had no effect on tumor values. **Conclusions:** The new CCK₂R-antagonist based radiotracer [^{99m}Tc]DGA1 displayed strong tumor-targeting in mice, showing excellent prospects for use in the diagnosis of CCK₂R-expressing human tumors with SPECT. Clinical translation of [^{99m}Tc]DGA1 is warranted and currently pursued. **Acknowledgements:** This study was realized in the frameworks of IKY scholarship which was funded from the Action «Reinforcement of Postdoctoral Researchers», with the resources of the Operational Program “Human Resources Development, Education and Lifelong Learning” with priority axes 6,8,9, co-financed by the European Social Fund (ESF) and the Greek State.

EP-0849

New candidate high-affinity full agonist PET radioligands for imaging 5-HT_{1B} receptors have very low brain uptake and no signal

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Aims: The serotonin-1B receptor (5-HT_{1B}R) is a G-protein coupled receptor (GPCR) that has been studied with positron emission tomography (PET) in both monkey and human. GPCR's such as 5-HT_{1B}R exist in two affinity states that affect the binding of agonists more than the binding of antagonists. All known effective PET radioligands for 5-HT_{1B}R have antagonist activity and are therefore expected to bind with similar affinity to G-protein coupled and uncoupled receptors. An effective agonist 5-HT_{1B}R PET radioligand might be more sensitive to synaptic 5-HT concentration and useful for studying the 5-HT system. Notwithstanding, there is a question as to whether a full agonist can be a successful 5-HT_{1B}R PET radioligand. We identified two ligands for 5-HT_{1B}R (AZ11136118; AZ11895987) having full agonist activity with absence of antagonist activity, sub-nM affinity and moderate lipophilicity. Here we report their labeling with carbon-11 ($t_{1/2} = 20.4$ min) and evaluation as candidate PET radioligands in monkey. **Materials and Methods:** Labeling of [¹¹C]AZ11136118 was achieved at an amide bond through [¹¹C]carbon monoxide insertion between prepared iodophenyl methanesulfonate and a homochiral amine precursor. [¹¹C]AZ11895987 was labeled by treatment of the *N*-desmethyl analogue with [¹¹C]methyl triflate. In PET experiments, high molar activity radioligand was administered intravenously to monkey and brain radioactivity was recorded up to 120 min. Venous or arterial blood was sampled serially during scans for HPLC analysis of radiometabolites. [¹¹C]AZ11136118 was studied with PET in monkey a) at baseline; b) after 5-HT_{1B}R block with the antagonist AR-A000002 (2.0 mg/kg); c) after block of P-gp with tariquidar (8.0 mg/kg); d) after similar blocking of both P-gp and 5-HT_{1B}R. [¹¹C]AZ11895987 was studied in monkey at baseline only. **Results:** In baseline PET experiments, both radioligands showed poor peak brain uptake (< 0.2 SUV). After blocking the P-gp efflux transporter with tariquidar, brain uptake increased for [¹¹C]AZ11136118 but only to 0.8 SUV. No specific binding of either radioligand to brain 5-HT_{1B}R could be detected. **Conclusion:** [¹¹C]AZ11136118 and [¹¹C]AZ11895987 are topologically very similar to other successful 5-HT_{1B}R PET radioligands and their lack of brain entry is unexpected. [¹¹C]AZ11136118 appears to be a substrate for P-gp. Brain-penetrant full agonist radioligands are needed to test whether they may be useful for PET imaging of brain 5-HT_{1B}R.

EP-0850

⁶⁴Cu and fluorescein labeled anti-miRNA peptide nucleic acids for the detection of miRNA expression in living cells

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Introduction: MiRNA are single stranded RNAs of 18-22 nucleotides and they have been found to be promising diagnostic and prognostic markers for several pathologies, such as tumors, neurodegenerative, cardiovascular and autoimmune disease. In

the present work the development and characterization of the first anti-miRNA ⁶⁴Cu-radiolabeled probes based on PNA for a potential non-invasive molecular imaging *in vivo* of giant cell arteritis and thyroid carcinoma are described. **Materials and Methods:** MiR-146a and miR-146b-5p were selected as targets because they have been found up-regulated in these disease. Anti-miR-PNA and scramble-PNA probes were synthesized and linked to carboxyfluorescein or DOTA. The affinity of the probes for the targets was assessed by circular dichroism and melting temperature. Differential uptake and functional activity of fluoresceinated anti-miRNA probes were tested on BCPAP and A549 cell lines, expressing different levels of miR-146a and -146b-5p. DOTA anti-miRNA probes were then labelled with copper-64 and their stability and uptake were assessed in the same cell lines. **Results:** From circular dichroism studies it was possible to note that both PNA sequences (anti-miR-146a and -146b-5p) were able to recognize both miRNA sequences. The scrambled PNA sequence did not show any ability instead. Fluorescence of both BCPAP and A549 cells treated with anti-miR PNAs was higher than that of cells treated with the negative control scrambled-PNA. ⁶⁴Cu-DOTA-anti-miR-146a PNA showed an almost doubled uptake in BCPAP cells with respect to the A549 cells after 42 hours. Conversely, the uptake of the ⁶⁴Cu-DOTA-anti-miR-146b-5p PNA was comparable in the two cell lines. The uptake of the ⁶⁴Cu-DOTA-scramble PNA was really low in both the cell lines and can be assigned to unspecific binding. **Conclusions:** The experiments confirmed that anti-miR-146a PNA can selectively bound the miRNA target and its uptake is higher in miRNA overexpressing cells *in vitro*. ⁶⁴Cu-anti-miR-146a PNA might be further investigated for non-invasive PET imaging of miR-146a and miR-146b-5p overexpressing diseases.

EP-0851

The evaluation of a novel PET ligand for colony stimulating factor 1 receptor in status epilepticus model rat brains

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Introduction: Neuroinflammation is involved in the pathophysiology of neurodegenerative diseases including Alzheimer's diseases. Neuroinflammation has recently been recognized as a promising target for the treatment of neurodegenerative diseases. Thus, positron emission tomography (PET) imaging for a specific molecule related to neuroinflammation could provide useful information for the drug development targeting neuroinflammation. We are developing a novel PET ligand for the colony stimulating factor 1 receptor (CSF1R). CSF1R is expressed only on microglia in the central nervous system. In this study, we evaluated the potential of the PET ligand to detect neuroinflammation in pilocarpine-induced status epilepticus model rat brains. **Materials and Methods:** [¹¹C]NCGG401, our CSF1R PET ligand, was synthesized with a high radiochemical purity (>99%). We conducted 120-min dynamic PET scans to evaluate its kinetics in the brain after intravenous administration of [¹¹C]NCGG401

(~10 MBq) in four normal rats (Crl:CD (SD), male, 8-week old) with or without a blocking agent (BLZ945, 1.0 mg/kg body weight), which selectively inhibits CSF1R. Subsequently, we conducted 60-min dynamic PET scans in two status epilepticus model rats (Crl:CD (SD), male, 8-week old, 10 days after 400 mg/kg pilocarpine i.p.) to evaluate the ability of the ligand to detect neuroinflammation in the brain. **Results:** After the intravenous administration of [^{11}C]NCGG401, brain radioactivity showed a fast initial peak (SUV 1.0) and good washout thereafter in the normal rats. Administration of a blocking agent increased the rate of washout significantly suggesting that there is specific binding of the ligand to CSF1R in the normal rat brain. The status epilepticus model rats showed a higher uptake with a slower rate of washout than the normal rats did, reflecting increased binding of the ligand to the brain with neuroinflammation. **Conclusion:** [^{11}C]NCGG401 showed a favorable kinetics and presence of specific binding to CSF1R in the rat brain. The uptake of the ligand reflected increased binding sites in the brain with neuroinflammation. Thus, [^{11}C]NCGG401 appears to be a promising PET ligand for CSF1R to detect neuroinflammation in the brain.

EP-0852

Evaluation Of Trivalent ^{68}Ga -NOTA-(2-deoxy-D-glucosamine)₃ As A Potential Probe For Tumor Imaging In A Lung Tumor Xenograft Model

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Objective: This study aims to evaluate trivalent ^{68}Ga -NOTA-(2-deoxy-D-glucosamine)₃ (^{68}Ga -NOTA-G3) as a PET probe for tumor imaging in lung carcinoma-bearing mouse model. **Methods:** ^{68}Ga -NOTA-G3 was prepared by labeling the NOTA conjugate with freshly eluted ^{68}Ga at room temperature. Subcutaneous tumor xenografts were produced by inoculation of NCI-H292 lung cancer cells in the right flank of 6-week-old nude male mice under anesthesia. Biological characterization studies of ^{68}Ga -NOTA-G3 including in-vitro cellular uptake and dynamic nanoPET/CT imaging of NCI-H292 tumor-bearing mice were performed (0–2 h post-intravenous injection). ROIs analysis was performed with Pmode software. **Results:** ^{68}Ga -NOTA-G3 was prepared in high specific radioactivity (> 67 GBq/ μmol) and high radiochemical purity (> 95%) without purification. The accumulation of ^{68}Ga -NOTA-G3 in NCI-H292 cells was obvious and increased with time. Dynamic nanoPET/CT imaging studies in NCI-H292 lung carcinoma-bearing mice clearly delineated the tumor lesions. PET images showed low uptake ^{68}Ga -NOTA-G3 in brain and heart, and high accumulation in liver and kidney. ROIs analysis of PET images showed that the tumor-to-muscle ratio was 5.1 at 2 h post-injection. **Conclusion:** In this study, the trivalent glucosamine derivative ^{68}Ga -NOTA-G3 was successfully prepared with high yield and radiochemical purity. Both results of cellular study and PET/CT imaging showed that ^{68}Ga -NOTA-G3 was accumulated in tumor cells with desirable uptakes. ^{68}Ga -NOTA-G3 is demonstrated as a potential radio-probe for tumor imaging. These results warrant further investigation for biological characters and modifications of this multivalent glycoligand.

EP-0853

Preliminary Biological Evaluation of Radioligands for PET Imaging of Histone Deacetylase 6

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Introduction: Histone deacetylases (HDACs) are enzymes responsible for lysine deacetylation of histones. In particular, HDAC6, a class IIb HDAC, is a unique enzyme that is mainly found in the cytosol and regulates deacetylation of cytosolic proteins including α -tubulin, HSP90 and tau protein. HDAC6 has also been implicated in cancer metastasis and neurodegeneration. Thus, research into the role of HDAC6 with in vivo imaging will facilitate development of drugs targeting HDAC6. In the present study, we performed preliminary biological evaluation of radiolabeled analogues ([^{11}C]**1** and [^{18}F]**2**) of Tubastatin A, an HDAC6-selective inhibitor, for positron emission tomography (PET) imaging of HDAC6. **Methods:** ^{11}C -Methylated **1** was synthesized from desmethyl precursor using [^{11}C]CH₃OTf. ^{18}F -Fluoroethylated **2** was synthesized from a tosylate precursor by a two-step, one-pot reaction including fluorination and conversion of a methyl ester group into a hydroxamic acid group. To estimate the binding affinity of the compounds for HDAC1 as a representative of the HDAC family and HDAC6, IC₅₀ values were determined by an HDAC activity assay. Biodistribution at 1, 5, 10, 30 and 60 min post-injection was evaluated in normal mice. Radiometabolites in mouse plasma after intravenous injection of [^{18}F]**2** were assessed by high performance liquid chromatography (HPLC). **Results:** The two compounds showed similar binding selectivities for HDAC6 over HDAC1 (IC₅₀ values of **1**: 904 nM for HDAC1 and 30.4 nM for HDAC6; IC₅₀ values of **2**: 996 nM for HDAC1 and 33.1 nM for HDAC6). They also resembled each other in biodistribution in the mouse major organs including liver and kidney. Brain uptake of [^{11}C]**1** and [^{18}F]**2** was less than 0.6% injected dose (ID)/g throughout the 60-min period. Bone radioactivity was stable at around 2% ID/g after injection of [^{18}F]**2**, suggesting in vivo defluorination of [^{18}F]**2** was not significant. Metabolic stability in mouse plasma was assessed for [^{18}F]**2** because ^{18}F -labeled ligands are more clinically useful than ^{11}C -labeled ligands due to the longer half-life of fluorine-18. HPLC analysis revealed the presence of two polar radiometabolites in addition to the intact form. Percentages of the intact form to total radioactivity in mouse plasma were $76 \pm 3\%$ and $70 \pm 12\%$ at 15 and 30 min post-injection, respectively. **Conclusion:** [^{18}F]**2** showed potential utility for HDAC6 PET imaging. However, its poor blood-brain barrier permeability limits its use in research into neurodegenerative diseases.

EP-0854

In vitro evaluation of pretargeting system with anti-CD20 mAb for targeting non-Hodgkin's lymphoma

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Purpose: Pretargeting technique using bioorthogonal chemistry was investigated to improve targeting efficacy. In this study, a pretargeting system of DBCO-conjugated rituximab and ^{64}Cu -la-

beled azide was investigated *in vitro*. **Methods:** Rituximab (anti-CD20 mAb) was conjugated with DBCO-PEG₅-NHS ester or DBCO-PEG₁₃-NHS ester in 0.1M NaHCO₃ (pH = 8.3), purified afterward by PD-10 column. NODA-PEG₄-azide for ⁶⁴Cu labeling was prepared by mixing azido-PEG₄-NHS ester with NODA-GA, followed by purification using HPLC. The feasibility of specific pretargeting of rituximab was evaluated using CD20 expressing B-cell lymphoma cell line (Daudi). Cells were pre-incubated with DBCO-PEG_n-rituximab for 60 min. Thereafter, ⁶⁴Cu-azide was added to the cells. After incubation for 60 min at 37°C, cell-associated radioactivity was measured. ⁶⁴Cu-azide was added directly to the cells without the addition of DBCO-rituximab as control experiment. **Results:** The yield of NODA-PEG₄-TCO was 30%. The HPLC purification of the conjugate provided a purity of greater than 90%. NODA-PEG₄-azide was labeled with ⁶⁴Cu. The labeling yield was >99.8%, and the specific activity was 19.1 MBq/nmol. ⁶⁴Cu-labeled azide was stable in PBS and human plasma for 72 hours at 37 °C (>95%). The number of DBCO-PEG_{5or13} conjugated on rituximab were 4.3 and 4.4, respectively which confirmed using MALDI-TOF. **In vitro** pretargeting binding of ⁶⁴Cu-azide to DBCO-rituximab pretreated CD20 positive cells was higher than that of ⁶⁴Cu-azide without the addition of DBCO-rituximab. These data demonstrate that ⁶⁴Cu-azide/DBCO-mAb reaction can occur inside of in vitro systems and confirm *in vitro* pretargeting. **Conclusion:** We successfully prepared the ⁶⁴Cu-labeled azide/DBCO-rituximab for pretargeting technique. *In vitro* pretargeting study demonstrates a proof of concept for the prepared molecules. Further, *in vivo* studies are needed to evaluate pretargeting strategy using these ligands. Research Support: This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government (Ministry of Science, ICT) (NRF-2013M2C2A1074238).

EP-0855

Development of LDLR peptide vectors for tumor targeting

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VECT-HORUS has developed a proprietary technology platform, VECTrans^{}, that facilitates the targeting and delivery of imaging or therapeutic agents into the brain and tumors using receptor mediated transport. The ⁶⁸Ga-VH peptide is a small imaging agent that targets the low-density lipoprotein receptor (LDLR) overexpressed on the surface of various cancer-cells. **Aim:** The objective of the present study is to assess using PET-Scan the biodistribution of a peptide targeting LDLR coupled to a NODA-GA cage (VH-NO31), compared to a referent molecule, following intravenous administration to mice implanted with adrenal gland cancer (NCI-H295R, xenograft model) or glioblastoma (U87MG, intracranial injection). **Material and Methods:** VH-NO31 was synthesized and characterized by ESI Mass Spectrometry, by *in vitro* binding experiments with recombinant LDLR (SPR) and by *in vitro* uptake in the U87MG cell line. Mice were implanted subcutaneously in the upper flanks with NCI-H295R cells or orthotopically (intracerebrally) with U87MG cells. Imaging experiments were carried out when the tumours reached a

volume comprised between 200-600 mm³ for NCI-H295R (about 32 days) or after 21 days post-implantation for U87MG. Animals (n =6) received the test substance by intravenous single bolus injection at a dose of 10± 4MBq and PET/CT scans were acquired at 1h post-injection. PET/CT studies were performed on a microPET/microCT rodent model scanner (Mediso). A radiolabeling reaction was conducted by reacting 20g of VH-NO31 with 74-148 MBq of ⁶⁸Ga. The day after, the same group of nude mice was administered with either 10± 4MBq of ¹⁸F-FDG (adrenal model) or ¹⁸F-RGD (glioblastoma), as referent molecules. Quantitative region-of-interest (ROI) analysis of the PET images was performed on the attenuation and decay corrected PET images using Vivoquant software and tissue uptake values are presented as a ratio Tumor on Muscle (T/M). **Results:** For both studied models, imaging and quantification showed a significant accumulation of VH-NO31 in comparison with the referent molecules. The ratio T/M of VH-NO31 was 2.2 on day 14 versus 0.7 for ¹⁸F-FDG and 6.1 on day 32 for the adrenal gland model. For glioblastoma, the tumor/contralateral hemisphere ratio was 10.5 on day 21 versus 2.8 for ¹⁸F-RGD. The capture of VH-NO31 were 3.1 and 3.7 more important than ¹⁸F-FDG and ⁶⁸Ga-RGD. **Conclusion:** *In vivo* biodistribution profiles show strong tumor accumulation of VH-NO31 compare to healthy tissues and accumulation in non-target excretion organs kidney and liver. Our data suggest that VH-NO31 is a promising tracer for imaging/diagnostics of tumors that overexpress LDLR.

EP-0856

Testing The Feasibility of a Dihydro Thiazolo Ring-fused 2-pyridone Derivative As a Possible PET Ligand to Target Alpha-synuclein in Neurodegenerative Disorders

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Introduction: Development of a PET radioligand for imaging alpha-synuclein (-syn) in Parkinson's disease (PD) and Multi system atrophy (MSA) is a clinical unmet need. Recently, a small molecule with a dihydro-thiazolo ring-fused 2-pyridone, FN075, was found to be a modulator of -syn fibrillation *in vitro* and *in vivo*. PS648, a FN075 derivative with competitive binding properties for thioflavin T, has improved physicochemical properties than FN075 with lower lipophilicity. The goal of this study was to label PS648 with ³H and evaluate its binding characteristics using post-mortem autoradiography (ARG) and binding assay techniques. **Methods:** [³H]PS648 was synthesised from 1.2 mg of the bromide precursor by reductive dehalogenation using 10% Pd/C and 254 GBq of T₂ to afford 938 MBq of the target compound with a specific activity of 834 GBq/mmol and a radiochemical purity of 97.3%. ARG was performed using human brain sections from PD, MSA and controls obtained from the Netherlands brain bank. The tissue was incubated in Tris HCl (50 mM, pH 7.4) at 3nM in the presence and the absence of

non-labelled PS648 compound (10 μ M). Immunohistochemical analyses were carried out in adjacent tissue sections to examine α -syn, amyloid β and Tau pathologies. The affinity of PS638 was determined by saturation binding assay using *in vitro* α -syn fibrils (1 μ M) incubated with 10 serial dilutions of [3 H] PS648 (0.1 - 300 nM) in the presence of unlabeled compound (10 μ M). **Results and Discussion:** [3 H]PS648 displayed binding in PD, MSA and control tissue that was decreased after the co-incubation with unlabeled compound. In the grey matter, higher specific binding was measured in the cingulate cortex of PD (46.5 fmol/mg, n=1) as compared with the cerebellar cortex of MSA (25.8 $\pm$ 11.9 fmol/mg, n=2) and the cingulate cortex of control tissue (26.8 $\pm$ 11.5 fmol/mg, n=2). On the other hand, higher specific binding was measured in the cerebellar white matter of MSA (35.8 $\pm$ 6.3 fmol/mg, n=2) as compared with the white matter of the cingulate cortex of PD (11.57 fmol/mg, n=1) and controls (13.6 $\pm$ 1.3 fmol/mg, n=2). K_D was 49 nM using α -syn fibrils. **Conclusion:** These preliminary data showed that PS648 binds in post-mortem PD and MSA tissue and *in vitro* to α -syn fibrils and. The compound displays however low binding affinity to α -syn fibrils and most likely binds also to amyloid- β . Although this class of molecules has the capability of binding α -syn *in vitro*, further investigation is needed in order to improve their affinity and selectivity for possible applications as PET radioligands.

EP-0857

Development of imaging agent for glutamic acid transporter by off-target exclusion using computational chemical method

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Background / Aims: Positron emission tomography (PET) imaging is a useful method for analyzing the biological functions of receptors and transporters in the CNS. The Demonstration of functional changes will lead to early diagnosis of various brain diseases. However, it is only accumulation of radioactivity that can be followed by PET, and it is difficult to separate it from off-target binding. For example, it has been found that some useful agents that bind to the glutamate transporter (GLT) also bind to the estrogen receptor (ER α). We excluded off-target binding using computational chemistry techniques and worked on the development of glutamate transporter PET imaging agents. **Methods:** First, we performed an *in silico*-binding assay using tamoxifen, which binds to both GLT and ER α proteins using our protein-ligand docking calculations. Next, Structural modifications were then carried out with tetrahydrobenzopyran derivatives predominant in GLT binding, taking note of the bind-

ing to ER α . Furthermore, we investigated the position where [18 F] or [11 C] which is a PET nuclide can be introduced. **Result:** *In silico* - binding assay, we designed tamoxifen and derivatives of tetrahydrobenzopyran. I believe that these can be used as ligands for GLT. In our group, design of labeling precursors and examination of labeling conditions are also under way. **Conclusions:** We performed *in silico* binding assay and synthesized labeled derivatives of tamoxifen and tetrahydrobenzopyran. This may be a ligand for glutamate transporter. Currently, we are preparing for animal experiments using epilepsy model animals with glutamate metabolism inhibition.

EP-62

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Drug development -> Radiopharmacokinetics and drug development

EP-0858

Do we Really Need Another Rule to Predict Blood Brain Barrier Penetration?

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Introduction: A plethora of concepts and so called “rules of five” (Ro5) are stated in literature and supposed to predict blood brain barrier (BBB) penetration. One of the earliest concepts dates back to 1968 and the most current one was published in 2017 (1,2). Aim of the study was to systematically review these published rules by applying them to a heterogeneous compound library. Furthermore, the creation of these rules will be discussed with respect to their chosen methods (experimental and calculated) and compound selections. **Materials & Methods:** 131 substances were experimentally tested (five features) (3) and calculated properties were collected (17 features using two different software). The resulting database was categorized into three groups (BBB penetrating, non-penetrating and a subgroup of compounds interacting with efflux transporters) and statistically analysed (ANOVA) in GraphPad Prism or based on machine learning approaches (4). **Results & Conclusion:** So far, none of the published rules focussed on PET brain tracers, plenty of them did not compare different drug groups, and all of them used different methods to evaluate the same feature (e.g. logP), which lead to a diversity of interpretations. Hence, these facts lead to numerous rules over the last decades based on unsatisfied *in vitro* and *in silico* measurements of brain uptake. The application of the diversity of published rules to our dataset resulted in a high false positive (up to 52%) and false negative number of cases (up to 88%). The topological polar surface area (tPSA) generated by ChemBioDraw was the molecule property with the highest weight on BBB penetration prognosis in

contrast to the tPSA value taken from ACD/ChemSpider. The selected tPSA cut-off of 60 Å leads to a total default rate of less than 24%. The hydrogen bond donors (HBD) was found to be another high weighted value. This is related to the fact that the number of HBD is part of the tPSA calculation. Accordingly, the biodistribution of a tracer cannot be easily defined by a given rule. Successful prediction of BBB penetration of newly developed tracers require standardized methods, the knowledge and rationale behind the experimental as well as calculated properties and an unbiased selection of tested compounds. **References:** 1. Hansch C et al. *J Med Chem.* 1968;11:1-11. 2. Rankovic Z. *J Med Chem.* 2017;60:5943-5954. 3. Vranka C et al. *Nucl Med Biol.* 2017;58:20-32. 4. Papp L et al. *J Nucl Med Off Publ Soc Nucl Med.* 2017.

EP-0859

A novel method for conjugation of PNA to antibodies for radionuclide based pretargeting: proof of principal.

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Aim: Pretargeting is a promising strategy to shorten time for sufficient imaging contrast compared to directly radiolabeled monoclonal antibodies (mAbs). Pretargeting based on hybridization between Peptide Nucleic Acids (PNAs) provides several advantages such as fast hybridization rates, bioorthogonal properties and biocompatibility. Site-specific conjugation of PNA to antibodies would provide a homogenous product with a defined degree of modification and predictable pharmacokinetics. Z-domain, a 58-a.a protein, derived from the IgG-binding B-domain of S.aureus protein A is known to have a well characterized binding site in the Fc-region of IgG. In this study we tested if Z-PNA chimera is suitable for site-specific decoration of mAbs with a PNA-based hybridization probe. We then evaluated feasibility of pretargeting using site-specifically PNA-modified mAb(trastuzumab). **Methods:** The 15-mer PNA-hybridization probe **HP1** was conjugated to Z_{BPA}-domain using a sortase A-mediated ligation. Z_{BPA}-**HP1** chimera was site-specifically conjugated to the Fc-region of trastuzumab and fixed using UV-induced photoactivation. **In vitro** binding specificity of ¹²⁵I-trastuzumab-Z_{BPA}-**HP1** to HER2-expressing cells was tested by saturation of HER2. Specificity of ⁵⁷Co-labeled **HP2**-binding to trastuzumab-Z_{BPA}-**HP1** pretreated cells was tested using competitive binding with large excess of trastuzumab, non-labelled **HP2** or by adding ⁵⁷Co-**HP2** only. Binding affinities of ¹²⁵I-trastuzumab-Z_{BPA}-**HP1** to HER2-expressing cells and affinities of ⁵⁷Co-**HP2** to trastuzumab-Z_{BPA}-**HP1** pretreated cells were measured using LigandTracer. Feasibility of in vivo pretargeting was evaluated in Balb/C mice bearing HER2-overexpressing SKOV-3 xenografts. For this, mice were injected with 80 µg (0.5 nmol) ¹²⁵I-trastuzumab-Z_{BPA}-**HP1** followed by injection of 3.5, 10 or 20 µg ⁵⁷Co-**HP2**, 48 h later. Mice were dissected at 24 h post-⁵⁷Co-**HP2** injection. Control experiments included presaturation of HER2-receptors using excess-fold molar of trastuzumab and injection of ⁵⁷Co-

HP2 without preinjection of trastuzumab-Z_{BPA}-**HP1**. **Results:** Photoconjugation resulted in 40% efficiency yielding one Z_{BPA}-**HP1** per antibody molecule. ¹²⁵I-trastuzumab-Z_{BPA}-**HP1** bound specifically to HER2-expressing cells with nanomolar affinity (1-2 nM). Binding of ⁵⁷Co-**HP2** to HER2 expressing cells was dependent on the presence of trastuzumab-Z_{BPA}-**HP1**. The affinity of binding of ⁵⁷Co-**HP2** to trastuzumab-Z_{BPA}-**HP1**-pretreated cells was in pM range. Tumor uptake of ¹²⁵I-trastuzumab-Z_{BPA}-**HP1** was 0.33±0.06 %ID/g 72 h.p.i and HER2-mediated. Optimal tumor targeting (0.8±0.2 %ID/g) was achieved when 3.5 µg (0.7 nmol) ⁵⁷Co-**HP2** was injected 48 h after trastuzumab-Z_{BPA}-**HP1** injection. Tumor accumulation of ⁵⁷Co-**HP2** was reduced by 2- (0.33±0.06 %ID/g) and 27- (0.03±0.01 %ID/g) folds after presaturation with trastuzumab or when no trastuzumab-Z_{BPA}-**HP1** was preinjected. A tumor-to-blood uptake ratio of 1.5±0.3 was achieved resulting in a clear visualization of HER2-expressing xenografts by SPECT. **Conclusion:** Site-specific conjugation of **HP1** to trastuzumab was possible. The feasibility of trastuzumab-based PNA-mediated pretargeting has been demonstrated.

EP-0860

Brain exposure of ATM inhibitor AZD1390: positron emission tomography (PET) study in healthy human subjects

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Introduction: The protein kinase ATM (ataxia telangiectasia mutated) is a key mediator in the cellular response to cytotoxic DNA double strand breaks induced by radiation (1). Activated ATM facilitates DNA damage repair (DDR). Hence ATM inhibition decreases DNA damage repair and ultimately affects tumor growth. AZD1390 is a novel, highly potent and selective ATM inhibitor (ATMi), targeting active DDR pathways, and currently examined in a phase 1 study in combination with radiation therapy for the treatment of *glioblastoma multiforme* and brain metastases (NCT03423628). **Aim:** The primary objective of this phase I PET study (NCT03215381) was to measure the brain exposure of ¹¹C-labelled AZD1390 after intravenous administration of a microdose in healthy subjects with an intact blood-brain barrier (BBB). **Methods:** A single microdose of [¹¹C]AZD1390 (mean injected mass 1.21 µg, range 0.46-4.67 µg; radioactivity 288 MBq, range 232-369 MBq) was administered intravenously in each of 8 healthy male subjects (age 21-65 years). The radioactivity concentration of [¹¹C]AZD1390 in brain was followed for 90 minutes using a high resolution PET system. Brain MRI (3D

T1-weighted) was used for co-registration of PET and automated delineation of regions of interest. Radioactivity in arterial blood was measured to obtain a metabolite corrected arterial input function for quantitative compartment analysis of [^{11}C]AZD1390. The calculated parameters were: maximum brain radioactivity concentration, ($C_{\text{max}(\text{brain})}$ percent of injected radioactivity, %ID); time of maximum brain radioactivity concentration, $T_{\text{max}(\text{brain})}$; brain to plasma ratio (K_p) assessed as the total distribution volume, V_T ; and free brain to plasma ratio ($K_{\text{pu,u}}$) calculated based on V_T and the free fractions in brain and plasma (2). Safety was monitored by laboratory health examinations, and recording of vital signs, ECG and adverse events (AEs). **Results:** The brain radioactivity after injection of [^{11}C]AZD1390 reached a $C_{\text{max}(\text{brain})}$ of 1.00 %ID (mean, range 0.54–1.33) at a T_{max} of 21 min (mean, range 17–30) min. The mean V_T for the whole brain was 5.20 (2.31–9.19) $\text{mL}\cdot\text{cm}^{-3}$ and $K_{\text{pu,u}}$ was 0.24 (0.11–0.42). No AEs related to administration of a microdose of [^{11}C]AZD1390 were reported during the study. **Conclusions:** The results of this study show that [^{11}C]AZD1390 passes the blood-brain-barrier and provides good brain exposure in human subjects. Further studies in patients with CNS malignancies are warranted to evaluate therapeutic effect of pharmacologic doses of the ATMi AZD1390 in combination with radiation therapy. **References:** (1) Bakkenist CJ, Kastan MB. *Nature*. 2003; 421: 499–506; (2) Schou M et al. *Int J Neuropsychopharmacol*. 2015; 18:pyv036

EP-0861

^{90}Y -labeled of phosphates-coated magnetic nanoparticles as a potential tumor treatment radiopharmaceuticals

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Magnetic nanoparticles (MNPs) have been intensively used for a wide variety of biomedical applications. In the present study, MNPs coated with imidodiphosphate (IDP) or inositol hexaphosphate (IHP) were synthesized and labeled with ^{90}Y . The aim is to investigate the possibility of radiolabeled coated MNPs use in the therapy as multifunctional agents capable to localize both radioactivity and magnetic energy at a tumor site. MNPs were synthesized by co-precipitation of ferric and ferrous salts in a basic solution. Characterization of the MNPs was performed using X-ray powder diffraction, transmission electron microscopy, Fourier transform infrared spectroscopy, dynamic light scattering and laser Doppler electrophoresis. The heating ability of MNPs was quantified through the specific power absorption (SPA) measurements. The MNPs were labeled with $^{90}\text{YCl}_3$ and used in *in vitro* stability studies in saline and human serum and *in vivo* studies in normal and NOD/SCID mice bearing human LS174T colon carcinoma tumors. The coating of MNPs with phosphates made them biocompatible, increased their colloidal stability and allowed the binding of the radionuclide ^{90}Y to the available functional groups on the surface of the MNPs. IDP and IHP have not hitherto been used for coating of MNPs and the results of this study showed that the phosphate groups influenced the modification of the surface of MNPs. The obtained values for the specific power absorption of MNPs (46.95–80.76

W/g) in different physiological media indicated their possible application for hyperthermia treatment. Both types of coated MNPs were ^{90}Y -labeled in a reproducible high yield (>98 %). *In vitro* studies of ^{90}Y -MNP in saline and human serum showed their high stability after 72 h. The biodistribution analyses of $^{90}\text{Y}\text{-Fe}_3\text{O}_4\text{-IDP}$ and $^{90}\text{Y}\text{-Fe}_3\text{O}_4\text{-IHP}$ MNPs after intravenous administration to normal nude mice revealed that the maximum of the injected dose was observed in the liver (91.78% and 85.23%), followed by the spleen (3.53% and 7.89%) and the lungs (2.16% and 2.60%) at 72 h post injection, respectively. An insignificant amount of radioactivity after 72 h was detected in femur, a target organ for free ^{90}Y , indicating that ^{90}Y was tightly attached to the surface of the MNPs. Compared to intravenous injection, intratumoral injection of both nanoparticles can directly deposit large doses to tumor site, without the toxicity to other organs. The results of this comprehensive study showed the great promise of radiolabeled biocompatible phosphate magnetic complexes for therapeutic uses combining magnetic hyperthermia and radiotherapy.

EP-0862

[^{18}F]RPS-547: Improving the pharmacokinetics of [^{18}F]RPS-544 for CXCR4 targeted PET Imaging

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Aim: The recently reported [^{18}F]RPS-544 showed good, CXCR4-specific uptake in tumors, but high activity in the hepatobiliary pathway. Therefore we aimed to make specific structural modifications in order to obtain an improved [^{18}F]labeled with superior tumor/tissue ratios for high contrast imaging of CXCR4 expression. **Materials and Methods:** RPS-546, -547 and -552 were designed to replace the 2-fluoropyridyl moiety of RPS-544 with a fluoroethyltriazole. The ligands and their alkyne precursors for radiolabeling were synthesized in 3 steps. *In vitro* evaluation of the ligands included a competitive binding assay against [^{68}Ga]pentixafor, determination of K_d and internalization in PC3-CXCR4 cells. Radiofluorination was achieved following a click reaction using 2-[^{18}F]fluoroethylazide. Labeled compounds were screened by $\mu\text{PET}/\text{CT}$ imaging at 1 h post injection (p.i.). Biodistributions ($n=5/\text{compound}$) of [^{18}F]RPS-552 (1 h p.i.) and [^{18}F]RPS-547 (1 and 2 h p.i.) were performed BALB/C nu/nu mice bearing bilateral PC3-WT/PC3-CXCR4 tumors. Specificity for CXCR4 was determined by co-injection of AMD-3100 (5 mg/kg). **Results:** The labeling via click chemistry was accomplished manually in a 2 h, non-optimized synthesis with an overall yield of $44.3\pm 7.1\%$ (decay corrected, $n=8$) and molar activity $>185\text{ GBq}/\mu\text{mol}$. Although the IC_{50} of RPS-547 ($601\pm 118\text{ nM}$) and RPS-552 ($515\pm 68\text{ nM}$) was considerably lower than that of RPS-544 ($4.9\pm 0.3\text{ nM}$), imaging by $\mu\text{PET}/\text{CT}$ evidenced similar tumor uptake for all three tracers but faster renal excretion, leading to better contrast, for [^{18}F]RPS-547 and [^{18}F]RPS-552. [^{18}F]RPS-546, with $\text{IC}_{50}\approx 1500\text{ nM}$, showed no specific targeting *in vivo*. Biodistribution studies confirmed PC3-CXCR4 tumor uptake to be $3.1\pm 0.5\%$ ID/g for [^{18}F]RPS-547 and $2.5\pm 0.1\%$ ID/g for

[^{18}F]RPS-552, comparable to uptake of [^{18}F]RPS-544 in the same animal model ($p=0.57$ and 0.16 respectively). Activity levels in the liver and intestines were 5x lower than that of [^{18}F]RPS-544. All tumor/tissue ratios were significantly improved ($p<0.01$) for [^{18}F]RPS-547 relative to [^{18}F]RPS-544. Co-injection of AMD-3100 reduced uptake in the PC3-CXCR4 tumor by 60–70% and by nearly 100% in the bone and spleen. Levels of [^{18}F]RPS-552 in the bone and spleen were substantially, but not completely, reduced by AMD-3100. **Conclusions:** [^{18}F]RPS-547, a structural analog of [^{18}F]RPS-544, shows CXCR4-specific uptake in tumors and improved pharmacokinetics relative the parent compound. The substitution of a fluoroethyltriazole moiety for a 2-fluoropyridyl moiety reduced binding affinity *in vitro* when compared to [^{18}F]RPS-544, but resulted in improved images with comparable tumor uptake but much better contrast to normal tissue.

EP-0863

In vivo imaging of Tau deposition using a new tracer- ^{18}F -S16 in comparison with ^{18}F -THK5317 in Alzheimer's disease

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Purpose: The purpose of this pilot human study was to evaluate the effectiveness of a new tau tracer ((S)-1-(4-(6-(dimethylamino) naphthalen-2-yl)phenoxy)-3-fluoropropan-2-ol, ^{18}F -S16) in identifying AD patients from healthy controls (HCs) as compared with ^{18}F -THK5317. **Methods:** The study cohort consisted of 5 AD, 1 FTLD, 1 PSP, 1 DLB, 6 HCs and 2 young volunteers (Youngs). Dynamic PET was performed over a period of 90 min after injection of tracers in HCs and Youngs. Static data acquisitions with a duration of 20-min from 40 min to 60 min after tracers' administration were performed in all patients to analyze the standardized uptake value (SUV) and cortical-to-cerebellum SUV ratios (SUVRs). Voxel-based analysis of both tracers was employed to assess their uptake differences between populations. **Results:** Both tracers were distributed to the brain of all controls rapidly but the clearance of ^{18}F -S16 was slower than ^{18}F -THK5317 within 90 min acquisition. In addition, ^{18}F -S16 displayed higher grey matter but lower white matter uptake than ^{18}F -THK5317 in controls. Nonspecific uptake was observed in both tracers in basal ganglia and brain stem, but the eyeball uptake was observed only in ^{18}F -THK5317. In comparative studies, the cortical average SUVr of ^{18}F -THK5317 was 1.22 ± 0.06 for AD versus 1.13 ± 0.03 for HCs ($F = 5.73$, $P < 0.05$), and for ^{18}F -S16, that was 1.19 ± 0.10 versus 1.17 ± 0.06 ($F = 1.54$, $P > 0.05$). In voxelwise analysis, AD patients showed significant increased cortical ^{18}F -S16 binding in the bilateral basal temporal cortex, hippocampus, prefrontal cortex, insular, ACC and lateral parietal cortex; ^{18}F -THK5317 displayed increased abnormal retention in bilateral basal temporal cortex, lateral temporal cortex, prefrontal cortex, PCC/precuneus and lateral parietal cortex. The patterns of uptake of both tracers were similar in FTLD and PSP patients and no obvious

abnormal uptake was found in the DLB patient. **Conclusions:** Although the binding intensity and distribution of ^{18}F -S16 were different with that of ^{18}F -THK5317 in controls, the significant difference between AD and HCs in cortical regions indicates that ^{18}F -S16 might be a promising Tau-tracer for PET imaging.

EP-0864

A dual-modality tracer design for peptides based on bioorthogonal click chemistry

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Introduction: Dual-modality—or rather hybrid—tracers containing both fluorescence and radioactivity imaging labels have demonstrated potential during surgical guidance. Given that such molecular imaging procedures require the introduction of two imaging labels on a single targeting vector, the molecular design is of utmost importance for the tracer performance. The aim of this study was to research the possibility to move towards bioorthogonal click chemistry as a tool for designing hybrid tracers for *in vivo* use. **Methods:** Consistency with previous works was kept by utilising a standardised cyclic RGD peptide as targeting vector. Cyclic RGD peptides (c[RGDyK]) were functionalised with a custom azide-containing Cy5 dye followed by subsequent conjugation *via* click chemistry to BCN- or DBCO-functionalized DTPA and radiolabelling with ^{111}In . The prepared hybrid tracers were studied for chemical stability, serum interaction and photophysical characteristics, followed by *in vitro* (Geß3 cells; flow cytometry, fluorescence microscopy) and *in vivo* (orthotopic 4T1 mouse tumour model; SPECT imaging, fluorescence imaging and %ID/g distribution studies). **Results:** The quantum yield of $\text{N}_3\text{-Cy5-(SO}_3\text{)-COOH}$ was $\Phi_f = 6\%$, which increased by 116 or 250% after click chemistry (DTPA-DBCO- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$ $\Phi_f = 13\%$ and DTPA-BCN- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$ $\Phi_f = 21\%$). Both tracers proved to be chemically stable and displayed a comparable serum interaction (40 ± 2 and $44 \pm 2\%$ bound for DTPA-DBCO- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$ and DTPA-BCN- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$, respectively). *In vitro* studies indicated that the BCN click handle negatively influenced the affinity for $\alpha_v\beta_3$ ($K_D = 158 \pm 119$ nmol) as compared to the DBCO handle ($K_D = 26 \pm 6$). With both tracers, orthotopic 4T1 tumours could be visualised using SPECT imaging. High renal accumulation was observed for both analogues (22 ± 6 vs. 15 ± 3 %ID/g) and renal excretion was favoured over hepatobiliary excretion. Tumour-to-muscle ratios were similar (4.8 ± 2.1 and 5.1 ± 1.5 ; DBCO- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$ and DTPA-BCN- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$, respectively), but tumour-to-fat ratios were again poorer for the BCN analogue (5.0 ± 3.4 and 2.7 ± 1.8 ; DBCO- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$ and DTPA-BCN- $\text{N}_3\text{-Cy5-(SO}_3\text{)-c[RGDyK]}$, respectively). **Conclusion:** Use of bioorthogonal click chemistry enables the progressive design of hybrid tracers. Although our findings indicate the DBCO-based design holds most potential, the findings indicate that further structural refinement may positively influence tracer performance in the future.

EP-0865

A Novel Molecule for the Systemic Imaging and Treatment of Rheumatoid Arthritis

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Introduction: A Tc-99m labeled mannosyl-dextran molecule (Tc-99m tilmanocept) has demonstrated specificity for targeting CD206 macrophages associated with sentinel nodes in breast cancer patients. The CD206 receptor is also expressed on inflammatory cells in the joints of patients with rheumatoid arthritis (RA) and in other inflammatory conditions (such as atherosclerosis) [1]. In patients with advanced RA, direct injections of radiocolloid into affected joints are used therapeutically to relieve pain and increase mobility. RA rarely effects a single joint, so multiple injections at multiple sites are required. If the radiocolloid could be administered systemically, it may be possible to treat multiple joints simultaneously. We combined a therapeutic isotope, Sn-117m (γ 159 keV, 86% ; e^- ~140 keV, 112% ; $t_{1/2}$ 14d) with mannosyl-dextran to test the ability of the therapeutic tracer to localize in sites of inflammation in similar fashion to Tc-99m tilmanocept. **Methods:** Sn-117m was chelated with aminobenzyl-DOTA. Mannose coupled dextran amine was combined with the Sn-117m chelate and the pH was adjusted and the final product purified with a size exclusion column. Yields ranged from 30 to 60%. A sterile abscess (containing CD206 macrophages) was induced in eight BALB/c mice (injection of 20 μ L of turpentine into the gastrocnemius muscle). Twenty-four hours later mice were each injected with 20 μ L (~200 kBq) of Sn-117m composition into the lateral tail vein. Four mice were sacrificed at 2 hours after and the other four at 24 hours after the injection. Identical parallel experiments were also performed with 8 additional mice using the commercial preparation of Tc-99m tilmanocept. Biodistribution analyses were performed of tissues and fluids. **Results:** A comparison demonstrated similar elevated abscess to normal muscle uptake with both compounds. Biodistribution profiles were similar although an increase in liver uptake was observed for the Sn-117m molecule. **Conclusions:** These studies suggest that systemic administration of a Sn-117m tilmanocept analogue localizes in inflamed RA tissue. 1. "The inextricable axis of targeted diagnostic imaging and therapy: An immunological natural history approach", F.O Cope *et al.*, Nuclear Medicine and Biology 43, (2016) 215-225

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Pharmacokinetic properties of Gallium-68 labeled hydroxypropyl-beta-cyclodextrin

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Introduction: A new renaissance started in the research and application of cyclodextrins a few years ago. The number of novel derivatives are increasing and new applications has been appeared. Fluorescent and radiolabeled cyclodextrin derivatives are new tools in cyclodextrin research. By the help of these molecules the cellular interactions, biological activity, pharmacokinetics and *in vivo* distribution can be monitored by imaging techniques. The aim of our study was to synthesize the ⁶⁸Ga-labeled NODAGA-hydroxypropyl-beta-cyclodextrin (⁶⁸Ga-NODAGA-HPBCD) and test the pharmacokinetic properties and *in vivo* distribution of this radiolabeled molecules.

Methods: p-NCS-benzyl-NODA-GA (NODAGA) was conjugated to the 6-deoxy-6-monoamino-(2-Hydroxypropyl)- β -cyclodextrin (NH₂-HPBCD). The product (NODAGA-HPBCD) was analyzed by analytical RP-HPLC and verified with high resolution mass spectrometry. In the next step the NODAGA-HPBCD was labeled with Gallium-68 (⁶⁸Ga). The ⁶⁸Ga labeled NODAGA-HPBCD (⁶⁸Ga-NODAGA-HPBCD) was characterized. The radiochemical purity (RCP%), partition coefficient (log *P* values), and *in vitro* stability of ⁶⁸Ga-NODAGA-HPBCD was determined. Thereafter *in vivo* distribution and pharmacokinetic properties of ⁶⁸Ga-NODAGA-HPBCD was monitored by positron emission tomography (PET). **Results:** NODAGA-HPBCD was purified by preparative RP-HPLC and the purity was better than 99%. The radiochemical purity of the ⁶⁸Ga-NODAGA-HPBCD was higher than 98%, the specific activity was 16.72 ± 2.34 GBq/ μ mol, and the decay corrected yield was $75.64 \pm 6.21\%$ (n = 8). The octanol/water partition coefficient of ⁶⁸Ga labeled NODAGA-HPBCD was found to be -3.08 ± 0.12 . For *in vitro* stability measurements the ⁶⁸Ga-NODAGA-HPBCD were added to mouse plasma at 37°C and measured with analytical radio-HPLC. Aliquots were taken at 15, 30, 60 and 90 minutes and the radiochemical purity results were higher than 95% in all cases. *In vivo* dynamic and *ex vivo* biodistribution studies using control BALB/c mice revealed that ⁶⁸Ga labeled NODAGA-HPBCD was mainly excreted by the kidney, due to its hydrophilic properties that has been proved by the partition coefficient. The accumulation of the radiotracer in abdominal organs was very low, and no uptake was found in the brain. **Conclusion:** In this study, ⁶⁸Ga labeled NODAGA-HPBCD was successfully produced and tested *in vitro* and *in vivo*. The synthesized NODAGA-HPBCD was characterized and labeled with ⁶⁸Ga successfully. Overall, the outcome of our study indicates that the *in vivo* behavior of radiolabeled cyclodextrins can be examined by PET techniques, thus these derivatives are suitable for further pharmacokinetic measurements. This study was supported by FK_17 (FK124634) research grant of the National Research, Development and Innovation Office, Budapest, Hungary

EP-0867

Towards an improved radiotracer to study P-glycoprotein function at the blood-brain barrier: first human PET data with [¹¹C]metoclopramide

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Aim: At the human blood-brain barrier (BBB), P-glycoprotein (ABCB1) limits brain distribution of diverse drugs. Currently available PET tracers to study cerebral ABCB1 function ((*R*)-[¹¹C] verapamil, [¹¹C]*N*-desmethyl-loperamide) are avid ABCB1 substrates with low brain uptake, which possess inadequate sensitivity to detect moderate changes in ABCB1 function at the BBB. Metoclopramide is a weak ABCB1 substrate with sufficiently high passive permeability to cross the BBB. The aim of this study was to assess the influence of ABCB1 on the neuropharmacokinetics of [¹¹C]metoclopramide. **Materials and Methods:** Ten drug free, healthy volunteers (mean age: 26±4 years) underwent 60 min PET scans with [¹¹C]metoclopramide before and during a 2 hour infusion of the ABCB1 inhibitor cyclosporine A (CsA) at a dose of 2.5 mg/kg body weight/hour. Arterial plasma concentrations of [¹¹C]metoclopramide and its radiolabelled metabolites were determined with radio-HPLC to derive a metabolite-corrected arterial input function. Individual, MRI-based whole brain grey matter region of interest was used to extract PET activity values. PET and plasma data were modeled employing a reversible 1-tissue-2-rate constant compartmental model. In addition, the elimination rate constant of radioactivity from the brain (k_p) was determined by linear regression analysis. **Results:** In baseline scans, [¹¹C]metoclopramide showed appreciable brain uptake (total volume of distribution V_T : 2.11±0.33 mL/cm³), which was approximately 3-fold higher than that of [¹¹C]verapamil. During CsA infusion, there was a significant decrease in radioactivity elimination from the brain (change in k_p : -40±20%, $p<0.0001$, paired t test). Moreover, K_1 was increased by +9±12% ($p=0.0533$), k_2 was decreased by -15±5% ($p<0.0001$) and V_T was increased by +29±17% ($p=0.0002$). Forty minutes after radiotracer injection, 53±14% and 51±13% of total radioactivity in plasma consisted of unchanged parent tracer in scan 1 and scan 2, respectively. **Discussion:** We found a significant increase in brain distribution of [¹¹C]metoclopramide under conditions of partial ABCB1 inhibition, which confirms that [¹¹C]metoclopramide is transported by ABCB1 at the human BBB. The same CsA infusion protocol caused in humans an approximately 65% increase in K_1 and V_T and no change in k_2 of [¹¹C]verapamil (Muzi et al. JNM 2009;50:1267-75). In contrast to currently available avid ABCB1 substrate radiotracers, ABCB1 inhibition led to a decrease in radiotracer elimination from the brain, which suggests that ABCB1 exerts a pharmacokinetically different impact on brain distribution of weak as compared with avid ABCB1 substrates. [¹¹C]Metoclopramide may be better suited to detect disease-induced alterations in ABCB1 function at the BBB than avid ABCB1 substrates.

EP-0868

In vivo PET imaging and Kinetic Profile of ¹⁸F-FC119S in 5xFAD Mouse model: a preliminary study

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Purpose: ¹⁸F-FC119S is a positron emission tomography (PET) tracer for imaging β -amyloid (A β) plaques in Alzheimer's disease (AD). The aim of this study is to evaluate the efficacy of ¹⁸F-FC119S in quantitating A β deposition in a mouse model of

AD by PET. **Method:** Dynamic ¹⁸F-FC119S PET images were obtained in 5xFAD ($n = 5$) and wild-type (WT) mice ($n = 7$). The brain PET images were spatially normalized to the M. Mirrione T2-weighted mouse brain MR template, and the volumes of interest were then automatically drawn on the cortex, hippocampus and cerebellum. The specific binding of ¹⁸F-FC119S to A β was quantified as the distribution volume ratio using Logan graphical analysis with the cerebellum as a reference tissue. The A β levels in the brain were also confirmed by immunohistochemical analysis. **Results:** For the 5xFAD group, radioactivity levels in the cortex and the hippocampus were higher than those for the WT group. In these regions, specific binding was approximately 1.2-fold higher in 5xFAD mice than in normal mice. Immunohistochemistry supported these findings; the AD group showed severe A β deposition in the cortex and hippocampus in contrast to the WT group. **Conclusion:** These results demonstrated that ¹⁸F-FC119S PET can differentiate amyloid deposition in 5xFAD mice from that in WT mice. **Acknowledgements:** FutureChem (Korea) is acknowledged for the synthesis of ¹⁸F-FC119S. This study was supported by a grant from the Korea Institute of Radiological and Medical Sciences (KIRAMS), which is funded by the Ministry of Science and ICT(MSIT), Republic of Korea (1711062441/50461-2018, 50536-2018).

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Can we image Malignant Pleural Mesothelioma with ⁶⁸Ga-DOTA-Neurotensine analogue? In vitro study

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Aim: Malignant Pleural Mesothelioma (MPM) is an aggressive tumor with increasing incidence as a result of widespread exposure to asbestos. Most of the patients with MPM do not experience symptoms until the late-stage. Additionally, MPM is commonly unresponsive to conventional chemo-radiotherapy and most patients die within 7-9 months of diagnosis. Up to date, ¹⁸F-FDG PET/CT imaging does not significantly increase the accuracy of early diagnosis of MPM. Due to the high neurotensin receptor-1 (especially NTSR1) expression of MPM cells, we decided to evaluate the diagnostic relevance of a new and promising imaging molecular PET probe: a neurotensin fragment derivatized with DOTA and labeled with ⁶⁸Ga, named DO-TA-NT-20.3. We evaluated this drug in vitro on the mesothelioma cell line MSTO-211H, by cell kinetic uptake assay. **Materials and Methods:** ⁶⁸Ge/⁶⁸Ga Generator was eluted with 8mL 0.1M HCl. A cleaning elution was carried out to eliminate the ⁶⁸Zn present in the generator, which can affect the synthesis yield. For the preparation of ⁶⁸Ga-DOTA-NT-20.3 fragment, 150-800MBq of ⁶⁸GaCl₃ (app. 8.0mL) and 50 μ g of precursor, dissolved in 50 μ L TraceSelect Water, were used in an automatic synthesis module. The ⁶⁸Ga elution was pre-purified on SCX column. The purified ⁶⁸Ga³⁺ was obtained eluting the column with 0.8mL of NaCl/HCl 3M solution (pH=1). 2mL of CH₃COONa/CH₃COOH 0.8M buffer

and 400 μ L EtOH/H₂O at 50/50% (v/v) was added to 50 μ g NT-20.3 and to 0.8 mL $^{68}\text{Ga}^{3+}$ solution eluted from column. The reactor was heated to $80 \pm 2^\circ\text{C}$ for 3 min and then to $110 \pm 2^\circ\text{C}$ for 7 min. The product was diluted to 8 mL with 0.9% saline solution. Final product pH ranged between 4.0 and 5.0. MSTO-211H cells were incubated with 100 kBq of ^{68}Ga -DOTA-NT-20.3 and uptake was measured at different time points (60, 80, 100, 140 min), with a 3" x 3" NaI(Tl) pinhole gamma counter. **Results:** Our results showed that ^{68}Ga -DOTA-NT-20.3 uptake plateaued 80 min after incubation. Saturation binding experiments were performed and statistical analysis revealed a Hill slope of h between 0 and 1, thus indicating that the radiolabeled compound has multiple binding sites without a positive cooperativity. **Conclusion:** The new radioligand ^{68}Ga -DOTA-NT-20.3 can have an important role in the early diagnostic procedure of patients with MPM. Furthermore, the substitution of the ^{68}Ga diagnostic isotope with a therapeutic one (such as ^{223}Ra , ^{90}Y , ^{177}Lu , ^{111}In) could lead this tracer being used as a new specific therapeutic agent for patients with MPM.

EP-0870

A Pre-targeting Approach For Liver Radioembolization

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Aim: Theranostic applications such as hepatic radioembolization for the treatment of liver metastasis can suffer from discrepancies between diagnostic planning (scout-scan) and the therapeutic delivery itself, resulting in unwanted side-effects such as pulmonary shunting. We reasoned nanotechnology based supramolecular interactions could help overcome this shortcoming, thereby directly linking pre-interventional diagnostics to the local delivery of therapy. We here present a theranostic pre-targeting concept based on host-guest interactions. With this concept the distribution observed in the scout scan provides a target for a secondary (therapeutic) vector. **Materials & Methods:** Adamantane functionalized macroaggregated albumin particles (MAA), acted as guest-vector and were (optionally) labeled with technetium-99m (^{99m}Tc -MAA-Ad). The secondary host-vector, $\text{Cy}5_{0.5}\text{CD}_9\text{PIBMA}_{39}$ was labeled with either ^{99m}Tc or ^{111}In . In vitro serum stability of host-guest complexes were studied during 44h at 37°C . For pre-targeting (^{99m}Tc)-MAA-Ad was intra-hepatically administered in mice. Two hours thereafter, ^{99m}Tc - or ^{111}In - $\text{Cy}5_{0.5}\text{CD}_9\text{PIBMA}_{39}$ was administered I.V. Between 2 and 44h p.i. (dual-isotope) SPECT imaging was performed and the %ID/g in various tissues was determined. Pre-targeting with non-functionalized MAA or injections with mere PBS served as controls. **Results:** *In vitro* MAA-Ad and $\text{Cy}5_{0.5}\text{CD}_9\text{PIBMA}_{39}$ were stable, only showing 10-20% dissociation at 44h incubation. *In vivo* (dual-isotope) SPECT imaging of host-guest interactions in mice confirmed co-localization between $\text{Cy}5_{0.5}\text{CD}_9\text{PIBMA}_{39}$ and MAA-Ad in the liver. Hepatic uptake of radiolabeled $\text{Cy}5_{0.5}\text{CD}_9\text{PIBMA}_{39}$ amounted to $14.9 \pm 6.1\%$ ID/g at 2h p.i. which increased to $26.2 \pm 2.1\%$ ID/g at 44h p.i.. Hepatic uptake values as result of pre-targeting were significantly higher compared to those

in control mice. Uniquely, for the first time, this data indicates that the formation of multivalent supramolecular interactions between cyclodextrin and adamantane can be used to drive complex formation in the chemically challenging *in vivo* environment. **Conclusion:** Our data demonstrates pre-targeting strategies could help innovate radioembolization procedures, in particular those based on multivalent supramolecular interactions. The potential of early preclinical findings warrant further chemical optimization of the individual components, possibly followed by clinical translation.

EP-0871

Gold nanoparticles coated with antibodies lead to ROS-dependent apoptotic cell death in non-cancerous human cell lines

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In cancer radiotherapy, gold nanoparticles (AuNPs) have emerged as promising radiosensitizers increasing the effectiveness of external beam radiotherapy by local production of reactive oxygen species (ROS) and secondary electrons upon irradiation. At UNamur, 5 nm gold nanoparticles coated with an organic shell of polyallylamine are produced by plasma vapor deposition (AuNPs@PPAA). Optionally, the AuNPs@PPAA can be conjugated to anti-EGFR antibodies (Cetuximab) (AuNPs@PPAA-Ctxb) which actively target EGFR-overexpressing cancer cells *in vitro* and *in vivo*. However, *in vivo* biodistribution studies have demonstrated a significant accumulation in the liver and the spleen. Therefore, the cytotoxicity profile of the gold nanoparticles should be properly investigated in healthy cell types prior to use the AuNPs@PPAA-Ctxb in clinical applications. Human kidney (HK-2) cells and Human telomerase-immortalized microvascular endothelial (TIME) cells were studied as first examples of healthy cells. We performed MTS cytotoxicity assays after 3 hours and 24 hours of incubation and live cell imaging with apoptotic markers Annexin V and caspase 3/7 during 72 hours of incubation with AuNPs@PPAA(-Ctxb). Transmission electron microscopy (TEM) was performed to visualize nanoparticle uptake after 30 minutes, 3 hours and 24 hours in the presence of nanoparticles with a concentration of 0.005 mg/ml of gold. TEM imaging demonstrated gold nanoparticle uptake in the cytoplasm already after 30 minutes of incubation with AuNPs@PPAA-Ctxb and a further increase after 3 hours and 24 hours of incubation. The MTS cytotoxicity assay showed a significant concentration-dependent reduction in cell viability of TIME cells after 3 hours and 24 hours of incubation with AuNPs@PPAA(-Ctxb), and of HK-2 cells after 24 hours of incubation. For the latter time point, TIME cells showed a lower EC50 value than that of HK-2 cells (0.006 mg/ml vs 0.009 mg/ml for AuNPs@PPAA, and 0.011 mg/ml vs 0.017 mg/ml for AuNPs@PPAA-Ctxb). Using live cell imaging, we observed a significant increase in Annexin V and caspase 3/7 activation in HK2 cells and TIME cells after 8 and 10 hours respectively in a concentration- and time-depen-

dent manner, indicating apoptosis as the process of cell death. Co-exposure of cells with gold nanoparticles and N-acetyl-L cysteine, an antioxidant, significantly reduced or delayed apoptosis indicating that AuNPs@PPAA(-Ct**xb**) induces oxidative stress. In the future, we will quantify the cellular AuNPs@PPAA-Ct**xb** uptake by means of ICP-MS. Furthermore, ELISA and western blot will give more details on damages induced by the oxidative stress.

EP-0872

Preparation and radiolabeling of surface-modified magnetic nanoparticles with technetium-99m as potential radiopharmaceuticals in nuclear medicine

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Recent advances in nuclear medicine have explored nanoscale carriers for targeted delivery of various radionuclides in specific manners to improve the effect of diagnosis and therapy of diseases. Magnetic nanoparticles (MNPs) have been widely developed for medical applications due to their high versatility, excellent functional properties, with the possibility to control different topological parameters relevant for multidisciplinary applications. The aim of the present study was to characterize MNPs coated with two hydrophilic bisphosphonate ligands, i.e., methylene diphosphonate (MDP) and 1-hydroxyethylidene diphosphonate (HEDP) and labeled with ^{99m}Tc . The purpose of this study was to examine if the above nanoparticles, can be used, for hyperthermia application and nuclear medicine imaging. The bisphosphonate coated MNPs were synthesized using co-precipitation method. Characterization of the MNPs was performed using X-ray powder diffraction, transmission electron microscopy, Fourier transform infrared spectroscopy, dynamic light scattering and laser Doppler electrophoresis. The heating ability for cancer hyperthermia therapy application was quantified through the specific power absorption (SPA) measurement. Radiolabeling of both bisphosphonate-coated Fe_3O_4 nanoparticles with ^{99m}Tc were carried out using SnCl_2 as a reducing agent. ^{99m}Tc -MNPs were additionally used for *in vitro* stability studies in saline and human serum and *in vivo* biodistribution studies in normal and NOD/SCID mice bearing human LS174T colon carcinoma tumors. The obtained SPA values of aqueous solutions Fe_3O_4 -MDP and Fe_3O_4 -HEDP are 67.3-183 and 55-131 W/g respectively for increasing field frequency between 252 kHz and 577 kHz indicated their possible application for hyperthermia treatment. Both radiolabeled MNPs were obtained in high radiochemical yield (>95%) and proved stable *in vitro*. The *in vivo* studies for both ^{99m}Tc -MNPs have shown significant liver and spleen uptake at all examined time points in normal mice, due to their colloidal nature. Accumulation of both labeled MNPs in other organs was negligible. We compared the uptake of both ^{99m}Tc labeled MNPs in tumor bearing mice from different administration routes (intratumoral or tail vein injection). In comparison, the overall tumor concentrations of both ^{99m}Tc -MNPs were significantly higher after intratumoral than after intravenous administration ($P < 0.001$). The tumor uptake values after intrave-

nous injection were negligible. The obtained results of specific power absorption demonstrate potential therapeutic applications of Fe_3O_4 -MDP and Fe_3O_4 -HEDP MNPs. Such radiolabeled biocompatible bisphosphonate MNPs with high labeling yield, *in vitro* and *in vivo* stability, showed the great promise as theranostic nanoagents which combines magnetic hyperthermia and SPECT imaging.

EP-0873

Efficient encapsulation of therapeutic radionuclides in liposomes based on analysis of radionuclide-chelating ligand complex formation

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Aim: Liposomes, well-known drug carriers, are also promising tools for both diagnostic tumor imaging and radionuclide therapy, because they can in principle encapsulate any radionuclides and deliver them to the tumor. We aim to develop liposomes as a platform of radiotheranostics. For that, efficient radionuclide encapsulation is needed, especially therapeutic radionuclides, such as ^{90}Y , ^{177}Lu and $^{64/67}\text{Cu}$. The remote loading method enables efficient labeling of liposomes in which ionophores carry radionuclides across the liposomal membrane and pass them to pre-encapsulated chelating ligands. However, only labeling efficiency was focused and little was reported on the complex formation between nuclides and ligands and their stability in liposomes. In this study, we determined their analysis conditions by using HPLC system, and then examined efficient encapsulation of therapeutic nuclides in liposomes. **Methods:** Liposomes were composed of DSPC and cholesterol, or PEGylated (10%), and preloaded 10 mM DOTA or NOTA. The remote loading was done firstly with stable isotopes of Cu^{2+} and Y^{3+} , and then ^{64}Cu or ^{89}Y were used with or without stable carriers. Oxine and tropolone were used as ionophore. Liposomal aqueous phase was obtained by chloroform-water extraction of liposomes. **Results:** HPLC separation and quantification of NOTA, Cu^{2+} and Cu -NOTA has successfully been done by combination of cation exchange column (CapcellPak CR) and unique ODS column (Capcell Core ADME) with HPLC system equipped with aerosol-based detector NQAD, as each of them had no UV absorption. Each peak was validated by mass spectrometry and ^{64}Cu radioactivity. Then remote loading of Cu^{2+} in liposomes was evaluated. Complex formation of Cu -NOTA increased depending on amount of added Cu . Loading temperature over 40°C was needed for high loading efficiency. The loading was completed within 10 min. Under these conditions, ^{64}Cu was successfully encapsulated in liposomes with high efficiency (>90%). Encapsulation of ^{64}Cu of the 10 GBq equivalency or more was possible. In the similar way, HPLC separation of DOTA, Y^{3+} and Y -DOTA was succeeded and ^{89}Y encapsulated liposomes were obtained with high efficiency. No leakage of loaded radionuclides was observed upon storage and after serum incubation for 24 h at 37°C. Their biodistribution and tumor accumulation were similar with ^{67}Ga -NOTA-liposomes and ^{111}In -DOTA-liposomes. Good tumor accumulation was obtained (5.8 %AD/g) in FaDu-bearing mice. **Conclusions:** HPLC analysis of nuclide-ligand complex formation was useful

for effective encapsulation of therapeutic radionuclides in liposomes. **Research support:** This study was supported by Grants-in-Aid from JSPS, HLSR Grant by MHLW and NCC Research and Development Fund.

EP-0874

One-step ^{18}F -fluorination of furin activatable probe for PET imaging of tumor

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Introduction: Peptide analogies have generated great interest as tumor positron emission tomography (PET) imaging agents due to their attractive property. Nevertheless, the complicated radio-labeled process and fast metabolism make the final clinical application of peptide probes challenging. A novel probe Acetyl-Arg-Val-Arg-Arg-Cys(StBu)-Gly(^{18}F -AmBF₃)-CBT (^{18}F -1), was designed by introducing AmMBF₃ into the conjugation of RVRP peptide and CBT motif for the one-step ^{18}F -fluorination.

Methods: The radiosynthesis of ^{18}F -1 was under facile conditions in pyridazine-HCl buffer (pH~2.5, 1 M) at 80 °C within 30 min. The enzyme-controlled condensation was studied in MDA-MB-468 cell lysates. The cellular uptake of ^{18}F -1 and ^{18}F -1-ctrl was studied by the measurement of radioactivity intracellular by a γ -counter after incubating with ^{18}F -1 or ^{18}F -1-ctrl (1 μCi) in MDA-MB-468 cells. The in vivo behavior of ^{18}F -1 was examined by PET imaging using MDA-MB-468 tumor-xenografted mice and was compared to that of the ^{18}F -1-ctrl and co-injection of unlabeled compound 1. **Results:** The final radiochemical yield (RCY) was determined at $65.3 \pm 1.75\%$ with an excellent radiochemical purity (RCP>99%). Moreover, under the action of furin and GSH, the probe suffered the condensation reaction to form dimers and self-assembly into nanoparticles for enduring signals. The cellular uptake of ^{18}F -1 and ^{18}F -1-ctrl were determined to be $10.2 \pm 0.37\%$ and $1.19 \pm 0.25\%$ at 120 min respectively. For in vivo PET imaging, ^{18}F -1 exhibited a $39 \pm 0.31\%$ ID/g tumor uptake and 2.93 ± 0.92 tumor-to-muscle ratio at the beginning of the injection, which was lowered at 60 min. The co-injection of ^{18}F -1 and 1 kept a stable tumor uptake ranging 2.83 ± 0.23 to $3.40 \pm 0.18\%$ ID/g within 60 min. **Conclusions:** The one-step labeling method shows advantages in the simple labeling process with high RCY and short labeling time, which enables a real kit process for the synthesis of ^{18}F -radiopharmaceuticals and significant for the large scale production of clinic application. Funding: This work was supported by Natural Science Foundation of Jiangsu (BK20151118), 333 Project of Jiangsu Province (BRA2016518) and the Key Youth Medical Talent Project of Jiangsu Province (grants QNRC2016626 and QNRC2016629).

EP-0875

A population pharmacokinetics approach to evaluate the impact of the antibody dose in a context of lymphoma radioimmunotherapy (RIT) on dogs

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In lymphoma RIT, the administration of a dose of unlabelled antibody given as a pre-dose before or in co-infusion with the radiolabelled antibody reduces splenic uptake and slows the radioconjugate's clearance from blood. In clinical studies, however, it has been complex to evaluate the amount of cold antibody required to saturate normal and malignant B-cells in spleen. Our study aims at using a population pharmacokinetics (PPK) approach to estimate this amount in dogs injected with an anti-CD22 MAb and derive the parameters that influence the antibody distribution. Seven dogs (6 healthy dogs and 1 dog bearing CD22+ B-cell lymphoma) were injected with an anti-canine CD22 antibody radiolabelled with indium-111. The six healthy dogs were separated in three groups receiving different amounts of antibody (17.75mg, 5mg and 0.75mg). The lymphoma dog received 0.75mg of antibody. SPECT/CT images were acquired at different time-points following the administration (from 1h to 164h). Blood samples were also collected after injection. SPECT images were then quantified to derive the antibody pharmacokinetics. We modelled the experimental data with a PPK approach. The pharmacokinetic model considers an immediate uptake in spleen after injection and a potential tumour uptake in major organs for the lymphoma dog. Data from the seven dogs were gathered and used to identify the adjustable parameters of the model following a PPK approach. In healthy animals, the antibody clearance for blood was much faster for healthy dogs receiving the lowest dose of antibody. Activity uptake in the spleen was also dependant on the amount of injected antibody with higher uptake for the dogs receiving 0.75 mg of antibody ($3.8 \pm 0.4\%$ IA/g at 45h) compared with the dogs receiving 17.75mg of antibody ($1.2 \pm 0.7\%$ IA/g at 47h). A much higher uptake was observed in the spleen of the lymphoma dog, infiltrated with disease as assessed with ultra-sound imaging (11.1% IA/g at 45h). Despite the sparsity of data, our PPK approach made possible the identification of the adjustable parameters of the model and fitted well the experimental data. Two covariates that influenced the spleen uptake were identified: the spleen mass and the presence of splenic tumours. In healthy dogs, model predicts that an antibody dose around 0.5 mg/kg is sufficient to saturate the splenic uptake. Our PPK approach revealed successful to model pharmacokinetics data from healthy and lymphoma dogs in a RIT context. This could be used to adapt the amount of antibody to inject to patients and thus optimize this therapy.

EP-0876

Transcapillary Escape Rate of ^{125}I -Albumin in Relation to Timing of Blood Sampling

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Introduction: Increased vascular permeability is an early sign of vascular damage. Transcapillary escape rate of albumin (TER_{alb}) can be measured using the disappearance of radioactive recombinant human serum albumin (rHSA), according to

either a one or two compartmental kinetic model. The aim of the study is to evaluate the influence of different blood sampling schemes and the use of different compartmental analyses for the calculation of TER_{alb} . **Materials and Methods:** Study subjects were part of a cross-over intervention study protocol, that investigated the effect of a chronic dietary sodium load on blood pressure, the endothelial surface layer and microcirculation. Blood samples were drawn after 3, 4, 5, 10, 15, 20, 30, 45 and 60 minutes after intravenous administration of 100 kBq I-125 rHSA. TER_{alb} was calculated according different blood sampling schemes, beginning at 3 - 20 till 60 minutes. **Results:** Only 85% of the subjects reached maximum concentration (C_{max}) within 10 minutes, while all participants reached C_{max} within 20 minutes. The calculated TER_{alb} of the one compartmental analysis using blood samples from $T_{20\ min}$ and later ($T_{20\ min}$ scheme) ($n=35$, mean TER_{alb} $5.62 \pm 2.24\%$) was significant lower compared to the analysis with samples from $T_{3\ min}$ ($T_{3\ min}$ scheme) ($n=15$, mean TER_{alb} $7.31 \pm 1.50\%$, $p=0.020$). The TER_{alb} of the two compartmental analysis of the $T_{20\ min}$ scheme ($n=35$, mean TER_{alb} $6.09 \pm 2.24\%$) was significant lower compared to the $T_{3\ min}$ scheme ($n=13$, mean TER_{alb} $7.22 \pm 1.47\%$, $p=0.047$) and $T_{5\ min}$ scheme ($n=22$, mean TER_{alb} $6.69 \pm 1.59\%$, $p=0.000$). There were no significant differences between the mean TER_{alb} of the $T_{20\ min}$ scheme using one compartmental analysis compared to a two compartment model (mean difference = $-0.368 \pm 2.372\%$, $p=0.455$). In addition, the TER_{alb} based on only two samples ($T_{20\ min}$ and $T_{60\ min}$) was not significant different compared to the TER_{alb} using multiple samples ($T_{20\ min}$, $T_{30\ min}$, $T_{45\ min}$ and $T_{60\ min}$). **Conclusion:** To allow for a maximum concentration of rHSA in all the subjects, sampling schemes must start at least 20 minutes after administration of rHSA. The mean TER_{alb} using the $T_{20\ min}$ sampling scheme was significant lower compared to sampling schemes starting at earlier time points. There was no significant difference in TER_{alb} using one or two compartmental analysis or based on two samples only ($T_{20\ min}$ and $T_{60\ min}$) compared to multiple samples.

EP-63

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Radiochemistry -> Radionuclide production

EP-0877

Results of the production of ^{68}Ga with biomedical cyclotron by liquid target

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Introduction: Following our preliminary feasibility study, this work is aimed to evaluate the production of ^{68}Ga ($t_{1/2}=67.63$ min, β^+ 88.88%), via the $^{68}Zn(p,n)^{68}Ga$ reaction by proton irradiation of an enriched zinc nitrate solution, using a biomedical cyclotron, as an alternative to current expensive generators. The production of ^{68}Ga by liquid target has different advantages: it makes ^{68}Ga routinely available and it is relatively inexpensive. **Methods:** The target material was prepared by dissolving metallic ^{68}Zn (isotopic enrichment of 99.26%) in HNO_3 6N and then diluting it with HNO_3 0.2N (to get the pressure in the target under control during irradiation) to obtain a 1.7M solution of $^{68}Zn(NO_3)_2$. Using the cross-section data (EXFOR database) and the proton stopping power (SRIM software), the ^{68}Ga saturation yield and its impurities were estimated and this allowed us to find the optimal irradiation condition for production of ^{68}Ga and minimizing the isotopical impurities. Irradiations were performed with a GE PETtrace cyclotron using a slightly modified liquid target. The 16.5 MeV proton beam is degraded using a material suitable to improve resistance of the target to acidity of the target material, down to an energy of 12 MeV, in order to minimize the production of ^{67}Ga through the $^{68}Zn(p,2n)^{67}Ga$ reaction. Irradiations were carried out for 32 ± 1 minutes at 47 ± 2 μA beam current. During all runs target pressure was stable at 445 ± 10 psi. The product's activity was measured using an activity meter calibrated with a standard of ^{68}Ge traceable to NIST, while radionuclide purity was evaluated by using gamma-ray spectrometry with an HPGe detector. **Results:** The produced activity of ^{68}Ga for each irradiation amount to 4.4 ± 0.4 GBq. The average saturation yield of ^{68}Ga amounts to 330 ± 30 MBq/ μA . These results are equal in the amount of 70% of our yields calculated using theoretical cross sections. The gamma-spectra of the irradiated samples showed the presence of different isotopes of Ga, Cu and Co, as predicted by the theoretical estimates. Radionuclide purity is within the limits of EU Pharmacopeia up to 3 hours after end of bombardment. Separation and recovery up to a yield of $90 \pm 9\%$ was obtained. **Conclusions:** In summary, this approach provides clinically relevant amounts of ^{68}Ga by cyclotron irradiation of a liquid target, in adequate chemical form and radionuclidic purity, as a competitive, cost effective alternative to the $^{68}Ge/^{68}Ga$ generators.

EP-0878

Optimization of Zr-89 Production with RFT-30 Cyclotron

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Aim: Zr-89 ($t_{1/2}=3.3$ d) is one of the appealing unconventional PET radiometal with the favorable nuclear decay kinetics and chemical properties for its application in time-consuming bio-distribution studies and tumor targeting procedures. Rising demand of ultrahigh purity and high-specific activity Zr-89 has propelled the isotope production community worldwide to develop an overall efficacious method for its promising production and constant supply. In this work, we have summarized the efforts made by our team in optimizing the production of Zr-89 by $^{89}Y(p,n)^{89}Zr$ using a 30 MeV prototype cyclotron (RFT-

30) installed at Korea Atomic Energy Research Institute. Furthermore, semi-automated separation process optimization based on syringe pump was developed to obtain high-purity ^{89}Zr for research applications. **Material and Methods:** Production was optimized by irradiating varying thickness (0.1–0.65 mm) of high purity ^{89}Y targets with 12–14 MeV protons using 10 μA –30 μA current at solid target irradiation station and production of 1.6 mCi/ μAh ^{89}Zr was achieved. After cooling the target for one hour its rapid dissolution was achieved in 6 M HCl. Separation and purification of ^{89}Zr in oxalate as well as chloride form from the target matrix was achieved by employing commercially available hydroxamate based resin and QMA cartridge respectively. The comparative and comprehensive column operation studies using gravity flow, vacuum system and syringe pump were carried out. Radionuclidic and radiochemical purity was ascertained by HPGe and radio TLC respectively. **Results and Conclusions:** Using the above mentioned methodology we developed advanced optimized method using which we were able to produce high activity (~130 mCi) of ^{89}Zr in one batch. Amongst the studied methods syringe pump assisted semi-automated separation process was quite stable. The separation was achieved using lower HCl (≤ 1.5 M) and $\text{H}_2\text{C}_2\text{O}_4$ (0.05 M) concentrations. Furthermore, optimized separation provided 99% of loaded ^{89}Zr in ≤ 1 mL with high radionuclidic and radiochemical purity ($\geq 99.99\%$) proving its potentials as the effective methodology for routine ^{89}Zr production. The produced ^{89}Zr at our facility is supplied domestically for the research purposes since February 2018.

EP-0879

Production Of ^{47}Sc In Maria Reactor In Polatom

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Introduction: Scandium-47, with a half-life of 3.35 days is a beta emitter ($E_{\beta-\text{max}} = 600$ keV), which is suitable for targeted radionuclide therapy. It also emits γ radiation ($E_\gamma = 159$ keV, 68.3%), which could be utilized for imaging using SPECT. There are also other scandium isotopes emitting β^+ particles such as ^{43}Sc , ^{44}Sc . Therefore, ^{47}Sc can be used in combination with its positron emitting “twins”, forming diagnostic-therapeutic pairs. Still availability of ^{47}Sc is limited. It can be produced in nuclear reactors in result of ^{46}Ca neutron irradiation, giving ^{47}Ca which in turn decays to ^{47}Sc with a half-life of 4.5 day. Therefore, a few days after irradiated target processing, the separation cycle can be repeated in order to recover the ^{47}Sc . The aim of this work was to investigate the possibility to manufacture ^{47}Sc with purity sufficient for medical application by neutron irradiation of ^{46}Ca enriched calcium targets. **Method:** ^{47}Sc was produced by irradiation of ^{46}Ca target (48.5 mg of CaCO_3 , 5.2% enrichment in ^{46}Ca) for 150 h in a thermal neutron flux of $1.2 \cdot 10^{14} \text{ cm}^{-2}\text{s}^{-1}$ in Maria reactor. The irradiated target was dissolved in 3M HCl. Separation of ^{47}Sc from calcium excess was performed by its precipitation in hydroxide form and filtration, followed by purification on the AG 50W-X4 resin, and finally washed out in 0.25 M NaOAc solution. All calcium containing fractions collected during Sc separation,

were used in repeated separation of Sc after 7 days. In order to verify the quality of obtained ^{47}Sc solution, the radiolabeling of two peptides: DOTATATE and DOTA-Substance-P was performed and radiochemical purity was assessed by TLC and HPLC. **Results:** Irradiation of ^{46}Ca resulted in approximately 600 MBq of ^{47}Sc . The separation yield was in the range from 54 to 72 %. In all cases, also in the repeated recovery of ^{47}Sc , the obtained ^{47}Sc solution was pure in terms of radionuclide and chemical purity, as shown by the results of peptides radiolabeling. The ^{47}Ca were measured in ^{47}Sc solution only, however its content did not exceed 0.04%. DOTATATE and DOTA-Substance-P were radio-labeled with over 99% radiochemical purity. **Conclusions:** The ^{47}Sc solution obtained with our method proved to be suitable for the direct labeling of biomolecules with good radiochemical purity. Acknowledgements: This project was supported with the funds awarded by the Ministry of Science and Higher Education in Poland within the agreement Nr 3639/FAO/IAEA/16/2017/0

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The INFN-TROPIC project: Target for Radioisotope Production via Anti-Channeling

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The research for novel production techniques of radioisotopes is a field of special interest for modern nuclear medicine, in order to overcome some possible limitations in the supply chain of Mo-99 [1]. In particular, the production of radioisotopes in cyclotrons is spreading worldwide, despite its higher cost with respect to the production in nuclear reactors. Simulations performed with the Geant4 Monte Carlo code showed the possibility to improve radioisotopes production by using crystalline targets [2]. Indeed, ordered and oriented structures can modify the trajectories of incoming beam particles interacting with them. The intense electromagnetic field between two crystalline planes can act as a lens to focalize particles onto target nuclei, thus enhancing the probability of nuclear interactions. This phenomenon is called “anti-channeling”, and its intensity depends either on the energy and charge of incoming beam particle, and on the type of crystalline structure of the target. The INFN-TROPIC project aims to the characterization in laboratory- and production- environment of a crystalline target for the production of radioisotopes in cyclotrons. In particular, a dedicated study of the anti-channeling phenomenon through Monte Carlo simulations is required. Alongside, the research of a commercially-available crystals with a chemical and isotopical composition suitable for the production of an isotope of interest, with at the same time a crystalline quality sufficiently high to observe the anti-channeling effect is mandatory. First crystals to be studied are Yttrium and Rhodium. They are supplied in crystalline form by some specialized manufacturers, and they have the advantage of nat-

urally occurring in only one isotope, being used respectively for the production of Zirconium-89 and Palladium-103, with a high cross section for protons at ≈ 15 MeV (hundreds of millibarns). Preliminary simulations with the Monte Carlo N-Particle (MCNP6) code confirm the possibility of measuring online the production rate with a gamma spectrometer, by selecting photons emitted by excited nuclei produced with the nuclear reaction. [1] <http://www.oecd-neo.org/ndd/reports/2010/nea6967-radioisotopes-full-report.pdf> [2] *Exploiting Channeling of Charged Particles for the Enhancement of the Ni64 to Cu64 Reaction Yield*, 7 June 2015, Society of Nuclear Medicine and Molecular Imaging Meeting 2015, Baltimore (US)

EP-0881

Successful development for separating ^{99m}Tc from ^{99}Mo generated by accelerator driven neutrons

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^{99}Mo , the mother radionuclide of ^{99m}Tc , is in strong demand in nuclear medicine and has been produced by a limited number of research reactors. An alternative method of accelerator production is being promoted to ensure a supply of ^{99}Mo . A common problem in accelerator production without fission, however, is to separate ^{99m}Tc from low specific activity ^{99}Mo . Thermo-chromatographic separation method to take advantage of the difference in sublimation temperature between ^{99m}Tc oxide and ^{99}Mo oxide has drawn attention by previous studies to overcome the problem, yet there has been a long standing problem in processing a large quantity of MoO_3 with repetitive high separation efficiency. ^{99}Mo produced by irradiating a $^{100}\text{MoO}_3$ sample with accelerator driven neutrons offers high radioactivity but has specific activity below five-thousandth of the fission produced ^{99}Mo from ^{235}U . In this study, we succeeded to overcome the problem by developing a new thermo-chromatographic separation procedure suitable for the accelerator generated ^{99}Mo . Irradiated MoO_3 was melted in crucibles, from which ^{99m}Tc is released and condensed as ^{99m}Tc oxide separated from ^{99}Mo . Moist oxygen gas was used to enhance oxidation of ^{99m}Tc and separation efficiency. The constant separation efficiency of 80% was obtained with repeated milkings. It was found that using molten, but not powder MoO_3 , was essential for ^{99m}Tc to be separated by diffusing out of MoO_3 within an hour at high separation efficiency. $^{99m}\text{TcO}_4^-$ solution can be finally eluted with a few millilitres of physiological saline. The quality of the final ^{99m}Tc ($\text{Na}^{99m}\text{TcO}_4$) was found to be compatible to a commercially available product. Recovery test showed that over 90% of the irradiated $^{100}\text{MoO}_3$ remained in the crucibles after separation which was simply recoverable. By collecting the remaining trapped as a crystal deposit within the apparatus, 99% of the total $^{100}\text{MoO}_3$ was recovered without changing the chemical form of $^{100}\text{MoO}_3$ nor was it contaminated by the addition of chemicals. The result demonstrated that a large sample quantity of $^{100}\text{MoO}_3$ over 100 g can be processed and recovered with thermo-chromatographic separation in a good separation/recovery yield.

The method offers a reliable high yield, a high quality ^{99m}Tc and high recovery of the sample which are crucial with respect to economically sustainable production of ^{99m}Tc . It can also be applied to ^{99}Mo produced by other nuclear reaction including $^{98}\text{Mo}(n, \gamma)^{99}\text{Mo}$, $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ as well as $^{100}\text{Mo}(n, 2n)^{99}\text{Mo}$ reaction.

EP-0882

Productions of ^{99}Mo and ^{67}Cu using accelerator neutrons for domestic use

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In Japan, about 0.9 million diagnostic procedures per year are carried out using ^{99m}Tc obtained from a $^{99}\text{Mo}/^{99m}\text{Tc}$ generator. Japan imports all of its required ^{99}Mo . A reliable and constant supply of ^{99}Mo is a key issue to ensuring the routine application of ^{99m}Tc . The current production chain of ^{99}Mo is fragile. The situation encouraged to study alternative methods for producing ^{99}Mo without highly enriched ^{235}U . As for PET imaging, ^{64}Cu with a half-life longer than ^{18}F has been also used. ^{67}Cu , which emits low energy γ -rays suitable for SPECT imaging and β -rays with a mean energy of 0.141 MeV to kill targeted cancer cells, is a promising radionuclide for theranostics. ^{64}Cu and ^{67}Cu are theragnostic radionuclide pairs, suitable to do personalized medicine. A proper production method of ^{67}Cu remains a challenging problem. We proposed new routes to produce ^{99}Mo and ^{67}Cu by irradiating ^{100}Mo and ^{68}Zn samples, respectively, with accelerator neutrons, provided by bombarding a carbon target with a deuteron beam of 40 - 50 MeV. ^{99m}Tc was separated from the ^{99}Mo with a low specific-activity by a thermochromatography apparatus. ^{99m}Tc -radiopharmaceuticals was confirmed to pass the quality control tests recommended by the United States Pharmacopeia. By measuring the yield of ^{99}Mo , we claim that about 30 - 50% of the demand for ^{99m}Tc in Japan would be met using a single accelerator of 40 MeV, 2 mA deuteron beams. As for ^{67}Cu , the radionuclide purity, labeling efficiency, and specific activity of ^{67}Cu were measured. ^{67}Cu chloride dissolved in saline was injected into the colorectal tumor-bearing mice to determine the biodistribution, and a high uptake of ^{67}Cu in the tumor was found, suggesting that $^{67}\text{CuCl}_2$ can be a potential radionuclide agent for cancer radiotherapy. We will present characteristic points of accelerator neutrons for producing a wide variety of medical radioisotopes of high quality together with the results mentioned. References: 1. The supply of Medical Radioisotopes: Report by Nuclear Energy Agency (June 2011). 2. I. Novak-Hofer and P. A. Schubiger, Eur. J. Nucl. Med. 29 (2002) 821. 3. S.C. Srivastava and L.F. Mausner, Therapeutic Nuclear Medicine, Springer-Verlag Berlin Heidelberg (2013) 11. 4. Y. Nagai and Y. Hatsukawa, J. Phys. Soc. Jpn. 78 (2009) 033201-1. 5. Y. Nagai et al., J. Phys. Soc. Jpn. 86 (2017) 053202-1. 7. K. Tsukada et al., J. Phys. Soc. Jpn. 87 (2018) 043201. 8. Y. Sugo et al., J. Phys. Soc. Jpn. 86 (2017) 023201-1.

EP-0883

Production, quality control of non-standard PET nuclide iodine-124 and thyroid micro-PET imaging

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Purpose: Iodine-124 (I-124) has become one of the most fascinating PET nuclides because of its long-life ($T_{1/2} = 4.2$ days) compared with fluorine-18 ($T_{1/2} = 110$ min)/ carbon-11 ($T_{1/2} = 20.4$ min). It's very helpful for using I-124 labeled pharmaceuticals to carry out many long-term clinical examinations & experiments. Here we state a routine production & quality control of I-124 in order to provide sufficient good quality non-standard novel PET nuclide I-124. Then, thyroid imaging of normal mice injected Na¹²⁴I solution was obtained by micro-PET/CT scan. **Method:** ¹²⁴Te(p,n)¹²⁴I nuclide reaction was employed for the I-124 production. Firstly, the target material ¹²⁴TeO₂ powder was mixed with Al₂O₃ together, then pressed into pellet on the round platinum target substrate followed by a sintering process in an electric furnace. The ¹²⁴TeO₂ target was irradiated by 20 μ A proton current at 12.5 MeV energy on a Sumitomo HM-20 cyclotron for about 6-10 hours. After the irradiation, radiated target was placed for 12 hours to decay the radioactive impurity material. I-124 was extracted by dry distillation based on different thermal behavior. Then the radionuclide purity of the produced I-124 solution was measured by γ -ray spectroscopy. To investigate the metabolism properties of I-124, Na¹²⁴I solution was injected into normal mice for thyroid imaging by micro-PET/CT. **Results:** The ¹²⁴TeO₂ mixture on Pt-disk was about 185 ± 5.8 mg without obviously pits & cracks on the surface, assuming a uniform thickness on the disk. There was about 370~1110 MBq activity of production obtained after 8 hours irradiation with 12.5 MeV proton (@20 μ A current). At last, 370~740 MBq high specific activity I-124 was collected after dry distillation separation & radio-chemical purification. The gamma spectrum of the produced I-124 solution showed that radionuclide purity was over 90%. Micro-PET imaging of Na¹²⁴I in normal mice exhibited the thyroid, stomach accumulations & kidney metabolism. **Conclusion:** In this study, ¹²⁴TeO₂ solid target was successfully prepared by the pressing/sintering process. I-124 was successfully extracted from the cyclotron irradiated ¹²⁴TeO₂ target by the dry distillation based on their different thermal behavior. After radio-chemical purification, we successfully produced good quality ¹²⁴I. The micro-PET thyroid imaging indicated that ¹²⁴I we produced could be used as a good novel PET nuclide for probe labeling. To the best of our knowledge, it's the first production of I-124 report in China.

EP-0884

In-loop carbonylation - a novel and simplified method for carbon-11 labeling of drugs and radioligands

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Aim: Transition-metal-mediated carbonylation is a versatile method for introducing carbon-11 (¹¹C) into druglike molecules and radioligands. We herein report the development of a novel and simplified approach for [¹¹C]carbon monoxide ([¹¹C]CO) carbonylation, in which the radiolabeling reaction takes place on the interior surface of an ordinary stainless-steel loop commonly used for high-performance liquid chromatography (HPLC). **Materials and Methods:** The reaction mixture (aryl halide, palladium-source, supporting ligand and nucleophile in anhydrous solvent) was loaded into the stainless-steel HPLC loop (2 mL) prior to the start-of-synthesis. No-carrier-added [¹¹C]CO was prepared by online reduction of [¹¹C]carbon dioxide over heated Molybdenum (850°C) and transferred into the HPLC loop using a stream of Helium at ambient temperature. The loop was kept for 5 min at the desired temperature (r.t. to 110 °C). After completed reaction, the contents were rinsed into a sealed tube by purging the loop with THF. The radiochemical yield (RCY) was assessed by radio-HPLC and the trapping efficiency (TE) was calculated as the radioactivity remaining in the tube after sparging the reaction mixture with Helium. RCYs and TEs are given as an average of two experiments, unless otherwise stated. **Results:** The ¹¹C-amino-carbonylation of iodobenzene with benzylamine was used as a model reaction. After optimization, [¹¹C]N-benzylbenzamide was obtained in a near quantitative RCY ($99 \pm 0.5\%$, $n=3$) and TE ($99 \pm 0.5\%$, $n=3$). The "in-loop" methodology was next applied in the synthesis of [¹¹C]benzoic acid (RCY > 99%, TE > 91%) as well as a series of ¹¹C-labelled esters, namely [¹¹C]methyl benzoate (RCY>99%, TE > 93%), [¹¹C]ethyl benzoate (RCY>99%, TE>93%) and [¹¹C]phtalide (RCY>99%, TE>88%). Finally, a set of drug molecules were radiolabeled using un-optimized conditions. Modest yields were obtained for FLB 457 (RCY= 80%, TE=54%) and AZD3676 (RCY=55%, TE= 65%), whereas excellent yields were obtained for the H₃ receptor radioligand AZ13198083 (RCY>93%, TE>96%) and the PARP inhibitor olaparib (RCY>99%, TE>97%). **Conclusions:** The presented "in-loop" process proved to be useful for diverse ¹¹C-carbonylation, providing [¹¹C]amides, [¹¹C]esters and [¹¹C]carboxylic acids in moderate to excellent RCYs. Given its simplicity and efficiency, we anticipate this methodology to be widely implemented in the development of tracer molecules for PET imaging. **Acknowledgements:** This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement N°675071

EP-64

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Radiochemistry -> Radiopharmaceutical preparation

EP-0885

In-loop carbonylation - a novel and simplified method for carbon-11 labeling of drugs and radioligandsM. Ferrat¹, Y. El Khoury¹, K. Dahl², C. Halldin¹, M. Schou^{3,1};¹Department of Clinical Neuroscience, Center for Psychiatry Research, Karolinska Institutet and Stockholm County Council, Stockholm, SWEDEN, ²CAMH & University of Toronto, Toronto, ON, CANADA, ³AstraZeneca PET Science Centre, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, SWEDEN.

Aim: Transition-metal-mediated carbonylation is a versatile method for introducing carbon-11 (¹¹C) into druglike molecules and radioligands. We herein report the development of a novel and simplified approach for [¹¹C]carbon monoxide ([¹¹C]CO) carbonylation, in which the radiolabeling reaction takes place on the interior surface of an ordinary stainless-steel loop commonly used for high-performance liquid chromatography (HPLC).

Materials and Methods: The reaction mixture (aryl halide, palladium-source, supporting ligand and nucleophile in anhydrous solvent) was loaded into the stainless-steel HPLC loop (2 mL) prior to the start-of-synthesis. No-carrier-added [¹¹C]CO was prepared by online reduction of [¹¹C]carbon dioxide over heated Molybdenum (850°C) and transferred into the HPLC loop using a stream of Helium at ambient temperature. The loop was kept for 5 min at the desired temperature (r.t. to 110 °C). After completed reaction, the contents were rinsed into a sealed tube by purging the loop with THF. The radiochemical yield (RCY) was assessed by radio-HPLC and the trapping efficiency (TE) was calculated as the radioactivity remaining in the tube after sparging the reaction mixture with Helium. RCYs and TEs are given as an average of two experiments, unless otherwise stated. **Results:** The ¹¹C-aminocarbonylation of iodobenzene with benzylamine was used as a model reaction. After optimization, [¹¹C]*N*-benzylbenzamide was obtained in a near quantitative RCY (99±0.5% n=3) and TE (99±0.5%, n=3). The “in-loop” methodology was next applied in the synthesis of [¹¹C]benzoic acid (RCY>99%, TE>91%) as well as a series of ¹¹C-labelled esters, namely [¹¹C]methyl benzoate (RCY>99%, TE>93%), [¹¹C]ethyl benzoate (RCY>99%, TE>93%) and [¹¹C]phthalide (RCY>99%, TE>88%). Finally, a set of drug molecules were radiolabeled using un-optimized conditions. Modest yields were obtained for FLB 457 (RCY=80%, TE=54%) and AZD3676 (RCY=55%, TE=65%), whereas excellent yields were obtained for the H₃ receptor radioligand AZ13198083 (RCY>93%, TE>96%) and the PARP inhibitor olaparib (RCY>99%, TE>97%). **Conclusions:** The presented “in-loop” process proved to be useful for diverse ¹¹C-carbonylation, providing [¹¹C]amides, [¹¹C]esters and [¹¹C]carboxylic acids in moderate to excellent RCYs. Given its simplicity and efficiency, we anticipate this methodology to be widely implemented in the development of tracer molecules for PET imaging. **Acknowledgements:** This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement N°675071

EP-0886

Rapid and efficient BEMP-mediated synthesis of ¹¹C-labelled benzimidazolones using [¹¹C]carbon dioxideK. Horkka¹, K. Dahl², C. Halldin¹, M. Schou^{1,3}; ¹Karolinska Institutet, Stockholm, SWEDEN, ²CAMH & University of Toronto, Toronto, ON, CANADA, ³AstraZeneca PET Science Centre, Stockholm, SWEDEN.

Aim: Benzimidazolones are common structural motifs in drug-like molecules and radioligands. The current project aimed to develop a novel method for radiolabeling these motifs starting from cyclotron produced [¹¹C]carbon dioxide ([¹¹C]CO₂), and thereby precluding the use of ¹¹C-labelled phosgene for this purpose. **Materials and Methods:** No-carrier-added [¹¹C]CO₂ was produced using an on-site PETtrace cyclotron (GEMS, Uppsala Sweden). The produced [¹¹C]CO₂ was further concentrated and introduced in a stream of helium into a reaction vessel pre-charged with the appropriate *o*-phenylenediamine and BEMP in acetonitrile. After 2 minutes, a solution of DBAD and tributylphosphine in acetonitrile were added. The reaction was quenched after 4 minutes and the radiochemical yield (RCY) was determined by radio-HPLC. The trapping efficiency (TE) was calculated by dividing the radioactivity remaining in the reaction mixture after the quench with that delivered to the vial. RCYs and TEs are presented as an average of two experiments, unless otherwise stated. **Results:** The formation of the unsubstituted [¹¹C]benzimidazolone was selected as model reaction, a compound that was obtained in a near quantitative RCY (99±0.5, n=3) and TE (98±0.5, n=3) at optimized conditions. With these reaction conditions in hand, a series (n=6) of substituted [¹¹C]benzimidazolones were obtained in excellent RCYs (83-99%) and TEs (91-97%). Electron-donating and withdrawing groups were well tolerated, as well as *N*-monoalkyl substituents. In addition to benzimidazolones, other heterocycles were also accessible using this novel strategy, as exemplified by the synthesis of [¹¹C]benzoxazolone (RCY=83%, TE=70%, n=3) and [¹¹C]benzothiazolone (RCY=95% and TE=97%, n=3). However, *N,N*-dimethyl-*o*-phenylenediamine failed to produce the corresponding [¹¹C]*N,N*-dimethylbenzimidazolone, thus suggesting the existence of an [¹¹C]isocyanate intermediate instead of direct attack on the phosphine oxonium ion. **Conclusions:** The herein reported method for the preparation of [¹¹C]benzimidazolones is an important addition to the thin library of available methods for ¹¹C-labelling. This novel [¹¹C]CO₂-fixation method is simple, efficient, and allows for a reliable production of [¹¹C]carbonylated radiotracers for PET imaging. **Acknowledgements:** This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement N°675071.

EP-0887

Evaluation of [¹¹C]PXT012253 and [¹⁸F]PXT012251 as PET radioligands for mGlu4 allosteric modulators in non-human primatesS. Nag¹, R. Arakawa¹, A. Takano¹, Z. Jia¹, M. Jahan², A. Forsberg¹, G. Duvey³, C. Halldin^{1,4}, D. Charvin³; ¹Karolinska Institutet, Stockholm, SWEDEN, ²Uppsala University Hospital, Uppsala, SWEDEN, ³Prexton Therapeutics, Geneva, SWITZERLAND, ⁴Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, SINGAPORE.

Introduction: Modulation of presynaptic metabotropic glutamate receptor 4 (mGlu4) has been proposed as a promising therapeutic target in several neurological disorders such as Parkinson's disease. Two PET radioligands, C11-labelled [^{11}C]PXT012253, and F18-labelled [^{18}F]PXT012251 have been recently developed and evaluated initially in rodents/non-human primates (NHP) (1,2). In this study, in order to characterize both radioligands for further application in clinical studies, we investigated the kinetics of [^{11}C]PXT012253 and [^{18}F]PXT012251 in NHP brains quantitatively. **Materials & Methods:** [^{11}C]PXT012253 was synthesized in one step using [^{11}C]CH₃OTf as methylating agent. Radiolabeling of [^{18}F]PXT012251 was achieved by classical one-step fluorine-18 nucleophilic substitution reaction. A total of five 93-minute brain PET measurements (three baseline, one blocking condition with [^{11}C]PXT012253 and one baseline condition with [^{18}F]PXT012251) were performed in four male cynomolgus monkeys (6.4–8.3 kg) using a High Resolution Research Tomograph (Siemens Molecular Imaging). As the blocking study, a mGlu4 positive allosteric modulator (PAM), PXT002331 (2 mg/kg), currently in clinical trial for Parkinson's disease, was administered intravenously with bolus infusion in one NHP. Radiometabolites were measured in NHP plasma using radio-HPLC. As the outcome measure, the total distribution volume (V_T) was calculated by two tissue compartment (2TC) model with metabolite corrected plasma radioactivity as the input function. **Results:** Synthesis of both radioligands were accomplished successfully with high radiochemical yield and purity > 99% for both radioligands. Molar activity was 139–4800 GBq/ μmol for [^{11}C]PXT012253 and 29 GBq/ μmol for [^{18}F]PXT012251 at the time of administration. Both radioligands were found to be stable, with a radiochemical purity of >99% at 2 h after formulation in a sterile phosphate buffered solution (pH = 7.4). Whole brain uptake of [^{11}C]PXT012253 was found higher (3.3–4.6 SUV at the peak) than that of [^{18}F]PXT012251 (2.0 SUV). V_T s among different brain regions at baseline condition ranged 5.4–9.1 (on average of three NHPs) for [^{11}C]PXT012253 and 0.9–1.3 for [^{18}F]PXT012251. Relative uptake differences among the brain regions were larger in [^{11}C]PXT012253 when compared with [^{18}F]PXT012251. These data indicate that [^{11}C]PXT012253 has higher specific binding than [^{18}F]PXT012251. After blocking with PXT002331, V_T s in all the examined brain regions decreased significantly, indicating specific binding for mGlu4. **Discussion/Conclusion:** The present results suggest [^{11}C]PXT012253 is a promising PET radioligand for mGlu4 allosteric modulators in the brain. Further development of [^{11}C]PXT012253 is warranted in human subjects. **References:** 1) Kil KE, et al. *Bioorg Med Chem Lett.* 2016;26(1):133–9. 2) Kil KE, et al. *J Med Chem.* 2014;57(21):9130–8.

EP-0888

Efficient synthesis and radiosynthesis of tetrazine probes for pretargeted imaging of peritoneal carcinomatosis

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Aim: Pretargeting offers a way to enhance target specificity while reducing off target radiation dose to healthy tissue during payload deliver. Among the different available bioorthogonal chemistry reactions described so far, the inverse electron demand Diels-Alder cycloaddition is the most suitable for an application in radioimmunotherapy given the fast, strong and biocompatible covalent interaction between tetrazine (Tz) and *trans*-cyclooctene (TCO) moieties (Rossin *et al.*, 2010; Houghton *et al.*, 2017). Moreover, tetrazine probes can be used for both optical and PET/SPECT imaging (fluorine-18, copper-64, gallium-68, indium-111, lutetium-177), as well as for therapy (177-lutetium, 225-actinium) when functionalized with a nitrogen chelating macrocycles such as DOTA. But, to date, little research has been done concerning the impact of the nature or the length of the linker between tetrazine and DOTA on the ligation efficiency (Rossin *et al.* 2014; Rahim *et al.* 2015; Lappchen *et al.* 2017). **Methods:** In order to study the influence of PEGylated linkers, we have developed the synthesis of three PEGs of varying lengths (i.e. PEG₄, PEG₈ and PEG₁₂). The NHBocPEG_nNH₂ precursors (n = 4, 8 or 12) were reacted with Tz-CO₂H *via* peptidic coupling to afford TzPEG_nNHBoc. After deprotection with TFA, TzPEG_nNH₂ were directly coupled with DOTA-NHS to give TzPEG_nDOTA after purification on Combiflash® system (60–65%). Tetrazines were then radiolabeled with indium-111 or lutetium-177 as followed: (i) heating of appropriated TzPEG_nDOTA dissolved in sodium acetate buffer (20 mM, pH 7) with non-carrier added [^{177}Lu]LuCl₃ or [^{111}In]InCl₃ for 20 min (iTLC control); (ii) purification on RP-HPLC coupled with a radioactivity detector system (Gabi star, Raytest®); (iii) formulation on Sep-Pak C18 cartridge. Stability of radiolabeled Tz probes was then studied in three different media (plasma, PBS and physiologic saline). **Results:** Radiolabeling precursors were efficiently obtained from TzPEG_nNH₂ with good yields ranging from 53 to 78% and were stable when stored as aliquots at -20 °C up to 6 months for further radiolabeling. ^{177}Lu -DOTA-PEG_nTz complexes were produced in 65–70% overall radiochemical yield (RCY) with an excellent radiochemical purity (RCP > 98%) and a high molar activity (> 8 GBq/ μmol). For now, we demonstrated that ^{177}Lu -DOTA-PEG₄Tz was 40%, 55% and 80% stable after 24 h incubation in plasma, PBS and physiological saline, respectively. **Conclusion:** We developed an efficient synthesis and radiosynthesis of tetrazine probes. Influence of these three different PEGylated linkers will be studied further by *in vivo* scintigraphic imaging.

EP-0889

2-[^{18}F]Fluoro-5-iodopyridine ([^{18}F]FIPy): a novel reactive prosthetic group for the fast site specific radiolabeling via Pd-catalyzed cross coupling reactions

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Aim: Numerous Pd-catalyzed cross-couplings like Sonogashira, Suzuki-Miyaura, Heck and Stille reactions proved to be valuable tools for the site specific labeling of biopolymers. The aim of this

work was the study of Pd-catalyzed cross coupling reactions using [^{18}F]FIPy as radiolabeled synthon and 2,2'-(1,2-phenylene)-bis-(4,4-dimethyl-4,5-dihydrooxazole)-*N,N'*-palladium dichloride (Pd-BOX-1) as catalyst. Pd-BOX-1 demonstrated exceptional air and moisture stability, and excellent catalytic activity in aqueous reaction media. **Methods:** The direct reaction of 2-bromo-5-iodopyridine with DABCO followed by anion metathesis using TMSOTf afforded 1-(5-iodopyridin-2-yl)-1,4-diazabicyclo[2.2.2]octan-1-ium triflate (**1**) used as precursor for the preparation of [^{18}F]FIPy. The latter was produced using the “minimalist” protocol. Accordingly, [^{18}F]fluoride was eluted from a QMA cartridge with a solution of **1** in MeOH. MeOH was evaporated at 45 °C (250 mbar) within 4 min, DMSO was added and the resulting solution was heated affording [^{18}F]FIPy which after the purification by SPE was conjugated to different model compounds by different Pd-catalyzed (1% of Pd-BOX-1) cross-couplings using aqueous MeCN or DMF as reaction solvent within 10 min. **Results:** ^{18}F recovery from an anion exchange resin using **1** (3 mg) amounted > 98%. Heating of the resulting [^{18}F]fluoride onium salt in DMSO at 100 °C for 15 min afforded [^{18}F]FIPy in excellent radiochemical conversions (RCCs) of 91±3%. [^{18}F]FIPy was isolated in 61±5% radiochemical yield (RCY) and excellent radiochemical purity (RCP) of > 98%. The subsequent Cu and phosphine free Pd-BOX-1 catalyzed Sonogashira cross-coupling with phenylacetylene afforded the corresponding conjugate in an excellent RCC of > 89%. Furthermore, Suzuki-Miyaura, Heck and Stille reactions with 4-methylphenyl boronic acid, methyl acrylate and trimethyl(phenyl)tin, respectively, applied as model coupling partners furnished the corresponding radiofluorinated conjugates in RCCs of 85–98%. **Conclusion:** [^{18}F]FIPy is a valuable radiolabeled prosthetic group easily accessible using the “minimalist” approach. Various Pd-BOX-1-catalyzed cross coupling reactions with [^{18}F]FIPy is a versatile procedure for a fast, high-yielding and site specific radiolabeling under relatively mild conditions.

EP-0890

[^{18}F]Olaparib: Precision Radiolabelling of PARP Inhibitors for In Vivo Imaging

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The direct ^{18}F -labeling of Olaparib (Lynparza, AstraZeneca, AZD2281), an FDA approved PARP inhibitor for the treatment of BRCA-mutant ovarian cancer, has proven to be elusive, in part due to the limitations found within the field of radiochemistry.¹ This has led to a compromise either in the radiolabeled structure or the stability of the corresponding precursor, as exemplified by Reiner and Skrydstrup for the labelling of [^{18}F]PARPi and [^{11}C]Olaparib respectively.^{2,3} Recently, Gouverneur *et al.* developed a wide range of novel radiofluorination reactions, enabling radiolabeling otherwise challenging motifs.⁴ Most significant amongst these is the Cu-mediated aromatic nucleophilic ^{18}F -fluorination of aryl pinacol-derived boronic esters.⁵ Here, we demonstrate, for the first time, the successful labelling and

isolation of [^{18}F]Olaparib from the corresponding, bench stable, boronic ester precursor in a non-decay corrected radiochemical yield of 18% ± 3% (*n* = 5) and molar activity of 25 GBqμmol⁻¹. This isotopomer of the drug Olaparib, possesses the same PK, lipophilicity, bioavailability and PARP affinity and binding spectrum as the cold compound. As such, this has allowed for the direct measurement of biodistribution, tumour uptake, and PARP binding of Olaparib using PET imaging in mouse models of pancreatic ductal adenocarcinoma (PDAC) cell lines. **References:** 1. M. G. Campbell, J. Mercier, C. Genicot, V. Gouverneur, J. M. Hooker, T. Ritter *Nat. Chem.* 2017, **9**, 1–3 2. Reiner *et al.*, *Mol. Imaging. Biol.* 2016, **18**, 386–392. 3. T. L. Andersen, S. D. Friis, H. Audrain, P. Nordeman, G. Antoni, T. Skrydstrup, *J. Am. Chem. Soc.* 2015, **137**, 1548–1555 4. S. Preshlock, M. Tredwell, V. Gouverneur, *Chem. Rev.* 2016, **116**, 719–766. 5. Gouverneur *et al.* *J. Am. Chem. Soc.* 2017, **139**, 8267–8276.

EP-0891

Rapid, Nucleophilic Synthesis of [^{18}F]FDOPA Using A Microdroplet Reactor

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Aims: Increasing interest in the PET tracer 3,4-dihydroxy-6-[^{18}F]fluoro-L-phenylalanine ([^{18}F]FDOPA) to image neuroendocrine tumors, brain tumors, and Parkinson's disease, is increasing the demand for straightforward methods for its production. Several nucleophilic synthesis methods have been reported that avoid issues of electrophilic synthesis, i.e. low availability of [^{18}F]F₂ and low molar activity. Building on recent advances in microdroplet radiochemistry, we evaluated the feasibility of adapting the diaryliodonium salt synthesis method[1] to our microfluidic synthesizer[2] to provide a rapid, straightforward synthesis. **Methods:** Synthesis of [^{18}F]FDOPA was implemented on a silicon microfluidic chip (25x27.5 mm²), consisting of a hydrophilic reaction zone (4mm diameter) surrounded by a hydrophobic Teflon-coated surface, that was affixed to a temperature control platform. First, a 10μL droplet of [^{18}F]fluoride solution containing Kryptofix 222 (8.4mM) and K₂CO₃ (4.1mM) in 90:10 H₂O:MeCN(v/v) was loaded on the chip and dried at 100°C for 1min. Then, a 10μL droplet of precursor in diglyme containing 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) was added[3]. During the fluorination reaction, additional diglyme was added to replace solvent that had evaporated. Finally, a 10μL droplet of H₂SO₄ (6M) was added, and the reaction mixture covered with a Teflon-coated glass substrate, to perform the deprotection. The crude product was recovered with HPLC mobile phase (70μL) and purified with reversed-phase analytical-scale HPLC. **Results:** Initially the fluorination reaction was optimized by varying temperature (80–140°C), time (5–10min), precursor concentration (9–72mM), and amount of TEMPO (10–92mol%). The optimal conditions (100°C, 5min, 9mM precursor, 75mol%

TEMPO) resulted in a fluorination yield (as determined by radioactivity measurement and radio-TLC) of $24.0 \pm 2.0\%$ ($n=3$). The deprotection reaction was then optimized by varying type and concentration of acid, as well as reaction time and temperature. Deprotecting with $6\text{M H}_2\text{SO}_4$ at 110°C for 5 min gave a RCY (before purification) of $14.3 \pm 0.5\%$ ($n=2$). **Conclusion:** We have demonstrated the feasibility of synthesis of [^{18}F]FDOPA in micro-liter-sized droplets. Synthesis time was significantly shorter than the macroscale method ($\sim 40\text{min}$ vs $\sim 117\text{min}$, including purification)[1], and used considerably less precursor (0.08mg versus 12mg). The isolated yield was comparable to the macroscale method ($10.0 \pm 0.7\%$ ($n=2$) vs $14 \pm 4\%$), and improvements may be possible after optimizations of deprotection and purification. Reactions were performed starting with $\sim 22\text{MBq}$ of activity, but scale will be increased in the future by using an upstream [^{18}F]fluoride concentrator[4] to produce sufficient quantities for clinical imaging. **References:** [1] Kuik et al., *J.Nucl.Med.* 56:106–112, 2015. [2] Wang et al., *Lab.Chip.* 17:4342–4355, 2017. [3] Carroll et al., *J.Fluor.Chem.* 128:127–132, 2007. [4] Hoover et al., *Organo-metallics*, 35:1008–1014, 2016.

EP-0892

Synthesis of Triphenylphosphonium Cation and Folic acid Conjugated ^{89}Zr -Labelled Silica Nanoparticles for PET Imaging

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Introduction In this study, we investigated the internalization of nanoparticles in cancer cells by surface charge and overexpression receptors. We also examined the effects of TPP and folic acid. The positron emission nucleus, ^{89}Zr ($t_{1/2}$ 3.3d), was labeled on the surface of the SNP without a chelator in order to confirm the in vivo behavior of the nanoparticles according to the surface modified amount through PET. **Subjects & Methods** Amine-modified silica nanoparticles and DMF were added to five different reaction flasks. The amounts of TPP added to the flasks were varied to 0.2, 0.6, 1.8, 3.0 and $4.2\text{ }\mu\text{mol}$. Then 1.2 equivalents of EDC, 1.2 equivalents of NHS and 2.0 equivalents of TEA were added per equivalent of TPP. ST and DMSO were added to five reaction flasks. $4.2\text{ }\mu\text{mol}$ of folic acid was added after 1 min for sufficiently disperse the nanoparticles. Then 1.2 equivalents of EDC, 1.2 equivalents of NHS and 2.0 equivalents of TEA were added per equivalent of folic acid. In Zr-89 radiolabeling, Each of the five samples were placed in vials and was dispersed in HEPES. Then, 37 MBq of ^{89}Zr -oxalate was added into each vials and heated up to 95°C for 1 h. After completion of the reaction, the solvent and nanoparticles were separated from each other by centrifugation and washing with 50 mM DTPA solution and saline to remove free Zr-89. For cellular uptake, 1.0×10^5 of CT-26 cells were seeded into 24-well plates and grown in DMEM medium containing 10% (v/v) fetal bovine serum (FBS) at 37°C for 24 h. ^{89}Zr -STFs ($0.19\text{ MBq}/240\text{ }\mu\text{L}$) were added to CT-26 and incubated for 48 h at 37°C . The samples were washed with PBS, and ^{89}Zr -STFs uptake rates were detected using gamma

ray counter at 0.5, 1, 3, 24 and 48 h. **Results** Labeling yield was 80% and radiochemical purity of $> 99\%$ and stability of $> 80\%$ at 0.9% NaCl for 7 days. In the evaluation of cell uptake, SNP with the highest ratio of TPP and folic acid showed the highest intake. **Conclusion** Biological evaluation of SNPs according to the amount of surface modification of TPP and folic acid showed that endocytosis mechanism was different in vitro according to receptor overexpressed in cancer cells and charge, suggesting a method to effectively target tumor as a nanomedicine.

EP-0893

Investigations on the Inclusion of Copper During CuAAC-Assisted Radiofluorination of Liposomes

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Introduction: For the evaluation of macromolecular drug delivery systems suitable radiolabeling procedures are needed. The Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) as powerful, highly reliable and selective reaction, which allows for a rapid synthesis in high yields and under mild conditions (pH, temperature), is predestinated for the radiolabeling of such systems. However, the cytotoxic properties of copper require a complete removal prior to an application. Usually, macromolecular structures can easily be purified from light-weighted substances by size exclusion chromatography (SEC), unless the substances are retained by the macromolecular structure. In terms of a CuAAC, this would lead to a non-removable fraction of copper, making a usage of the drug delivery systems impossible. Thus, this work investigates a possible inclusion or adsorption of copper during the CuAAC-assisted ^{18}F -radiolabeling of liposomes. **Methods:** In this respect, liposomes were reacted with 1-azido-2-(2-(2-fluoroethoxy)ethoxy)ethane (F-TEG- N_3) in a CuAAC. In order to track the added copper, 1 ml of a Cu(II) nitrate solution (1 M in water) was irradiated with neutrons (flux of thermal neutrons was $7 \cdot 10^{11}\text{ n}\cdot\text{cm}^{-2}\cdot\text{s}^{-1}$ on average) at the TRIGA Mark II research reactor Mainz to obtain [^{64}Cu]Cu(II) nitrate. For the subsequent CuAAC, an aliquot of the irradiated solution was used without further purification. After the CuAAC, liposomes were purified via SEC. Combined liposome containing fractions as well as a sample containing the same amount of [^{64}Cu]Cu(II) nitrate solution that was used for the CuAAC were measured in a gamma detector. Comparison of the resulting values gave the amount of copper still associated with the liposomes after purification. **Results:** The calculated radioactivity generated by ^{64}Cu at the end of irradiation was 310 MBq . This related to a specific activity of $4.88\text{ MBq}/\text{mg}$. Gamma spectrometry revealed, that only 0.018% of the added radioactivity was still present in the liposome containing fractions after purification. This refers to a total amount of copper of 0.17 ng . First attempts to radiolabel liposomes directly with [^{18}F]F-TEG- N_3 gave radiochemical yields (RCY) up to 27.4% after 10 min. **Conclusion:** The ration of retained copper is so low, that an *in vivo* application of the liposomes is absolutely reasonable. This significantly simplifies the

radiosynthesis, which saves time, enables a higher amount of radioactivity per volume and results in a lesser radiation exposure for the experimentalist.

EP-0894

Biological Evaluation Of Novel ^{18}F -labeled Beta-amyloid Probes With A Neopentyl Labeling Group

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Objective: To facilitate the rapid purification of ^{18}F -labeled compounds using solid phase extraction methods, we developed labeling groups containing neopentyl glycol (JP2017-52713A). In this study, we applied these new labeling groups to a stilbene amyloid- β (A β) probe and evaluated how they affect the function and capacity of the A β probe. **Methods:** We synthesized four ^{18}F -labeled stilbene derivatives with different lengths of polyethylene glycol (PEG) chains that linked between the stilbene and the labeling group (number of PEGs = 0, 1, 2, 4). With saturation binding analysis, the binding affinity of each compounds to synthesized A β peptide aggregate was determined. To evaluate the biodistributions, the ^{18}F -labeled compound was injected into the mice, and the distributions of radioactivity into major tissues were determined as percent injected dose (ID)/g at different time points (2, 10, 30, 60, 120 minutes). In addition, we compared the brain uptake kinetics between each labeled compound up to 90 minutes after injection using small animal positron emission tomography (PET). **Results:** Regarding the binding affinity to A β aggregate, our data suggested that there is one ligand binding site for the PEGx0 derivative and two ligands binding sites for the other three derivatives. Dissociation constants (K_d) were as follows (value at binding site with higher binding affinity is shown when there are two ligands binding sites): PEGx0 = 23 nM; x1 = 3.6 nM; x2 = 5.0 nM; and x4 = 15 nM. Regarding the biodistributions in mice, the cerebral uptake of PEGx0, 1, and 2 derivatives was initially around 3% ID/g and subsequently declined over time. On the other hand, the initial cerebral uptake of PEGx4 was $\leq 1\%$ ID/g, revealing its poor blood-brain barrier permeability. Moreover, the accumulation of radioactivity in the bone was greater in the PEGx4 derivative (4.8% ID/g at 60 minutes) compared to other derivatives, suggesting its susceptibility for in vivo defluorination. PET studies in small animals also showed that the initial cerebral uptake was similar among PEGx0, 1, and 2 and that a 50% clearance level of peak cerebral radioactivity was reached in 30 minutes, 25 minutes, and 10 minutes, respectively, after the administration of the derivative. **Conclusion:** Of the derivatives we evaluated, PEGx1 and PEGx2 showed high A β binding affinity, blood-brain barrier permeability in mice, and rapid clearance from the brain. These results suggested that neopentyl labeling groups are applicable for ^{18}F -labelling of a stilbene A β probe.

EP-0895

Optimisation of the [^{18}F]AIF Radiolabelling Method on Trasis AiO Synthesis Platform

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Objectives: The aluminium ^{18}F -fluoride ([^{18}F]AIF) method for radiolabelling biologically relevant molecules has generated significant interest owing to the capacity to combine the convenient metal-based radiochemistry with the excellent decay characteristics of fluorine-18. Many examples of peptides and proteins radiolabelled with [^{18}F]AIF methodology can be found in the literature as well as a general procedure for the automated [^{18}F]AIF radiolabelling on two synthesis platforms.^{1,2} With interest in the translation to clinical application, our current study is aimed at developing an optimised automated [^{18}F]AIF radiolabelling process on the Trasis All in One (AiO) platform.

Methods: The previously described [^{18}F]AIF radiolabelling general method was investigated on the Trasis AiO platform using NOTA-Octreotide as a representative of azamacrocyclic-biomolecule conjugates. The focus was placed mainly on the reagents (peptide and AlCl_3), formulation and on the type of buffer. To a vial containing the two freeze-dried substrates, were added 1 mM ascorbate buffer and ethanol as organic co-solvent. The solvent mixture was used to buffer the QMA eluted ^{18}F -fluoride (ca 2 GBq) to the optimal pH of 4 and provide an efficient radioprotection to the peptide. Additionally, to avoid the need for laborious pH adjustments, the QMA cartridge was pre-converted to the chloride form and the ^{18}F -fluoride was eluted using 0.36% NaCl (aq). After incubating the radiolabelling mixture at 105°C for 15 minutes, a single purification step using HLB-SPE, provided the final radioconjugate in a water/ethanol solution. HPLC analysis of the product showed a high purity (RCP>98%) and high stability. **Results:** For each radiolabelling reaction performed, the ^{18}F -fluoride incorporation, radiochemical yield and molar activity of [^{18}F]AIF-NOTA-Octreotide were determined. When 60 nmol of the substrate and ca 2 GBq of ^{18}F -fluoride were used, an overall >50% incorporation, ca 35% radiochemical yield and molar activity of ca 15MBq/nmol were achieved. The total production time was 35–40 min. **Conclusions:** An optimised procedure for the automated [^{18}F]AIF radiolabelling on the Trasis All in One platform was achieved using a lyophilised NOTA-Octreotide and AlCl_3 mixture, ascorbate as buffer, and ethanol as organic co-solvent. The quick and reproducible method shows great potential for the cGMP production of [^{18}F]AIF radiopharmaceuticals for routine clinical use. 1. W. McBride, C. A. D'Souza, R. M. Sharkey, and D. M. Goldenberg, *Appl Radiat Isot.*, 2012; **70**, 200 2. L. Allott, C. Da Pieve, D. R. Turton and G. Smith, *React. Chem. Eng.*, 2017, **2**, 68

EP-0896

Radiolabeling of ramucirumab with lutetium-177: The influence of chelator type on radiochemical and binding parameters

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Aim: Ramucirumab (RAM) is a therapeutic monoclonal antibody targeted against the extracellular domain of vascular

endothelial growth factor receptor 2 (VEGFR2), which is a key receptor in neoangiogenesis. Several types of cancer (e.g. gastric, esophageal or lung cancer) are known for their overexpression of VEGFR2. RAM labeled with suitable radionuclides could be potentially useful for the imaging and/or targeted radiotherapy of oncological diseases. The aim of this work was to develop a method for radiolabeling of RAM with therapeutic radionuclide lutetium-177 and to determine *in vitro* binding of ^{177}Lu -RAM radiopreparate to the target cell receptor. **Materials and Methods:** The antibody RAM was indirectly labeled with lutetium-177. Three types of lutetium-177 binding chelators were evaluated during experiments: p-SCN-Bn-DOTA, p-SCN-Bn-NOTA and p-SCN-Bn-CHX-A"-DTPA. Optimal condition for antibody-chelator conjugation (Ab:chelator ratio, time, pH, temperature) were sought during the experiments. The radiochemical purity was tested by ITLC immediately after the radiolabeling. To evaluate the stability of labeled antibody, radioconjugate samples were analyzed on various times by size exclusion HPLC with radiometric detection. Manual saturation/internalization method and the automatic real-time radioimmunoassay were used to evaluate radioconjugates' binding to VEGFR2 *in vitro*. Two VEGFR2 expressing human cancer cell lines were used in the binding studies. **Results:** All tested chelators enabled labeling of RAM with lutetium-177. However, the labeling method using DTPA chelator provided the most promising results (radiochemical purity >95% and unchanged binding affinity). DOTA and NOTA chelators provided lower purity after the labeling (the purification step was necessary) and the binding affinity was slightly lowered. All the preparations were stable during the experimental interval of 72 h. **Conclusion:** We have found a convenient labeling method for RAM radiolabeling with lutetium-177. The prepared radioligands preserved binding affinity to the VEGFR2. The obtained experience may be utilized in further *in vitro* and/or *in vivo* studies on radiolabeled RAM. *This project was financially supported by Charles University (project GAUK 998216/C/2016, project SVV 260 414) and Progres Q42).*

EP-0897

Radio-synthesis and preclinical evaluation of [^{11}C]VA426, a Cyclooxygenase-2 selective ligand

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Introduction: In this work, a COX-2 analogue VA426 [1-(4-fluorophenyl)-3-(2-methoxyethyl)-2-methyl-5-(4-(methylsulfonyl)phenyl)-1H-pyrrole] was synthesized and radiolabelled with the radioisotope [^{11}C]. Moreover, preliminary *in vivo* biodistribution, specificity and stability were evaluated. **Subjects and Methods:** No carrier added [^{11}C]CO₂ was produced via the $^{14}\text{N}(\text{p},\alpha)^{11}\text{C}$ reaction using IBA Cyclone 18/9 cyclotron and transferred into a Ge-Healthcare TracerlabFXc-Pro module where it was catalytically hydrogenated to form [^{11}C]CH₄. Methane was iodinated to form [^{11}C]CH₃I and then transformed in the highly reactive [^{11}C]methyl triflate, by an on line flow-through process. It was bub-

bled into the reactor where 1-3mg of the precursor [VA425] were dissolved in anhydrous DMSO. Several basis like NaH, NaOH 1N, and potassium tert-butoxide were evaluated. The crude mixture was purified by means of semi-preparative radio HPLC system with a reversed phase column, followed by formulation through a tC18 SPE cartridge. Final solution was sterile-filtered. The purity of the labelled compound was analysed by HPLC column. Kinetic profile of [^{11}C]VA426 was evaluated in brain and periphery of healthy mice (by *ex vivo* biodistribution at 10, 30 and 60 minutes), after the injection of $111 \pm 8 \mu\text{Ci}$. Results was expressed as percentage of injected dose per gram of tissue (% ID/g). The specificity versus COX-2 enzyme was evaluated in control (vehicle) and in Celecoxib pre-treated mouse, by PET kinetics studies. Mice were pre-treated with Celecoxib or vehicle (DMSO), 5 minutes before radiotracer injection (50-100 μCi) and evaluated by PET imaging for 30 min. For stability assessment, in plasma and liver, 3 healthy mice were injected i.v. with $82 \pm 25 \mu\text{Ci}$ of [^{11}C]VA426, sacrificed 10 minutes later and samples processed for the HPLC analysis of radiometabolites. **Results:** Radiochemical yield based on triflate activity was $7 \pm 3 \%$ n.d.c. Radiochemical purity was >99 % and specific activity was $2 \pm 0.5 \text{ Ci}/\mu\text{mol}$. [^{11}C]VA426 accumulates mainly in peripheral tissues rich in COX-2, such as lungs, liver, kidney and heart, while lesser in the central areas where [^{11}C]VA426 reached the highest levels of radioactivity in pons, cerebellum, thalamus and striatum. At 10 min p.i. Celecoxib was not able to prevent radiotracer binding, the only effect was an increment of radioactivity concentration in kidney. Radiometabolites analysis performed at 10 min. p.i. showed that only than $40 \pm 10 \%$ (plasma) and $26 \pm 19 \%$ (liver) of radioactivity was due to the parent compound indicating that [^{11}C]VA426 is highly unstable *in vivo*. **Conclusions:** Preliminary studies indicate that compound [^{11}C]VA426 needs further implementation in stability formulation to be suitable for PET imaging.

EP-0898

Radio-synthesis and preclinical evaluation of [^{11}C]VA1011, a novel Cyclooxygenase-2 selective ligand

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Introduction: COX-2 can be induced by several mitogen factors and its upregulation have been implicated in a variety of human cancers, making it an important target for cancer treatment. Non-invasive imaging detection of COX-2 expression may provide unique opportunities to obtain information about disease progression and pathogenesis. In this work, the hitherto unknown VA1011 [1-(4-fluorophenyl)-2-methyl-5-(4-(methylsulfonyl)phenyl)-3-(2-(methylthio)ethyl)-1H-pyrrole], structurally related to coxibs, was synthesized and radiolabelled with the radioisotope [^{11}C]. VA 1011 and its superior homologues (e.g. ethyl- and propyl thioethers), were designed as bioisosteric sulfur-derivatives of a previously and successful series of highly selective COX-2 inhibitors, endowed with prominent anti-in-

flammatory and anti-proliferative activity in *in vitro* and *in vivo* testing. Moreover, preliminary post radiolabelling stability was evaluated. **Subjects and Methods:** No carrier added [^{11}C]CO $_2$ was produced via the $^{14}\text{N}(\text{p},\text{q})^{11}\text{C}$ reaction (on N $_2$ gas with 0.5% O $_2$ gas), using IBA Cyclone 18/9 cyclotron and transferred into a Ge-Healthcare TracerlabFXc-Pro module. Briefly [^{11}C]CO $_2$ was reduced over shimalite nickel at 350°C with hydrogen to [^{11}C]CH $_4$, followed by gas phase halogenation to obtain [^{11}C]CH $_3\text{I}$. [^{11}C]methyltriflate ([^{11}C]CH $_3\text{OTf}$) was prepared by sweeping [^{11}C]CH $_3\text{I}$ vapor through a heated peek column containing silvertriflate-impregnated graphitized carbon, as previously described in the literature. The [^{11}C]CH $_3\text{OTf}$ was trapped at room temperature in a vessel containing the precursor, where labelling occurred. It was bubbled into the reactor where 1–3 mg of the precursor VA1010 [2-(1-(4-fluorophenyl)-2-methyl-5-(4-(methylsulfonyl)phenyl)-1H-pyrrol-3-yl)ethanethiol], were dissolved in anhydrous DMSO and potassium tert-butoxide. The crude mixture was purified by means of semi-preparative radio HPLC system with a reversed phase column, ACE 5 μ C18, 250 x 10 mm id; mobile phase was CH $_3\text{CN}/\text{AcONH}_4$ 0.05M (60:40, v/v), connected with an UV detector in series with a radiochemistry detector. Analytical quality control was developed using a column ACE 5 μ C18, 250 x 4.8 mm (CPS Analytica), mobile phase was CH $_3\text{CN}/\text{AcONH}_4$ 0.025 M (70:30, v/v). Formulation was developed using a tC18 SPE cartridge. The compound VA1011 was sterile and apirogenic and the best filter tested was Millex GV, in particular way for the recovery of the labelled compound. **Results:** Radiochemical yield based on triflate activity was 8 $\pm$ 2 % n.d.c. Radiochemical purity was >99 % and specific activity was 2 $\pm$ 0.5 Ci/ μ mol. **Conclusions:** Preliminary results, of the radiolabelling indicate that the compound [^{11}C]VA1011 can be used for starting preclinical studies *in vivo*.

EP-0899

First time cassette-based production of [^{11}C]PiB

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Introduction: [^{11}C]PiB is a radiotracer that has demonstrated its fighting potential against Alzheimer's disease as an amyloid deposition PET imaging agent. We herein describe the first efficient automated and cassette-based production method of this compound. **Methods:** [^{11}C]PiB was prepared in three automated chemical steps on the Trasis AllinOne synthesizer. [^{11}C]CO $_2$ was obtained through the classical $^{14}\text{N}(\text{p},\text{q})^{11}\text{C}$ reaction and reduced to [^{11}C]Methanolate in a THF solution of LiAlH $_4$. The obtained [^{11}C]Methanolate was then reacted with concentrated HI to yield [^{11}C]CH $_3\text{I}$. [^{11}C]methyl iodide was distilled and converted to the more reactive [^{11}C]Methyl triflate using the supported AgOTf cartridge provided and operated with the module. The radiomethylation of [^{11}C]PiB was performed by flushing [^{11}C]CH $_3\text{OTf}$ onto the solid-phase-supported precursor (6-OH-BTA-0). The labelled tracer was then eluted and subsequently purified by HPLC, providing pure and injectable [^{11}C]PiB after reformulation. **Results:** this automated production method provided [^{11}C]PiB with very good yields (>10% n.d.c. in 22 minutes) and (radio)

chemical purities in compliance with ICH and Ph.Eur. guidelines.

Conclusion: Using the wet chemistry method, a quick and simple synthesis of [^{11}C]PiB was implemented on the Trasis AIO synthesizer. The availability of plug-and-play cassette-based reagent kits allows the routine (pre)clinical use of [^{11}C]PiB and enhances the global research capabilities on Alzheimer's disease.

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EP-0900

Preparation of ^{89}Zr -Oxalate Isotonic Solution for Nuclear Medicine

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Aim: The aim of this study is to develop handy procedure for production of ^{89}Zr -oxalate in physiologically acceptable form and evaluate its potential for using in PET radiopharmaceutical chemistry. The procedure should allow to obtain the chemically pure preparation with high molar activity and radionuclide purity. The solution should be isotonic (concentration of oxalate in it does not exceed 0.115 M) with shelf-life at least 10 days. **Materials and Methods:** All chemicals and solvents were of high-purity or pharmaceutical grade and were purchased from Sigma-Aldrich or Panreac. Quality control was carried out with TLC chromatography (iTLC-SG strips, different eluents; PET-MiniGita radio-TLC scanner). Dowex1, Chelex-100 (Sigma-Aldridge), ZR (Triskem), Chromafix-HCO $_3$ (Macherey-Nagel) resins were used. $^{89}\text{ZrCl}_4$ in 5 M HCl was purchased from Cyclotron Ltd, (Russia). *In vivo* experiments were carried out in BALB/C mice models with different pathologies. Wizard²2480 gamma-counter and G4-microPET (Sofie) were used for biological evaluation. **Results:** It was found that ZR resin allows to obtain ^{89}Zr -oxalate solution with highest yield and lowest metal impurities content. Chromafix-HCO $_3$ and Chelex-100 resins allow to obtain high purity as well, and Chelex-100 resin allows to formulate ^{89}Zr -oxalate in an acceptable form. However, ^{89}Zr -oxalate solution purified with ZR resin does not meet all the requirement for the PET radiopharmaceutical under development. Its virtues and shortcomings will be presented in detail. Thus, conjoint use of ZR and Chelex-100 resins allowed to develop the procedure for production of pH-neutral isotonic ^{89}Zr -oxalate solution with high purity and specific activity. Radiochemical yield of the preparation and purification procedure is $\geq$ 90%. ^{89}Zr complexes with other carboxylic acids were studied as well. Biological and toxicity tests were carried out as well. Experimental results will be presented in detail. **Conclusion:** Handy procedure of production of ^{89}Zr -oxalate physiologically acceptable solution was developed. Oxalate concentration in final solution is $\leq$ 0.115 M and does not interfere with further reactions of ^{89}Zr complexation with chelating agents. On the other hand this concentration prevents hydrolysis effectively long enough. Its suitability for radiopharmaceutical preparations was evaluated. Moreover, this concentration of oxalic acid allows to obtain stable ^{89}Zr -solutions with different pH values (1–8), whereas it's impossible to achieve pH>2 with

concentration of oxalic acid >0.27 M (due to precipitation of sodium oxalate). *The work was financially supported by Ministry of Education and Science of the Russian Federation - State Contract №14.N08.11.0162.*

EP-65

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Radiopharmacy -> Quality control & quality assurance

EP-0901

HPLC method for analysis of DOTA-TATE

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Introduction: Main impurities in the ^{90}Y -DOTA-TATE / ^{177}Lu -DOTA-TATE labelling process, apart from the “free” yttrium-90 or lutetium-177, are DOTA-TATE complexes with other metals that could be present in the solution. The most common method for determination of radiochemical purity (RCP) of labeled peptides is RP-HPLC. However, the standard gradient HPLC methods may not allow determination of the DOTA-TATE complexes with “cold” metals. The information about presence of cold metal complexes might be very important in particular for investigation of reasons of radiolabeling failure and poor RCP. The aim of the study was to develop a new HPLC method that would be suitable for determination of RCP as well as for identification and determination of cold metal complexes that could be present in $^{90}\text{Y}/^{177}\text{Lu}$ -DOTA-TATE. **Materials & Methods:** The new isocratic RP-HPLC method (Phenomenex Kinetex 150x4.6mm column and isocratic flow of 80% 0.1% TFA in water and 20% of 0.1% TFA in acetonitrile, 1mL/min) has been developed and validated. Accuracy, repeatability, precision, linearity and range of the method were checked. DOTA-TATE complexes with “hot” yttrium-90 and lutetium-177 and “cold” complexes with indium, lutetium, yttrium, gallium, zinc, copper, iron and lead were evaluated. The formation of complexes has been confirmed by LC-MS. **Results:** A very good chromatographic separation of the individual DOTA-TATE metal complexes has been achieved. Each of the metal complexes can be easily identified by their characteristic retention times and could be quantitated using estimated molar absorption coefficients. The method enabled quantitative determination of unlabeled peptide in the radioactive preparation in the range of linearity from 10 mcg to 100 mcg of DOTA-TATE ($R^2 = 0.999$). **Discussion/Conclusion:** The developed isocratic HPLC method is suitable for RCP determination of radiolabeled DOTA-TATE. In single HPLC run both the RCP and the contribution of DOTA-TATE complexes with cold metals can be assessed, thus reflecting the specific activity of the radiolabeled peptide. Validation confirmed that the method is accurate, repeatable and precise. **Acknowledgement:** *this work was partly financed by grant No. POIR/01.02.00-00-0041/15 from the National Centre for Research and Development*

EP-0902

Impact of oxidising sporicidal agents on radiochemical purity of Tc-99m Radiopharmaceuticals

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Introduction: Prevention of microbial contamination of aseptically prepared products is particularly important in Radiopharmacy due to the need to administer the product before completion of sterility testing. If present in Grade A area, viable organisms such as bacterial spores may pose a risk of contamination. The likelihood of contamination is low, however it can lead to severe harm to patients and therefore must be mitigated. In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) requires the incorporation of a sporicidal agent into a two stage disinfection process when transferring materials into Grade A areas. An exception remains for the manufacture of Radiopharmaceuticals, due to the risk that oxidising agents such as hydrogen peroxide pose to the radiochemical purity of the products. In practice, contamination of a $^{99\text{m}}\text{Tc}$ kit product with such an agent may result in incomplete reduction of $^{99\text{m}}\text{TcO}_4^-$ at the time of reconstitution, as well as re-oxidation of the former during the shelf life of the products, resulting in poor radiochemical purity. Our aim is to assess the impact of the use of a sporicidal agent as part of the material sanitisation procedure on the radiochemical purity of $^{99\text{m}}\text{Tc}$ radiopharmaceutical products and to determine the change in radiochemical purity over the course of the shelf life of the products. **Methods:** An assembly of cold kits and consumables representative of a routine manufacturing session underwent 4 stages of sanitisation as they were gradually transferred from EU GMP unclassified area to EU GMP Grade A Area. The first stage incorporated a sporicidal low residue peroxide and the subsequent stages consisted of a spray and wipe technique with 70% filtered IMS. All products manufactured were tested for radiochemical purity immediately after reconstitution as well as post end of shelf life. Sterility tests were also carried out for each product. **Results:** The results of radiochemical purity testing were consistently higher than those specified in the manufacturer's summary of the product characteristics (SPC), for all products and sampling times. Sterility test results were negative for all products tested. **Conclusion:** The incorporation of sporicidal low residue peroxide agent into materials sanitisation in Radiopharmacy can be achieved successfully without compromising the radiochemical purity of products, as long as steps to ensure effective removal of peroxide residue are in place. This represents a significant improvement in sterility assurance of aseptically prepared radiopharmaceuticals, which translates into enhanced patient safety.

EP-0903

Evaluation of Indigenously Sourced ^{90}Y -Acetate as a Clinical Grade Radiochemical for use in Radiopharmaceutical Formulations

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Aim: This work was aimed at establishing the quality of indigenously sourced ⁹⁰Y-Acetate as a clinical grade radiochemical precursor for use in radiopharmaceuticals formulations. This was carried out by performing various quality control studies and the results were compared with the acceptance criteria as stated in EP monograph for ⁹⁰Y-Chloride. ⁹⁰Y-Acetate used in the present case has been sourced from High Level Liquid Waste, using separation method based on Supported Liquid Membrane (SLM) technology. **Methods:** RCP was evaluated using TLC (60Å^o-silica-gel, 0.1M CH₃COONa buffer: pH-5.0) and HPLC (RP18, Isocratic-mode, 0.1%TFA in water/acetonitrile:80/20). Gross-γ determined by HPGe coupled 4k-MCA, while Gross-α by ZnS(Ag) method. ⁹⁰Sr content quantified by EPC and β-Spectrometry. Metallic impurities (Fe, Pb, Cu, Zn and Cd) determined by ICP-OES. Impurities from radiolytic damage of KSM-17 and 0.8M CMPO impregnated membranes analyzed by ³¹P-NMR. Since ⁹⁰Sr/⁹⁰Y equilibrated feed mixtures were in 0.02M/4M HNO₃, NO₃⁻ concentration determined by ion-chromatography. Gel-clot BET-assay and Sterility test were performed. The suitability of ⁹⁰Y-Acetate as an API radiochemical ascertained by radiolabeling with DOTATATE. Bio-distribution of ⁹⁰Y-DOTATATE carried out in normal Wistar rat by acquiring bremsstrahlung-image at 22h post-injection with photopeak centered at 95keV using high energy collimated gamma camera. **Results:** Indigenously sourced ⁹⁰Y-Acetate (n=11) was found to be clear and colorless. RAC was between 38-40 mCi/mL. T_{1/2} was between 64.10-64.17h. RCP of ⁹⁰Y-Acetate estimated by TLC was >98% with R_f 0.8-0.9. RCP derived by HPLC was >98% with R_t of radioactive-chromatogram at 4.3minutes which perfectly correlated with UV-chromatogram at 4.5minutes. No significant γ peak was observed except background X-rays (<100keV), ¹³⁷Cs (661keV) and ⁴⁰K (1460keV). ⁹⁰Sr content determined by EPC method was between 0.6-0.9 μCi/Ci of ⁹⁰Y, while β⁻ spectrum shows single peak with E_{max}: 2.28MeV. Gross-α levels were ~1.5 nCi/Ci of ⁹⁰Y. Metal contents (μg/Ci) in ⁹⁰Y-Acetate was 0.5-0.7(Fe), <0.6(Pb), <0.2(Cu), <0.5(Zn & Cd). Absence of any peak in ³¹P-NMR indicates no radiolytic damage of membranes. NO₃⁻ concentration was between 7-10 mg/mL. EL was <3 EU/mL and radiochemical was sterile. ⁹⁰Y-Acetate on radiolabeling with DOTATATE yielded ⁹⁰Y-DOTATATE with RCP >98% and RCY >90%. Bremsstrahlung image of Wistar rat shows localization of ⁹⁰Y-DOTATATE after 22h in kidney and liver with clearance from other major organs. **Conclusions:** The quality control parameters of ⁹⁰Y-Acetate were validated and compared to the pharmacopeia standard. The radiolabeling studies of DOTATATE yielding the product in acceptable RCP, with expected pharmacological behavior in in-vivo models establish the quality of the ⁹⁰Y-Acetate used and adds support to its use as a clinical grade radiochemical.

EP-0904

Validation of a triple method of Quality Control for routine human production of L-[¹¹C]Leucine

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Purpose: L-[¹¹C]Leucine is a radiotracer that can be used to monitor cerebral protein synthesis *in-vivo* by PET imaging. However its radiosynthesis produces a racemic mixture of D and L isomers, coupled with the product and its precursor isovaleraldehyde having weak UV absorptivity for analytical detection. Therefore, for routine QC testing of the final radiochemical product there is a need for three types of analytical methods to be applied. The aim of the project was to develop and validate according to the ICH harmonised tripartite guideline Q2(R1) these analytical methods for routine Quality Control of L-[¹¹C]Leucine.

Materials & Methods: Method 1: Analysis for chemical and radiochemical purity. Thermo Ultimate 3000 HPLC with isocratic pump, VWD at 338nm and radiodetection; Column Waters Spherisorb ODS2, 80Å, 250 x 4.6mm, 3μm, eluent 40% methanol in 10mM phosphate pH 7 at 1mL/min; 20μL injection. Derivatisation using Agilent OPA solution to enable UV detection, 2 min reaction followed by injection onto HPLC. **Method 2:** Analysis for enantiomeric purity. Thermo Dionex Ultimate 3000 HPLC with binary gradient pump, four channel VWD at 210nm and radiodetection; column ChiroSil SCA(-), 150 x 4.6mm, 5μm, eluent 70% methanol with 0.01% phosphoric acid at 1mL/min; 20μL injection. Sample co-injected at 500μg/mL to favour UV detection. **Method 3:** Analysis for the precursor chemical amount and residual solvent analysis. Thermo Focus GC with split injection ratio 6:1 and FID; column Thermo TG-624 30m x 0.32mm, 1.8μm; carrier helium 5mL/min on column with temperature gradient 40-130°C, fuel hydrogen/air; 1μL injection. **Results:** Methods 1 and 3 were validated for quantitative analysis for a range of 5-120% of the limit concentration in terms of linearity, accuracy, precision, specificity, repeatability, intermediate precision and stability of standard and precursor. L-Leucine-OPA as derivatised was stable for 4 hr at room temperature (peak area 3% RSD for 5μg/mL L-leucine standard). Method 2 was validated for specificity, the D and L-leucine isomers were well separated (R_s(EP) ≥ 3.3, limit ≥ 2); to maintain performance of this method the chiral column was reconditioned regularly with 10mM acetic acid. **Conclusion:** Three analytical methods for Quality Control testing of L-[¹¹C]Leucine were successfully validated to ICH guideline Q2(R1) using an extensive set of analytical techniques to assess the safety, quality, efficacy and identity of L-[¹¹C]Leucine for use in GMP human productions.

EP-0905

Single UHPLC-SEC method for the determination of radiochemical purity of ^{99m}Tc-radiopharmaceuticals

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Aim: Determination of the radiochemical purity (RCP) of radiopharmaceuticals is essential, as the presence of radiochemical impurities can affect the image quality leading to diagnostic inaccuracy. Radio Thin Layer Chromatography (r-TLC) is commonly used to measure the RCP of radiopharmaceuticals prepared in nuclear medicine. QC methods for radiopharmaceuticals should be as fast, robust and efficient as possible. Therefore, we investigated the possibility of using radio-Ultra High Performance

Liquid Chromatography (r-UHPLC) for the evaluation of the RCP of five different [^{99m}Tc]radiopharmaceuticals: [^{99m}Tc]albumin nanocolloids, [^{99m}Tc]human serum albumin, [^{99m}Tc]oxidronate, [^{99m}Tc]phytate and [^{99m}Tc]mertiatide. This single UHPLC-Size Exclusion Chromatography (SEC) method was evaluated in comparison with radio-TLC in daily routine practice. **Materials and Methods:** Analyses were carried out on an UPLC[®] (Waters) system coupled with a γ -radiodetector (LabLogic), using a BEH SEC column (Waters), and on a radio-TLC scanner (LabLogic). Coefficients of variation (CVs) were calculated to compare repeatability and reproducibility of both methods. The CVs were obtained from 6 different analyses collected on 5 different days. For the prospective comparison study of radiopharmaceuticals, r-UHPLC analyses were realized by a radio-pharmacist and r-TLC by electro-radiology technicians. An ANOVA test was used whenever samples were ≥ 30 and a Wilcoxon test if it wasn't the case. A 5 % risk was chosen for both of the tests. **Results and Discussion:** Using the UHPLC-SEC method, separation between the labeled products and the free [^{99m}Tc]pertechnetate could be achieved within 8 minutes with good resolutions. Repeatability and reproducibility were good (CVs $<1\%$) for both methods. The CVs were systematically lower with the r-UHPLC method. More than 200 radiopharmaceuticals were analyzed during the prospective study. No significant differences of RCP were observed, except for [^{99m}Tc]oxidronate ($p < 0.0001$). R-UHPLC also allowed to separate [^{99m}Tc]mertiatide from the hydrophilic impurities, which was not possible by r-TLC. Aside from mertiatide, 4 discrepancies of RCP conformity were reported between the two methods. No re-analysis was needed with r-UHPLC method compared to that with r-TLC ($n=18$). **Conclusion:** A reliable QC method is essential for guarantying a content release of radiopharmaceuticals. In daily routine, re-analyses of radiopharmaceuticals by r-TLC are sometimes required in case of contentious result. A r-UHPLC SEC method was developed and validated to measure the RCP of five different [^{99m}Tc]radiopharmaceuticals. Associated with other methods, r-UHPLC could probably replace traditional r-TLC in nuclear medicine. Thus, economic and radioprotection aspects should be evaluated to complete this technical side.

EP-0906

[^{18}F]-Fludeoxyglucose HPLC: A Liverpool Hospital optimisation study and investigation of unknowns

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Background / Aims: The Molecular Science Cyclotron Facility of Liverpool Hospital recently commenced in-house manufacture of [^{18}F]-Fludeoxyglucose (FDG). Development of the analytical method included a comparative study of 2 HPLC columns commonly used for carbohydrate analysis, investigating the NaOH mobile phase concentration and flow rate to give optimal resolution between FDG and FDM and a study aimed at identifying peaks in the ECD (electrochemical detector) chromatogram arising from alkali hydrolysis of labelled intermediate ([^{18}F]-FTAG) followed by acidic neutralisation and formulation in citrate buffer. **Methods:** FDG was produced from [^{18}F]F⁻ (GE

PETtrace, Huayi H₂¹⁸O) by automated synthesis (GE FASTlab-2). Formulated product was sterilised by filtration, sampled for QC, and dispensed into multidose vials for distribution. HPLC analysis of the chemical and radiochemical purity was conducted using a Shimadzu Prominence HPLC on a Dionex Carbopac PA 20 (150 x 3.0 mm, 6.5 μm) or a Hamilton RCX-10 (250 x 4.1 mm, 7 μm) column running 50 - 100 mM NaOH as the mobile phase at 0.5 mL /min. Chemical and radiochemical detection was achieved by EC (Antec Leyden Decade Elite) and scintillation (1' NaI, Flow-RAM LabLogic) detectors in series. Standards and other reference compounds were purchased from ABX, Sigma Aldrich and CarboSynth. Mannose triflate, citrate buffer, ethanol and acetonitrile were obtained from a used FASTlab cassette. All injections were 2 μL . **Results:** The Dionex Carbopac PA 20 (150 x 3.0 mm, 6.5 μm) and a NaOH concentration of 70 mM gave the best separation / retention time combination (total run time = 25 minutes), and an FDG / FDM resolution of 2.3. By comparison results obtained on the Hamilton RCX-10 (250 x 4.1 mm, 7 μm) were 40 minutes total run time with an FDG / FDM resolution of 1.9. To date glucose, 1,6-anhydroglucose and ethanol have been identified in the FDG ECD chromatogram while non-carbohydrate components of the formulation (acetonitrile, kryptofix, sodium citrate, sodium triflate and sodium acetate) do not afford peaks. **Conclusions:** Using 70 mM NaOH as the mobile phase (on PA20) gave excellent FDG / FDM resolution and a run time of <25 minutes. Regular reconditioning of the column with 200 mM NaOH reduced peak drift resulting from carbonate build up on the column. Ethanol, glucose and 1,6-anhydroglucose were identified as components of the FDG formulation, and work is continuing to identify other unknown compounds. **References:** GE Healthcare: White Paper, FASTlab Regulatory Support Information FDG Citrate Cassette. DOC1049454. 2011

EP-0907

Preparation and quality control of $^{177}\text{Lu}/^{90}\text{Y}$ -DOTATATE mix formulations for concurrent PRRT

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Introduction: Although the therapeutic activity of ^{177}Lu -DOTATATE has been proven in the phase 3 clinical trial, still there are options to improve therapy outcomes in NEN. Combination therapies with mixed doses of ^{177}Lu and ^{90}Y labelled DOTATATE are actively investigated proving the additional therapeutic benefit [1,2]. In personal medicine the administered doses should be individually adjusted. The driving idea is to administer to the patient the individually adjusted proportion of ^{90}Y and ^{177}Lu labelled drug for most efficient patient stratification. The aim of the study was the assessment of radioactivity ratio of ^{177}Lu - and ^{90}Y -DOTATATE in mixed formulations and implementation of the method in QC. **Materials & Methods:** MultiSom 0.1mg DOTATATE kit (POLATOM) was used for preparation of ^{177}Lu - or ^{90}Y -DOTATATE. The radiolabelling yield and peptide assay were checked according to the in-house established specifications. Then, these solutions were mixed to obtain activity ratio of ^{177}Lu - and ^{90}Y -DOTATATE: 50%:50%, 65%:35% and 80%:20%, and again subjected to QC using chromatographic methods (TLC, HPLC)

for RCP determination and assay of DOTATATE. For radioactivity measurements, the two-step measurement procedure was performed. The diluted samples were measured by gamma spectrometry with high purity germanium (HPGe) detector to determine the radioactivity of gamma-emitting ^{177}Lu . After addition of scintillation cocktail the sample was measured by liquid scintillation method in (LS) counter. Knowing the radioactivity of ^{177}Lu and its detection efficiency by LS, the ^{177}Lu signal was deducted from total counts registered and the remaining counts were attributed to the radioactivity of ^{90}Y . **Results:** The proposed and validated method for radioactivity determination of the ^{177}Lu - and ^{90}Y -DOTATATE in mixed formulations enables an accurate measurement with uncertainties below 5%. The RP-HPLC method using alfa-HIBA complexing agent in the mobile phase has been developed. The method enables separation ($R_s > 2.5$) and determination of unbound ^{177}Lu or ^{90}Y in $^{177}\text{Lu}/^{90}\text{Y}$ -DOTATATE mix formulations. The validation of the method is ongoing. **Conclusion:** QC methods for $^{177}\text{Lu}/^{90}\text{Y}$ -DOTATATE mixed formulations have been developed. **Acknowledgement:** *This work was partly financed by grant No. POIR/01.02.00-00-0041/15 from the National Centre for Research and Development* **References:** 1. Kunikowska et al, Clinical results of radionuclide therapy of neuroendocrine tumours with ^{90}Y -DOTATATE and tandem $^{90}\text{Y}/^{177}\text{Lu}$ -DOTATATE: which is a better therapy option? Eur J Nucl Med Mol Imaging (2011) 38:1788-1797 2. Seregini et al, Treatment with tandem ^{90}Y -DOTA-TATE and ^{177}Lu -DOTA-TATE of neuroendocrine tumours refractory to conventional therapy. Eur J Nucl Med Mol Imaging (2014) 41:223-230

EP-0908

E-learning as a tool to harmonize education and good quality assurance system in radiopharmacy

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Purpose: Basic education in radiopharmacy is an essential component of the scientific and technical background of a radiopharmacist and the inescapable route by which quality assurance in radiopharmacy can be implemented. The purpose of this study was to evaluate e-learning as a method to improve worldwide education in radiopharmacy and increase the awareness about concepts pertaining the quality of radiopharmaceuticals. **Design and Methodology:** To establish e-learning platform designed as an innovative learning apparatus that, working along side conventional teaching methods, integrates education in all aspects of Radiopharmacy into the curricula being offered by universities at existing education and training institutions is the step forward to the global recognition of the unified standards. In this study, a few lines of analysis for developing a suitable e-learning platform in radiopharmacy were as follows: Course flexibility to improve access and personalization

by Students, Rigorous definition of basic concepts and methods according to international standards, Significantly decrease costs for education in radiopharmacy, Enable fast practical implementation of theoretical concepts through virtual laboratory, Building up a worldwide available, virtual repository of learning resources in radiopharmacy. **Findings:** Each module is designed as a “basic unit of knowledge”, comprising a group of minimum competencies and knowledge about a specific subject and used independently or in combination with other modules or training resources, Students can select the module and the time that best suits his/her professional needs for accessing the materials, Diversity and interactions between different educational contexts are exploited to increase harmonization and integration. **Practical implications:** Two categories of practical implications important for implementation of the successful sustainable system of Quality Assurance could be envisaged as follows. Infrastructural: A new hardware infrastructure dedicated to radiopharmacy, Novel and upgradable e-learning solutions for education in radiopharmacy, Database and soft material repository: Basic concepts, definitions, theoretical models and analytical methods, Virtual training in radiopharmacy practice, Quality standards and quality assurance, Translational tools to adapt the e-learning platform to various educational systems. **Originality and value:** The present work is the first analysis to assess the feasibility of a global e-learning platform for education in radiopharmacy. It is expected that this approach would contribute to (a) overcome local differences in the interpretation of radiopharmacy practice and standards, (b) to spread worldwide knowledge in radiopharmacy, (c) to help harmonization of regulatory systems through education and (d) to implement good standard for quality assurance system.

EP-0909

Quality Control Of Rhenium-188 Eluates With High Volume Activity

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One of the most promising radionuclide for radionuclide therapy is rhenium-188, which produced from $^{188}\text{W}/^{188}\text{Re}$ generator. The therapeutic effect is achieved due to the radionuclide radiation of the pathological foci. Decay of ^{188}Re is accompanied by low-intensity gamma radiation, which makes possible to image the radionuclide in the body and determine doses in pathological foci by single-photon emission tomography and planar scintigraphy. RPhs for radionuclide therapy require the use of eluates with high volume activity. Preparation of «Synoren, ^{188}Re » (radiosynovectomy) require 130-6475 MBq/ml, for «Fosphoren, ^{188}Re » and «Zoleren, ^{188}Re » (palliative treatment of bone metastases) 370-2200 MBq/ml, Rph for hepatocellular carcinoma 4200-7500 MBq/ml. **Aim:** Concentration of $\text{Na}^{188}\text{ReO}_4$ solution is actual for increasing the operation of the generator and for production eluate with a high level of volume activity, followed by quality control of the obtained solutions. **Materials and Methods:** Solution of $\text{Na}^{188}\text{ReO}_4$ with high volume activity

ty were obtained from $^{188}\text{W}/^{188}\text{Re}$ generator with an automatic concentration module NEPTIS TH produced by IRE (Belgium). The radiochemical purity (RCP) was determined by thin layer chromatography on plates with a thin layer of silica gel in acetone. The content of inactive impurities in the $\text{Na}^{188}\text{ReO}_4$ solution was determined on atomic absorption spectrometer MGA-915M ("Lumex", Russia). The NaCl content was determined by potentiometric titration. **Results:** The quality control of $\text{Na}^{188}\text{ReO}_4$ solutions, obtained with using automatic concentration module was carried out in accordance with the State Pharmacopeia of the Russian Federation (GF XIII) for the following parameters: RCP, pH, NaCl content, content of chemical impurities. Due to decrease in RCP, we recommend not exceed volume activity of 7.4–8.0 GBq/ml in the obtained concentrates of the $\text{Na}^{188}\text{ReO}_4$ solution during routine use of the generator. RCP of the obtained concentrated solutions was not less than 99.0%. **Conclusion:** The level of metals in the obtained concentrated solutions is completely acceptable for the use of these eluates for the preparation of radiopharmaceuticals. In general, a proportional increase in the content of chemical impurities during the concentration process does not occur. It is possible to obtain more pure solutions for the content of such potentially competitive metals as Fe, Zn, Cu and others. It should also be noted that during concentration of $\text{Na}^{188}\text{ReO}_4$ solution to the levels of volume activity relatively high, the radiochemical purity of the eluate decreases, which is obviously associated with the partial formation of radiolysis products.

EP-66

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Radiopharmacy -> Radiopharmaceuticals - PET

EP-0910

Evaluation Of Arylpiperazinyl Derivatised Benzoxazolone And Benzothiazolone For 5-HT₇ Expression In Brain

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Aim & Objective: Serotonin (5-HT), is of particular interest because of its involvement in several psychiatric as well as neurological diseases. The latest addition 5-HT receptor subtype is 5-HT₇. It has supposed to a lot of role in many important functions such as sleep, mood, memory and cognition. Till date many researchers have attempted to develop PET ligands for 5-HT₇, but no radioligands have been reached at clinical level to study 5-HT₇ receptor in human. **Methods:** Here, we present biological evaluation of arylpiperazinyl derivatised bezoxzolone/

benzothiazolone for evaluation of 5HT₇. In addition 3-D pharmacophore evaluation/ docking studies was performed to confirm its high affinity for 5-HT₇ in comparison to 5-HT_{1A}, which was validated by in vitro and in vivo studies. **Results:** The radiochemical yield for these two compounds were $24 \pm 6\%$ and $31 \pm 5\%$ (decay-corrected) in 24 ± 12 min ($n = 7$). Preliminary PET study in SD rat brain showed fast accumulation of radioactivity in the brain much higher for bezoxzolone derivative, 2.75 SUV in comparison to benzothiazolone, 1.70 SUV. Similarly in sub brain regions cerebral cortex and thalamus the initial uptake was approximately 2 fold higher for the first compound. **Conclusion:** In summary these evaluation confirmed that arylpiperazinyl bezoxzolone/ benzothiazolones are promising skeleton to design PET ligand for 5-HT₇, further longitudinal animal studies may lead to first small molecule based PET ligand for 5-HT₇ in clinics.

EP-0911

Comparison of two different synthesis methods to label [Lys40,Nle14(Ahx-NODAGA)NH2]exendin-4 with Ga-68

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Glucagon-like peptide 1 receptor (GLP-1R) is preferentially expressed in pancreatic islets, especially in β -cells. Moreover, GLP-1R is highly expressed in human insulinomas and gastrinomas. In recent years several GLP-1 receptor-avid radioligands have been developed to image insulin-secreting tumors or to provide a tentative quantitative in vivo biomarker of pancreatic β -cell mass. Exendin-4 is a 39-amino acid high affinity ligand of the GLP-1R with full agonist activity. It was labeled with PET and SPECT isotopes for imaging purposes. Here, we report results of two synthesis methods to label [Lys40,Nle14(Ahx-NODAGA)NH2]exendin-4 with Ga-68, one using an automatic synthesis module and one manual procedure to label the peptide as a kit. To develop two different labeling methods for [Lys40,Nle14(Ahx-⁶⁸Ga-NODAGA)NH2]exendin-4 and to compare vis-à-vis their labeling quality, efficacy and feasibility. In both procedures, a TiO_2 -based generator (Eckert and Ziegler, E&Z) was eluted with 0.1M HCl and the $^{68}\text{GaCl}_3$ purified using a cationic-exchange cartridge. The kit vial (prepared by the Institute of Atomic Energy, Radioisotope Center POLATOM) was reconstituted with 1.0ml $^{68}\text{GaCl}_3$ (240MBq), using a needle vent, followed by 10min incubation at 100°C. Automatic synthesis was performed using an automated synthesis module (Scintomics GRP[®]) connected to the $^{68}\text{Ge}/^{68}\text{Ga}$ generator. The peptide was dissolved in HEPES solution and then labeled with 1.5ml $^{68}\text{GaCl}_3$ (300MBq) at 95°C for 10min. The radiopharmaceutical product was purified through a C18 cartridge, diluted with PBS buffer and sterilized by filtration through an inline 0.22 μm sterile filter. The RCP% was measured by TLC and HPLC (Ultimate 3000 Thermo fisher, 120 C18 column 3 μm 120Å). We also measured pH by a pH-meter.

The labeling kit is a 3-step “hot” procedure (elution, labeling, CQs aliquote). The automatic synthesis requires only one cold step (peptide dissolution) and one “hot” step (CQs aliquote). Mean RCP% and pH of resulting [Lys40, Nle14(Ahx-⁶⁸Ga-NODAGA)NH2]exendin-4 were 95.87% and 3.5–3.8, and 97.63% and 7.0, for the POLATOM labeling kit and for the automatic synthesis method, respectively. The [Lys40, Nle14(Ahx-NODAGA)NH2]exendin-4 was labeled successfully with ⁶⁸Ga both by the POLATOM labeling kit and by an automatic synthesis module. The POLATOM labeling kit procedure is easier and more rapid than the automatic synthesis method. The latter, however, provides a somewhat purer radiopharmaceutical product, with higher %RCP and entails a lower dose exposure to the operator. Therefore, the automated synthesis system provides an alternative reliable and straightforward approach to synthesize [Lys40, Nle14(Ahx-⁶⁸Ga-NODAGA)NH2]exendin-4.

EP-0912

Synthesis and Quality Control of a new probe [68Ga]-Pentixafor for PET imaging of CXCR4 expression

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The chemokine receptor 4 (CXCR4) is involved in tumor growth and progression, tumor invasiveness and metastasis in several types of human cancer. Recently, [⁶⁸Ga]-pentixafor has emerged as an excellent imaging agent for positron emission tomography (PET) of CXCR4 expression in vivo. The clinical interest in validation of ⁶⁸Ga-labeled agents has increased over time due to on-site production of Ga-68 from the ⁶⁸Ge/⁶⁸Ga generator and the use of automated synthesis systems. Radiopharmaceutical production process must adhere to current good manufacturing process compliance to ensure the quality of precursor and the final product that meet acceptance criteria. High quality PET imaging studies demand high quality radiopharmaceuticals. Numerous methods are used for the routine CQs testing of PET radiopharmaceuticals, including pH determination, radiation measurements, chromatographic methods, bacterial endotoxin/sterility tests. The goal was to develop and validate synthesis process and Quality Controls (CQs) of the radiopharmaceutical product [⁶⁸Ga]-pentixafor. Three consecutive synthesis of [⁶⁸Ga]-pentixafor were performed using an automated synthesis module (Scintomics GRP[®]). For all the synthesis, a TiO₂-based generator (Eckert and Ziegler) was eluted with 0.1M HCl and the ⁶⁸GaCl₃ purified using a cationic-exchange cartridge. The peptide (ABX) was dissolved with HEPES solution (1.5M) and heated at 95° for 10min, then purified through a C18 cartridge, diluted with PBS buffer and sterilized by filtration through a 0.22µm sterile filter. The development process also addressed acceptance criteria for the QC tests and user requirements. We conducted testing for the membrane filter integrity, pH, sterility, and pyrogenicity of drug product. Once a QC test was developed, validation studies were performed to ensure that the method is reproducible and reliable in routine use. We used chromatographic methods HPLC and TLC. The three synthesis procedures of [⁶⁸Ga]-pentixafor showed a RCP% of

99.86%, 99.83% and 100%. The radionuclidic (Ge-68) impurity was $4.8 \times 10^{-5}\%$, $4.9 \times 10^{-5}\%$ e $4.7 \times 10^{-5}\%$. The residual ethanol resulted 5.22%, 5.58% and 5.32% V/V and the spot of HEPES impurity was not more intense than the spot of the reference solution (200µg/V). Bacterial endotoxin testing was performed as the LAL-test and resulted <0.25Eum/ml. The pH of the final product was 7 for all samples. The results demonstrated a batch-to-batch reproducibility providing suitable RCP% and other CQs results, validating the whole synthesis process of [⁶⁸Ga]-pentixafor and allowing the use of this radiotracer as diagnostic probe for molecular imaging. The automated synthesis system provides a reliable approach to synthesize [⁶⁸Ga]-pentixafor in clinical routine.

EP-0913

Selection of optimal macrocyclic chelator for high contrast PET imaging of gastrin releasing peptide receptor using cobalt-labeled bombesin antagonist RM26

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Aim: Overexpression of gastrin-releasing peptide receptors (GRPR) is associated with several cancers. We have recently reported on a bombesin analog (NOTA-PEG₂-RM26) labeled with ⁵⁵Co for next day PET imaging of GRPR. The pharmacokinetics of peptides can be tuned by using different chelators: metal-chelator complexes can bring different overall charge and require co-ligands depending on metal's valency and chelator's denticity. Therefore, in an attempt to further optimize the pharmacokinetic profile, we have in this study evaluated the effect of four macrocyclic chelators (X-PEG₂-RM26, X=NOTA, NODAGA, DOTA, DOTAGA) on the targeting properties and biodistribution of radiocobalt-labeled bombesin antagonist RM26. Co-NOTA chelator should be neutral, Co-NODAGA and Co-DOTA should bring mono- and Co-DOTAGA - di-negative charge. **Methods:** RM26 analogs N-terminally conjugated with NOTA, NODAGA, DOTA or DOTAGA via a PEG₂ spacer were radiolabeled with ⁵⁷Co. Conjugates were evaluated toward stability, binding affinity, targeting specificity, and cellular processing. Biodistribution of labeled conjugates was studied in PC-3 xenografted mice 3 and 24 h pi. The tumor uptake was visualized by preclinical imaging. **Results:** All conjugates were successfully labeled with radiocobalt with high yields and demonstrated high stability. The radiopeptides retained binding specificity to GRPR and their cellular processing was characterized by low levels of internalized activity. The IC50 values were in the low nanomolar range. The kinetic binding studies showed KD values in the low picomolar range. The best binding capacity was found for DOTA-PEG₂-RM26. The biodistribution demonstrated rapid clearance of activity from blood and normal organs via renal excretion. Tumor uptake was similar for all conjugates 3 h pi, exceeding the uptake in all other organs (7.3±1.3 %ID/g for NOTA chelator, 6.3±1.2 %ID/g for NODAGA, 8.1±0.7 %ID/g for DOTA, and 6.9±2.7 %ID/g for DOTAGA). The activity accumulation in GRPR-expressing organs

was significantly higher for DOTA-containing conjugate. Kidney uptake and retention increased with the negative charge of cobalt-chelator complex. The rapid washout of activity from normal organs, including receptor-positive, together with the high retention in tumors resulted in an increase in tumor-to-organ ratios over time for all constructs. Concordant with affinity measurements, ^{57}Co -DOTA-PEG₂-RM26 had the best tumor retention of activity 24 h pi, resulting in the highest tumor-to-blood ratio (598 ± 70). The tumor uptake was confirmed by preclinical imaging. **Conclusion:** Chelators had a pronounced influence on the biodistribution profile of radiocobalt-labeled GRPR antagonists. The DOTA conjugate demonstrated the best binding affinity and the best retention of activity in tumors, having the highest contrast to blood 24 h pi.

EP-0914

Imaging contrast of HER3 expression using monomeric affibody-based imaging probe can be improved by co-injection of affibody trimer

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Introduction: Human epidermal receptor type 3 (HER3) plays a crucial role in progression of many cancer types and several HER3-targeting drugs are under development. Only specific cohort of patients with tumours expressing HER3 will benefit from such treatment. A reliable and repetitive method for detection of HER3 expression in tumours is desirable. In vivo radionuclide imaging meets such requirements. The main challenges in imaging of HER3 are relatively low expression in tumours and endogenous receptor expression in healthy tissue, particularly in liver. Anti-HER3 affibody molecule (7 kDa) labelled with radiocobalt using NOTA chelator demonstrated the most favourable biodistribution profile in terms of the lowest unspecific hepatic uptake and high and stable activity uptake in tumours. We have demonstrated that optimization of injected protein dose lead to improvement of tumour-to-liver ratio. We hypothesised that specific uptake of labelled affibody monomer can be saturated in liver but not in tumour by co-injection of non-labelled affibody trimer due to limited tissue penetration of trimer. **Methods:** Biodistribution of ^{57}Co -NOTA- $\text{Z}_{\text{HER3:08699}}$ was studied 4 h pi in BxPC-3 xenografted mice. ^{57}Co -NOTA- $\text{Z}_{\text{HER3:08699}}$ (fixed labelled protein mass of 0.5 $\mu\text{g}/\text{animal}$) was co-injected with unlabelled affibody trimer ($\text{Z}_{\text{HER3:8699}}_3$) at monomer:trimer molar ratios of 1:0, 1:1, 1:3 and 1:6. Further, biodistribution of ^{57}Co -NOTA- $\text{Z}_{\text{HER3:08699}}/(\text{Z}_{\text{HER3:8699}})_3$ co-injected with ratio 1:3 was head-to-head compared 24 h pi with the biodistribution of ^{57}Co -NOTA- $\text{Z}_{\text{HER3:08699}}$ injected with the best performing dose found previously (2 $\mu\text{g}/\text{animal}$). HER3 expression in BxPC-3 xenografts was imaged using neat ^{57}Co -NOTA- $\text{Z}_{\text{HER3:08699}}$ and ^{57}Co -NOTA- $\text{Z}_{\text{HER3:08699}}/(\text{Z}_{\text{HER3:8699}})_3$ (1:3). **Results:** Hepatic activity uptake 4 h after injection of ^{57}Co -NOTA- $\text{Z}_{\text{HER3:08699}}/(\text{Z}_{\text{HER3:8699}})_3$ decreased with increasing of monomer:trimer molar ratio, while tumour activity uptake was the highest for 1:3 ratio. The maximum tumour-to-liver ratio was found at 1:3 mono-

mer:trimer ratio, 1.0 ± 0.1 , which was significantly higher than for 1:0 (0.44 ± 0.08), 1:1 (0.7 ± 0.1) and 1:6 (0.67 ± 0.01) molar ratios. Head-to-head comparison 24 h pi of ^{57}Co -NOTA- $\text{Z}_{\text{HER3:8699}}$ and ^{57}Co -NOTA- $\text{Z}_{\text{HER3:8699}}/(\text{Z}_{\text{HER3:8699}})_3$ (1:3) demonstrated that tumour activity uptake was significantly higher in the case of co-injection trimer (2.8 ± 0.4 vs 2.1 ± 0.1 %ID/g). Tumour-to-liver ratio was 2.3 ± 0.5 for ^{57}Co -NOTA- $\text{Z}_{\text{HER3:8699}}/(\text{Z}_{\text{HER3:8699}})_3$. Tumour-to-organ ratios were significantly higher (except tumour-to-small intestine) for group co-injected with trimer: e.g., tumour-to blood ratios were 7 ± 2 vs 4.6 ± 0.3 , tumour-to-lung were 3.9 ± 0.1 vs 3.2 ± 0.1 , tumour-to-liver were 2.3 ± 0.5 vs 1.58 ± 0.05 , tumour-to-muscle were 16 ± 1 vs 11 ± 1 , and tumour-to-bone were 28 ± 3 vs 7 ± 4 . SPECT/CT images confirmed the biodistribution data. **Conclusions:** Imaging of HER3 expression can be improved by co-injection of radiolabelled monomeric affibody-based imaging probe with affibody trimer.

EP-0915

Preclinical Evaluation of [^{18}F]ML-10 to Assessment of Radioimmunotherapy with [^{177}Lu]Lu-Labeled Antibody

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Purpose: Radioimmunotherapy combined with radionuclides and monoclonal antibodies (mAb) is promising method of cancer treatment. Prior to perform radioimmunotherapy, immune-PET is conducted to selected patient and estimated dosimetry. PET imaging is also used to evaluate the therapeutic effect with [^{18}F]FDG and [^{18}F]FLT. 2-(5-[^{18}F]fluoro-pentyl)-2-methyl-malonic acid ([^{18}F]ML-10) is a promising radiotracer to detect the apoptosis by using PET imaging. We investigated [^{18}F]ML-10 PET imaging of apoptosis to estimated radioimmunotherapy with [^{177}Lu]Lu-labeled cetuximab in A431 tumor xenograft model. **Methods:** Cetuximab was conjugated with DOTA-NHS ester and was radiolabeled with [^{177}Lu]LuCl₃. [^{18}F]ML-10 was synthesized with 2-(5-methanesulfonyloxy-pentyl)-2-methyl-malonic acid di-*tert*-butyl ester precursor and was purified using C18 Sep-Pak. Radioimmunotherapy studied with [^{177}Lu]Lu-cetuximab was performed in the A431 Model. Therapeutic responses were monitored using microPET/MR imaging with [^{18}F]ML-10 and immunohistochemical staining. **Results:** DOTA conjugated cetuximab was obtained with reasonable radiochemical yield (>20%) after PD-10 purification. [^{177}Lu]Lu-cetuximab had high radiochemical purity (100%) and stability (100%, 6 hrs). [^{18}F]ML-10 was synthesized with high radiochemical yield and radiochemical purity as $24.1 \pm 3.8\%$ and 99.7 ± 0.5 , respectively. Radioimmunotherapy using [^{177}Lu]Lu-cetuximab significantly inhibited the tumor growth. Vehicle groups showed continuously increasing tumor size as 18.6 of relative tumor volume. In contrast, [^{177}Lu]Lu-cetuximab group showed decrease in tumor volume 9 days after the treatment and relative tumor volume was 3.3. [^{177}Lu]Lu-cetuximab showed meaningful increasing of [^{18}F]ML-10 SUVR (tumor to muscle ratio) compared with vehicle. **Conclusion:** [^{18}F]ML-10 is a promising radiotracer for detection of apoptosis and [^{18}F]ML-10 PET imaging is also good tool for assessment of RIT induced apoptosis.

EP-0916

Synthesis and in vitro evaluation of arecoline derivatives as PET tracers for muscarinic acetylcholine receptors

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Introduction and Aim: Muscarinic acetylcholine receptors (mAChRs) are G-protein coupled receptors and their signal transduction is associated with many neurodegenerative disorders such as Alzheimer's disease. Arecoline, a naturally occurring alkaloid, exhibits partial agonist properties towards mAChRs. With respect to PET tracer development arecoline represents a suitable lead structure, allowing for radiochemical labeling on the N-methyl moiety and for derivatization to tune suitable pharmacokinetic and pharmacodynamic properties. The aim of this project is the synthesis and preclinical evaluation of carbon-11 labeled arecoline derivatives as potential mAChR PET tracers. **Material and Methods:** Three novel arecoline derivatives DPMARE (diphenylmethyl 1-methyl-1,2,5,6-tetrahydropyridine-3-carboxylate), TEGARE (2-[2-(2-methoxyethoxy)ethoxy]ethyl 1-methyl-1,2,5,6-tetrahydropyridine-3-carboxylate) and DCCARE (N-cyclohexyl-N-(cyclohexylcarbonyl)-1-methyl-1,2,5,6-tetrahydropyridine-3-carboxamide) were synthesized by esterification or amidation of arecaidine. Precursors for carbon-11 radiolabeling of these substances, as well as reference compounds were characterized by 2D-NMR, ESI-MS, UV-HPLC and by X-ray crystallography if applicable. Radiolabelling was performed in a GE TRACERlab Fx Pro synthesis module via reaction with [¹¹C]CH₃I. Small scale reactions employing different solvents, reaction times and temperatures were performed to optimize reaction conditions. The *in vitro* binding affinity of the compounds was determined with a competitive radioligand binding assay using [methyl-³H]-N-methylscopolamine. Cell membranes were prepared from stable transfected CHO cells expressing the respective subtype of mAChRs. LogP values were assessed via HPLC. **Results:** Arecoline and its derivatives were successfully labelled by reaction with [¹¹C]CH₃I in DMSO at rt for 2 min (RCY = 4.3 ± 0.8 %; molar activity = 93 ± 30 GBq/μmol; n = 8; ±SD). DPMARE shows K_i values in the low nanomolar range towards all subtypes, whereas arecoline exhibits only micromolar affinities towards all subtypes. LogP values were 3.33, -0.66 and 2.27 for DPMARE, TEGARE and DCCARE. **Conclusion:** Radiolabelling of arecoline and its derivatives with ¹¹C could be performed in a straightforward manner. Compared to arecoline, DPMARE shows a drastic gain in mAChR affinity. Considering its K_i values in a suitable range for PET tracer development as well as its appropriate logP, we will further evaluate its potential use as mAChR tracer. Metabolic stability, ligand-receptor kinetics and plasma protein binding will be studied in due course. **References:** 1. Vranka, C. *et al.* Log P, a yesterday's value? *Nuclear Medicine and Biology* 50, 1-10 (2017).

EP-0917

RBC membrane reconstitution enabled formation of ⁸⁹Zr labeled biomimetic nanoparticles for long-term tracking

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Aim: The surface properties of the cell membrane, including their immune control proteins, play a crucial role in their biological applications. Particularly, Red blood cell (RBC) membrane (Rm) can overcome the immune barriers because CD47 antigens on Rm are recognized by the SIRPα receptor signal (Don't eat me) with macrophages. These signal can prohibit phagocytosis of macrophages. **Materials and Methods:** Hollow mesoporous silica nanosphere (HMSN) was dispersed in a HEPES buffer (pH 7.5) at various concentrations. The pH of zirconium-89 (⁸⁹Zr)-oxalate (~20 MBq) was adjusted to pH 7.5–8. After stirring at room-temperature for 24 hours, labeling efficiency was confirmed by radio thin-layer chromatography using 50 mM DTPA as the mobile phase. RBCs of the mouse were isolated using the blood withdrawn by cardiac puncture. Blood was collected and was centrifuged to separate the RBC. The RBC ghost was obtained by hypotonic treatment. RBC membrane fragments were extruded and co-extruded with HMSNs. **Results:** Rm coated HMSN was characterized for morphology, size, and properties. In addition, ⁸⁹Zr (Half-life: 3.3 d) was incorporated under the mild condition with labeling efficiency of >96% on the silanol group of HMSNs without chelator. After Rm coating, the release of ⁸⁹Zr was decreased for long-term tracking. Small animal PET images acquired after tail i.v. injection of ⁸⁹Zr-HMSN and Rm-⁸⁹Zr-HMSN were saturated on tumor site at 48 hr. **Conclusion:** Having distinguished potentials viz. fluidity, stability and long-term circulation ability in biological systems this strategy can be applied extensively to identify the long-term in vivo behavior of nano-drugs while enhancing their biocompatibility. Rm evaded macrophage-mediated phagocytosis, and the Rm coating has been shown to improve the ability to evade the reticuloendothelial system.

EP-0918

Comparative evaluation of anti-EGFR affibody molecules labelled with gallium-68 and zirconium-89 using desferrioxamine B as a chelator

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Aim: Epidermal growth factor receptor (EGFR) is a transmembrane receptor, which regulates cellular proliferation, motility and apoptosis. Radionuclide molecular imaging of EGFR expression in tumours should enable stratification of patients for EGFR-targeting therapies. Anti-EGFR affibody molecule ZEGFR:2377 is a promising probe for imaging of EGFR in vivo. Recently, we have demonstrated that ZEGFR:2377 labelled with the positron emitter ⁸⁹Zr using DFO chelator provides a specific imaging of EGFR-expressing xenografts. The use of the generator-produced positron-emitting radionuclide ⁶⁸Ga instead of ⁸⁹Zr offers advantages of better availability and reduced absorbed doses to healthy tissues. The goal of this study was to evaluate targeting

properties of ^{68}Ga -DFO-ZEGFR:2377 and compare them directly with the properties of ^{89}Zr -DFO-ZEGFR:2377. **Methods:** Maleimido-DFO was site-specifically conjugated to C-terminal cysteine of ZEGFR:2377. The DFO-ZEGFR:2377 was labelled with ^{68}Ga in 1.25 M sodium acetate buffer, pH 3.6, at 85°C. ^{89}Zr -labelling of the affibody molecule was performed by neutralization of ^{89}Zr solution with Na_2CO_3 followed by adding 0.5 M HEPES buffer, pH 6.9, at 85°C. In vitro stability of ^{68}Ga -DFO-ZEGFR:2377 was evaluated in PBS and in the presence of 1000-fold excess of EDTA. In vitro binding specificity of ^{68}Ga -DFO-ZEGFR:2377 was checked using two EGFR-expressing cell lines, A431 and PC3, by a saturation assay. The cellular processing of the labelled conjugate bound to A431 and PC3 cell lines was evaluated using an acid wash method. Biodistribution of conjugates was measured in BALB/C nu/nu mice bearing A431 xenografts. In vivo specificity of ^{68}Ga -DFO-ZEGFR:2377 was confirmed by saturation of EGFR receptor with anti-ZGFR antibody cetuximab. **Results:** The radiochemical yield of ^{68}Ga -DFO-ZEGFR:2377 was 77±5%. After size-exclusion purification, the radiochemical purity was higher than 96%. The conjugate was stable after 3h incubation in PBS and EDTA. ^{68}Ga -DFO-ZEGFR:2377 retained specific binding to EGFR-expressing cells. The cellular processing showed relatively slow internalization. The conjugate demonstrated EGFR-specific targeting of A431 xenografts. Biodistribution showed that tumour uptake of ^{68}Ga -DFO-ZEGFR:2377 (8±2 %ID/g) was significantly higher than ^{89}Zr -DFO-ZEGFR:2377 (5.1±0.6 %ID/g) at 3h after injection. ^{68}Ga -DFO-ZEGFR:2377 had significantly ($p<0.05$) lower uptake in bone and spleen. ^{68}Ga -DFO-ZEGFR:2377 had tumour-to-blood ratio of 7±3 at 3 h after injection. ^{68}Ga -DFO-ZEGFR:2377 provided significantly ($p<0.05$) higher tumour-to-organ ratios for liver, lung, bone, colon, spleen and muscle in comparison to ^{89}Zr -DFO-ZEGFR:2377 resulting in better imaging contrast. **Conclusion:** Our data showed that DFO is a suitable chelator for radiolabelling of EGFR-targeting affibody molecules with gallium-68. ^{68}Ga -DFO-ZEGFR:2377 is a potentially applicable probe for PET imaging of EGFR overexpressing tumours.

EP-0919

Design And Synthesis Of Pet Tracers For The Imaging P2X7 Receptors

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Purpose: P2X₇ is an ionotropic subtype of ATP (P2) receptors and involved in inflammatory pathways of peripheral and central nervous system (CNS). Upregulation of P2X₇ receptors is observed on glial cells in CNS injury and neurodegenerative diseases. PET tracers of P2X₇ receptors might be able to visualize glial cells activity and related diseases but suitable tracers have not developed yet. Pyroglutamic acid benzylamide derivatives GSK1370319 and GSK1482160 are selective antagonists of P2X₇, developed by GSK group and PET studies were conducted by us and others. These compounds have chloro substituent group at ortho position. Here we synthesized pyroglutamic acid 1-phenethylamide derivatives to evaluate the effect of methyl

group and configuration at benzyl position against P2X₇ affinity. Their ¹¹C-labeling and PET imaging by using a neuroinflammation model rat were also performed. **Methods:** The synthesis of *R* and *S* isomers of *m*-CF₃ substituted **1** and non-substituted **2** were carried out by condensation of pyroglutamic acid and the corresponding chiral phenethylamines, followed by the methylation of cyclic amides. The synthesis of ¹¹C-labeled *R* and *S* **1** ((*R*)-PGAA3 and (*S*)-PGAA3) were performed by treatment of 3.3 μmol of precursor and 3 μmol of *t*BuOK at room temperature in DMSO for 3 min. In vitro analysis of *R* and *S* isomers of **1** and **2** were conducted against human P2X₇ in the fluorescent calcium assay. We used the rat with hemispheric neuroinflammation induced by intrastriatal injection of lipopolysaccharide (LPS) to evaluate the tracers by PET. **Results:** We used the precursors without protective group at the acyclic amide position to shorten the total synthesis time. The ¹¹C-methylation of demethyl precursor gave (*R*)-PGAA3 and (*S*)-PGAA3 in more than 80% radiochemical conversions and almost products were ¹¹C-methylated at cyclic position in both cases. Inhibitory analysis of *R* and *S* isomers of **1** and **2** showed 10.2, 17.2, 387, and 349 μM as IC₅₀ values. Compared **1** with **2**, the *m*-CF₃ substitution improved the affinity to P2X₇, however this value was 2-3 order lessor than original GSK compounds. As seen in low affinity of **1**, PET studies did not exhibit significant high uptake of PGAA3 to inflammatory region of the rat brain in 72 hours after LPS administration. **Conclusion:** We synthesized ¹¹C-labeled pyroglutamic acid phenethylamide derivatives (*R*)-PGAA3 and (*S*)-PGAA3 efficiently. In vitro and PET studies suggested further improvement relevant to aromatic substitution was required.

EP-0920

Small Animal Positron Emission Imaging Of HER2-positive Tumor Xenografts With Anti-HER2 Diabody Labelled By Iodine-124

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Introduction: Whole-body, non-invasive, molecular imaging strategies have the potential to extend the analysis of HER2-status to biopsy-inaccessible lesions. PET imaging with antibody-based radiotracers represents a promising approach for detecting biomarkers and monitoring changes to biomarker expression that may correlate with response to therapy. In vitro experiments have shown that binding with tumor cells of anti-HER2 single chain Fv (scFv)-based antibody molecule, called C6.5db, labeled with iodine-124 depends on the density of HER-2 receptors on their membranes. **Aim:** In this study, we evaluate the ¹²⁴I-C6.5 diabody as a potential PET radiotracer in a mouse tumor xenograft model. **Materials and Methods:** The anti-HER2 diabody C6.5 (supplied by Shemykin-Ovchinnikov Institute of Bioorganic chemistry, Moscow, Russia) was radioiodinated with iodine-124 produced by RITVERC Isotope Products (St. Petersburg, Russia). The radioiodination of anti-HER2 diabody C6.5 was carried out using Iodogen with their subsequent separation from the solution on the column with Sephadex G-50.

Radiochemical purity was determined by ITLC in 0.9 % NaCl. 2.0 MBq ^{124}I -C6.5db was injected in BALB c/Nude mice bearing BT-474, SKOV3 and MCF7 xenografts. The procedure of scanning was carried out on a small animal PET with subsequent reconstruction and quantitative analysis of images. The scan time is 10 minutes. PET images were obtained in 1, 4, 24 and 48 hours after injection. **Results:** The yield of the reaction was about 18 %. Radiochemical purity was not less than 95%. In the course of the study, PET images of animals with experimental models of tumor growth were obtained. The SUV value for xenografts of HER2-positive tumors varied from 2.0 at 4 h to 3.95 at 48 h after injection. HER-2 negative xenografts in PET scans were not visualized. **Conclusion:** The specificity of the visualization of HER2-positive xenografts with the help of ^{124}I -C6.5db is proved.

EP-0921

^{68}Ga -DOTA-Hepta, An Albumin Binding Tracer, Targets Glioblastoma Tumor In Vivo PET/CT Imaging May Serve As A Novel Prognostic Imaging Agent

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Introduction: The tumor vasculature and dynamic angiogenesis with time may play a crucial role in tumor staging, treatment respond monitoring and prognostic evaluation in the early phase. Thus, if an imaging agent that can precisely quantify the tumor distribution volume (DV) change in time will prove to be useful for diagnostic purpose as well as the therapeutic evaluation of any cancer therapy. To test this hypothesis, the novel albumin binding PET imaging agent was developed and evaluated in mouse tumor models of human colon (DLD-1) and glioblastoma (U87-MG) cancers. **Methods:** U-87 MG (5×10^6) and DLD-1 (1×10^7) cells were subcutaneously injected into the front flanks of 6–8-week-old male nude mice. The resultant tumors were allowed to grow until they reached volumes of 400–600 mm³ in volume. The acquired PET/CT images through 15-minute static scans at 1h, 3h and 5h after tumor xenograft mice ($n = 12$) were injected with radiolabeled ^{68}Ga -DOTA-Heptap (6.6–7.4 MBq). All images were generated with scatter correction, random correction and attenuation correction (AC). The average radioactivity concentration within the tumor or organ of interest was obtained by determining the mean pixel values within the multiple ROIs (% ID/g). The radioactivity of normal major organs such as the muscles, heart, lung, liver, kidney, and brain, was also calculated for comparisons. **Results:** Other than the liver (6.2 ± 0.98 %ID/g), kidneys (10.92 ± 0.315 %ID/g) and urinary bladder, in which the level of radiolabeled tracer uptake was influenced by excretion, intriguingly, the significant tracer uptake occurred in U-87 MG tumors. The U-87 MG tumors were clearly delineated and displayed significant tumor-to-background contrast over time, the tracer uptake in malignancies were (2.54 ± 0.356 %ID/g, 3.78 ± 0.515 %ID/g, 4.69 ± 0.197 %ID/g) at 1h, 3h and 5h, respectively. However, non-significant tumor uptake was observed in DLD-1 colon tumor (1.33 ± 0.103 % ID/g) model during the whole imaging acquisition time period. Major organs such as heart (4.2 ± 0.135 %ID/g), spleen (1.45 ± 0.23 %ID/g), muscle (1.46 ± 0.43

%ID/g) and brain (1.16 ± 0.34 %ID/g) all displayed comparatively low levels of tracer uptake. **Conclusion:** These results suggest that there is significant tumor uptake in ^{68}Ga -DOTA-Heptap tracer accumulation along with the time period monitoring by PET/CT imaging. Thus, the non-invasive detection of tumor vascular leaking activity *in vivo* may permit a more precise definition of the roles of tumor vasculature status and yield insight regarding novel therapeutic strategies in molecular level.

EP-0922

A Composite Iron Oxide Nanoparticle Labelled with Zirconium-89 by Simple Self-Assembly System for Cancer Detection

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Aim: Zirconium-89 (^{89}Zr) utilized in Positron Emission Tomography (PET) has been the spotlight in nanomedicine due to relatively long half-life required for the measurement of long-term in vivo behavior of the nanoparticles. The metallic radioisotope usually needs the chelator for conjugation with bioactive nanomaterials as a radiopharmaceutical. However, the chelator attached on surface of nanoparticle could induce unprecedented alteration of its properties due to the variation in the surface charge of the nanoparticles and may reduce innate targeting system. The behavior of the nanoparticles after injection in the body is different and dependent on size, shape and its surface properties. Here, we tried to incorporate ^{89}Zr in the biocompatible iron oxide nanoparticle by the simple one-pot hydrothermal synthesis without radio-metal chelators to identify the in vivo distribution of the nanoparticle. **Materials and Methods:** The ^{89}Zr produced using an onsite cyclotron at the Institute of Korea Atomic Research was mixed in the prepared solution included with FeCl_3 , ZrOCl_2 , L-glutamic acid and formic acid. The reactant mixture was transferred into a PTFE autoclave bottle followed by placed in a preheated oven at 120°C for 24 h. The radiochemical yield of the ^{89}Zr incorporated in the iron oxide nanoparticle was determined using TLC. For the further characterization of the iron oxide nanoparticle, TEM, XRD, XPS, IR, DLS and Zeta-potential were utilized. To examine biological properties of the nanoparticle, we proceed with labelling stability in various biological mediums, cytotoxicity, cellular uptake for CT-26 and A549 cancer cells, and the measurement of PET images for CT-26 tumor bearing Balb/C mouse. **Results and Conclusion:** The non-spherical iron oxide nanoparticles having average length and width of 180 and 80 nm respectively was obtained after simple one-pot hydrothermal reaction. Controlling of the nanometer size was achieved by using formic acid as a capping agent. ^{89}Zr was well labelled in the iron oxide nanoparticle during their nucleation and crystal growth ($\geq 98\%$). The ^{89}Zr binding stability in the iron oxide nanoparticle was significantly high in biological mediums, but the nanoparticle was aggregated in PBS (pH 7.4) and serum. The radioactive nanoparticle was considerably nontoxic to the living system, and indirectly suggested the nanoparticle was

significantly biocompatible. In the biological evaluations, high in vitro cellular uptake was demonstrated, and based on the results of the in vivo PET imaging and biodistribution analysis, the radioactive iron oxide nanoparticle proved effective targeting of the CT-26 tumor.

EP-0923

Total solid-phase synthesis of DOTA-functionalized tumor targeting peptides for PET imaging and therapy

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Objective: The convenient synthesis of metal chelating agents couple with tumor targeting peptides is needed to accelerate the research and clinical translation in molecular imaging. DOTA is one of the most widely used macrocyclic ligands for development of new metal based imaging and therapeutic agents owing to its ability to form stable and inert complexes under physiological conditions making these radiopharmaceuticals useful for imaging/therapy. DOTA-tris-*t*-butyl ester is commercially available but it is expensive and contain impurities of both the di-alkylated and tetra-alkylated cyclen. There is a need to explore new methods for preparation of DOTA-tri-*t*-butyl ester which are less expensive and provides a high purity DOTA product. The aim of this study was to develop a convenient and cost effective synthetic approach for the preparation of DOTA peptides directly on solid support for tumor imaging and therapy.

Methods: The tumor targeting peptide (bombesin 7-14) was synthesized by Fmoc-based solid-phase synthesis. For DOTA coupling bromoacetic acid after activation with HOBt/DIC was coupled to free amino group of peptide. This was followed by monoalkylation of bromoacetylated peptide resin with cyclen (tetraazacyclododecane). The cyclen peptide was then alkylated with *tert*-butylbromoacetate to afford desired DOTA peptide. Additionally, the same peptide was prepared from commercially available tris-*t*-butyl-DOTA for comparison. These peptides after labeling with ^{68}Ga were evaluated for their ability to bind bombesin receptors overexpressed on human breast and prostate cancer cells. In vivo tumor targeting was examined in nude mice implanted with MDA-MB-231 xenografts. **Results:** The identity and purity of DOTA peptides was confirmed by mass spectrometry and HPLC. The peptides radiolabeled efficiently with ^{68}Ga (>90%) and exhibited high binding affinity to BN positive MDA-MB-231 and PC3 cancer cell lines (k_d < 20 nM). In nude mice with MDA-MB-231 xenografts, ^{68}Ga -labeled peptides displayed efficient clearance from the blood and uptake/retention in all the major organs was low to moderate (below 5%ID/g). The accumulation in the BN positive tumors was ~2% ID/g at 1 h p.i. with good tumor to blood and muscle ratios. The main route of excretion was renal pathway. Both peptides displayed comparable in vitro and in vivo behavior. **Conclusion:** We have described the preparation and in vitro and in vivo activity of two DOTA coupled peptides. The synthesized peptides hold good tumor affinity and tumor targeting potential. This successful and economical synthetic strategy can be applied to the facile synthesis of various tumor targeting peptides which ultimately can be translated into clinical settings.

EP-0924

Synthesis and Biological Evaluation of Diagnostic reagent for Prostate cancer using Copper-64 radioisotope Synthesis and Biological Evaluation of Diagnostic reagent for Prostate cancer using Copper-64 radioisotope

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Introduction: Prostate specific membrane antigen (PSMA) is a cell surface membrane protein, which is overexpressed in most prostate cancer. Recently, PET imaging with ^{68}Ga -PSMA-HBED-CC has been widely used for the diagnosis of recurrent prostate cancer. In addition, the studies on the diagnostic potential of ^{64}Cu -labeled PSMA ligand reported actively. In this study, we monitored with biological evaluation *in vivo* and PET imaging of ^{64}Cu -labeled PSMA ligand (^{64}Cu -PSMA-617). **Subject & Methods:** The radiolabelling efficiency and stability of ^{64}Cu -PSMA-617 were confirmed by thin layer chromatography. PET/CT imaging of ^{64}Cu -PSMA-617 were obtained within prostate cancer mice models. **Results:** The radiolabeling efficiency of ^{64}Cu -PSMA-617 was showed over 95%, and stabilities of ^{64}Cu -PSMA-617 was remained over 98% in both human and mouse serum for 48 h. In normal male mice, the *in vivo* uptake of ^{64}Cu -PSMA-617 into several organs was measured at 2, 4, 6, 24, 48h after injection. Rapid blood clearance was observed for ^{64}Cu -PSMA-617. The highest uptake ratio was observed in the lung, liver, intestines and kidneys at 2h, however low uptake ratio of 1-2%ID/g was observed in most of organ at 4h. PET images of 22RV1 tumor-bearing nude mice were acquired dynamic images and at 24 h, 48h after injection. In dynamic PET images, ^{64}Cu -PSMA-617 uptake ratio in tumors was increased with in the first 10 minutes, and continuously increased until 60 minutes, and showed retention in tumors at 48h. **Conclusion:** In these results, the PET/CT imaging using ^{64}Cu -PSMA-617 in prostate cancer is expected to be useful for the diagnosis and treatment of prostate cancer patients.

EP-0925

Development of a radiolabelling method of ^{68}Ga -Exendin-4(NODAGA) using the GAIA module from Elysia-Raytest[®]

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Introduction-Aim: ^{68}Ga -Exendin-4(NODAGA) (^{68}Ga -exendin) is a tracer for the detection of insulinomas with PET/CT. It has been developed by Betacure in the Netherlands. Currently, it is evaluated within an European clinical trial as part of the BetaCure consortium (EU FP7 grant number 602812) that the Nuclear Medicine department of Tenon Hospital participates in. Within the consortium a radiolabeling method was developed that was not adapted to our equipment (Radiolabelling yield less than 10%). The aim of this study was to develop a new method for the GAIA module. **Materials and Methods:** Exendin-4(NODAGA) was provided by Pichem[®] as a freeze-dried peptide and $^{68}\text{GaCl}_3$ was eluted from a GalliaPharm[®] generator. Single-use kits and reagents were provided by ABX[®]. Exendin, solubilized in sodium acetate solution 0.8 mol/L containing

ascorbic acid (1g/mL), was introduced directly into the reaction vial with a micropipette to avoid loss of peptide in the tubing. Then, GaCl₃ was directly eluted into the reaction vial without pre-purification and the mixture was heated for 15 min at 100°C. At the end of the cooling mixture, Tween 80 (0.15%) was added to improve the transfer on SPE (Solid Phase Extraction) column. Moreover, the purification step was optimized by adding sodium acetate 2.4 mol/L in the reaction mixture to increase the pH to 5–5.5 before transferring onto the cartridge. The radiochemical purity (RCP) was evaluated by TLC with DTPA 0.1 mol/L in ammonium acetate 0.25 mol/L as mobile phase and ITLC-SG as stationary phase. **Results:** The radiolabeling yield, not corrected from decay, was approximately 50% (sufficient for injection of patients) as compared to 10% with the conventional method (pre-purification). The addition of sodium acetate 2.4 mol/L at the end of the reaction improved the amount of ⁶⁸Ga-exendin in the final product. The RCP was over 97% with less than 3% of ⁶⁸Ga-impurities (free ⁶⁸Ga³⁺ and ⁶⁸Ga-colloid (⁶⁸Ga(OH)₃)). **Conclusion:** By deleting the step of pre-purification, introducing Exendin directly into the reaction vial and adding more concentrated sodium acetate at the end of the reaction, we increased the radiolabeling yield and the radiochemical purity of our product: ⁶⁸Ga-exendin.

EP-0926

PET Imaging of Joint Inflammation by Cyanine-based Probe (⁶⁸Ga-DOTA-NIR790) in a Mouse Model of Arthritis

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Arthritis is the most common joint disorder around the world. The aim of this work is to preliminarily evaluate whether PET/CT imaging with ⁶⁸Ga-DOTA-NIR790 is a useful probe for monitoring and quantifying joint inflammation in FCA-induced arthritis. **Methods:** We synthesized cyanine-based imaging probes (⁶⁸Ga-DOTA-NIR790) for NIR fluorescence and nuclear imaging (PET) of FCA-induced arthritis. **Results:** The PET/CT image showed high radioactivity in joint inflammation, which was in agreement with NIR fluorescence imaging and biodistribution. **Conclusion:** The ⁶⁸Ga-DOTA-NIR790 could target the joint inflammation in FCA-induced arthritis, and offer multi-modalities for NIR fluorescence and nuclear imaging (PET) to diagnose and monitor arthritis.

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Objective: The blood-brain barrier (BBB) is a major obstacle for drug delivery to the brain. Nucleolipid based liposomes are promising drug delivery systems allowing in vivo tracking using molecular imaging techniques and have proved promising theranostics agents especially for tumors. However, efficient liposomal preparations for theranostic of neuro-onco, neuro-infection and neurodegenerative diseases needs further research. Nucleolipidic liposomes (NL-Nps) are of great interest because of the site-recognition (nucleoside), lipophilicity (long alkyl chain) and better membrane translocation by interaction of fatty acid with the lipid bilayer. Thus, we have evaluated uridine derived nucleolipidic liposomes for encapsulation efficiencies of MTX (methotrexate) anti-cancer and sulfanilamide anti-infection drug and in vivo tracking by radiolabeling with ^{99m}Tc. **Materials and Method:** (NL-Nps) were prepared using NL-DTPA (synthesized), heated to 50° C when mixed with organic solvent and added to aqueous phase containing the surfactant Tween-80 and the co-surfactant soya lecithin. NL-Nps were encapsulated with MTX and sulfanilamide were similarly prepared by adding drugs (0.1 to 1.5%) to the formulation. NL-Nps were evaluated for release kinetics and brain targeting in BMG-1 (brain glioma) cell line in murine model. **Results:** Multi-step synthesis leads to the final compound (NL-DTPA) and its liposomal preparation (size 113 to 130 nm, zeta potential -14 to -28 mV) with EEs of 64% was achieved. Liposomes showed sustained drug release for 2–5 days negligible hemolytic activity, no cytotoxicity in HEK cells. Radiolabeling efficiency of 98% was achieved using ^{99m}Tc conferring prolonged systemic circulation and renal route excretion. The biodistribution showed 1.8% ID/gm to 2.3% ID/gm for intact versus disrupted BBB in mice models. (NL-Nps) also in BMG tumor mice depicted higher tumor uptake (2.3T/M). **Conclusion:** Nucleolipid functionalized liposomes as candidates to be used as biocompatible nanocarrier systems with high systemic retention and anti-tumour effects. Future work will concentrate on targeting of liposomes in brain tumor model using stereotaxis. **References:** 1) Vitiello G, *et. al*, *Journal of Materials Chemistry* 2015;3(15):3011–23. 2) Khiati S, *et. al*, *ACS nano*. 2011 Oct 11;5(11):8649–55.

EP-67

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Radiopharmacy -> Radiopharmaceuticals - SPECT

EP-0927

Evaluation Of BBB Permeable Nucleo-Liposomes (NL-Nps): A DI-C15-Ketalised Palmitone Appended Uridine As Neuro-Tracer For SPECT

EP-0928

Evaluation of Radioiodine and Technetium-Labeled DARPIn 9_29 for Molecular Imaging of HER2 Expression in Cancer Using SPECT

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Aim: Radionuclide molecular imaging may allow non-invasive repeated whole-body monitoring of HER2 expression and permit stratification of patients for HER2-targeted therapy. Imaging probes based on small scaffold proteins (e. g. DARPins) provide high sensitivity and good contrast due to fast clearance from blood. However, composition of a scaffold protein and a radionuclide label may influence off-target interactions, accumulation in normal tissues and clearance rate of an imaging probe. The goal of this study was to evaluate DARPIn 9_29 labeled with iodine-125 and technetium-99m as a targeting agent for imaging of HER2 using SPECT. **Methods:** DARPIn 9_29 was labeled with iodine-125 by direct radioiodination and with technetium-99m by tricarbonyl conjugation to the C-terminal hexahistidine tag. **In vitro** evaluation of both radiolabeled proteins was performed in SKOV3, BT474 and DU145 HER2-expressing cell lines. Binding specificity was tested by saturation of HER2. Binding affinities to living HER2-expressing cells were measured using LigandTracer. Cellular processing and retention of radiolabeled proteins was measured over time. Biodistribution of both radiolabeled proteins was studied in mice bearing HER2-expressing SKOV-3 xenografts at 6 h p.i. Specificity of HER2-targeting was evaluated in a HER2-negative Ramos xenograft model. SPECT imaging was used to confirm the results of biodistribution studies. **Results:** DARPIn 9_29 was labeled with [125 I] with $96 \pm 1\%$ radiochemical yield (RCY) and with [99m Tc]Tc(CO) $_3$ with $80 \pm 4\%$ RCY. Both labeled proteins retained nanomolar affinity to HER2. Binding to HER2-expressing cells was specific and proportional to expression level. Internalization of proteins by cells was slow. Both labeled proteins were rapidly cleared from blood and provided similar tumor uptake at 6 h p.i. (3.4 ± 0.7 %ID/g for [125 I] and 2.9 ± 0.7 %ID/g for [99m Tc]Tc(CO) $_3$). However, there were appreciable differences in non-specific uptake and retention in normal organs. DARPIn 9_29 labeled with technetium-99m had high hepatic uptake with hepatobiliary excretion. DARPIn 9_29 labeled with iodine-125 had significantly ($p < 0.05$) lower uptake in lung, liver, gut, spleen, kidneys and bone. The uptake of both labeled proteins in HER2-positive xenografts was significantly ($p < 0.00005$) higher than in HER2-negative xenografts. **Conclusion:** DARPIn 9_29 can be directly labeled with iodine-125 and [99m Tc]Tc(CO) $_3$ with good yields and high stability. Binding specificity and affinity to HER2 were preserved. Both labeled proteins provided similar tumor uptake, however, radioiodine provided better tumor-to-organ ratios compared to technetium-99m due to lower lipophilicity and non-residualizing properties of the label. Radioiodinated DARPIn 9_29 is a promising agent for same-day imaging of HER2 expression using SPECT.

EP-0929

New 99m Tc-labeled peptide for EGFR tumor targeting

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Introduction: The epidermal growth factor receptors (EGFRs) are a family of cell surface receptors that play multiple roles in normal cellular functions mainly including cell growth, proliferation and cell survival. Several reports indicated that enhances in EGFRs expression (e.g. HER1 and HER2) disrupt the mecha-

nism of normal cells and consequently lead to cellular proliferation, angiogenesis, migration and invasion. The aim of this study was to evaluate a new 99m Tc targeted GE 11 peptide that has high tendency to accumulate in tumors with high level of epidermal growth factor receptor (EGFR) expression. **Material and Methods:** The 12-mer GE11 peptide (YHWYGYTPQNVI) was modified on N-terminus using the serylserylserin amino acids and HYNIC as spacer and bifunctional chelating agent, respectively. The HYNIC-(Ser) $_3$ -GE11 peptide was purchased from ProteoGenix (Schiltigheim, France) and labeled with 99m Tc using tricine and mixture of EDDA/tricine as the coligands. The efficacy of radiolabeling of peptides were analyzed on ITLC-SG and also by reversed-phase high-performance liquid chromatography (RP-HPLC). **Results and Conclusion:** HYNIC-SSS-GE11 were labeled with 99m Tc using both labeling approaches with more than 95% efficiency and showed high stability in buffer and serum. The affinity of new radioconjugated peptides for binding to EGFR were investigated on various cell lines with different levels of EGFR expression in which human ovarian carcinoma cells showed higher affinity and was used for further in vitro and in vivo investigations. The **in vitro** experiments showed good affinity to human ovarian carcinoma cells using both radioconjugated peptides. Biodistribution studies in normal female mice and mice xenograft tumor model revealed that the both radioconjugated peptides had high in vivo stability and high renal excretion. However tricine-coliganded radiolabeled peptide showed higher liver and intestine uptake compared than EDDA/tricine coliganded radiolabeled peptide. The gamma scintigraphy showed good tumor visualization. From the results of this investigation it appears that, the new radioconjugated peptide might be a promising radiotracer for SPECT imaging of ovarian tumor.

EP-0930

Biodistribution and Imaging Evaluation of Cyclic Peptide RGD in 4T1 Breast Cancer Model

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Objectives: Upregulated expression of integrin $\alpha_v\beta_3$ in newly formed endothelial cells and some tumor cells plays a significant role in tumor growth, invasion and angiogenesis. Cyclic RGD, which is high affinity and selectivity for integrin $\alpha_v\beta_3$, is considered as targeting peptides by recognizing integrin $\alpha_v\beta_3$ on the newly formed endothelial cells surface of tumor cells. We synthesized the 111 In-DOTA-GSG-cCRGDfC, an 111 In-labeled RGD peptide derivative targeting $\alpha_v\beta_3$ for imaging tumor. In this study, we try to explore biodistribution of 111 In-DOTA-GSG-cCRGDfC in 4T1 breast cancer bearing mice and demonstrate that 111 In-DOTA-GSG-cCRGDfC may offer diagnostic images for breast tumor. **Methods:** DOTA-GSG-cCRGDfC was labelled with 111 In or in Institute of Nuclear Energy Research. Biodistribution and nanoSPET/CT studies were performed in 4T1-xenograft BALB/c mice. Tumor xenografts were performed in 6-wk-old female BALB/c mice by subcutaneous injection of 2×10^6 4T1 cells. At 14 days after tumor inoculation, nanoSPECT/CT imaging was performed at 0.5 h, 2 h, 4 h and 24 h after injection

of ^{111}In -DOTA-GSG-cCRGDfC. In biodistribution study, 4T1 tumor-bearing female mice was performed after i.v. injection of 18 MBq ^{111}In -DOTA-GSG-cCRGDfC ($n = 5$). The mice were sacrificed and dissected at 0.5 h, 2 h, 4 h and 24 h after injection of ^{111}In -DOTA-GSG-cCRGDfC. **Results:** The labeling efficiency of ^{111}In -DOTA-GSG-cCRGDfC was more than 90%. The high tumor-to-organ ratios for the ^{111}In -DOTA-GSG-cCRGDfC (at 4 h after injection: tumor-to-muscle ratio, 12.71; and tumor-to-liver ratio, 3.64) were confirmed by nanoSPECT/CT images in the subcutaneous 4T1 tumor model. Biodistribution studies also revealed a high tumor-to-muscle ratio of 12.88 after 4 h. **Conclusions:** These results of nanoSPECT/CT imaging and biodistribution data showed that ^{111}In -DOTA-GSG-cCRGDfC was high accumulated in the 4T1 tumor site. We are going to prove DOTA-GSG-cCRGDfC and derivatives have the capability as a diagnostic/radiotherapy tool for $\alpha_v\beta_3$ -positive tumors in the future.

EP-0931

A Novel Tumor Imaging Agent, Tc-99m and Fluorescence Labeled Gastrin-Releasing Peptide Analogues: In Vitro and In Vivo Comparison

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Aim: A variety of imaging probes have been developed for different molecular targets. The GRP analogues (GRP, GRP18-27 and GRP21-27) were investigated vigorously as a targeting peptide for tumor, however, the cancer targeting abilities of these GRP analogues had not been compared head-to-head. Direct comparison of characteristics of these analogues will provide a useful information for the design of molecular imaging agent associated with GRP and an insight within the mechanism of tumor targeting using GRP analogues. In the present study, we developed Tc-99m and TAMRA labeled GRP analogues containing three different peptides (TAMRA-GHEG-ECG-GRP, TAMRA-GHEG-ECG-GRP18-27 and TAMRA-GHEG-ECG-GRP21-27) to target the tumor cells and compared the tumor targeting abilities using in vitro and in vivo experiments. **Materials and Methods:** Peptides were synthesized using Fmoc solid-phase peptide synthesis. Radiolabeling of peptides with Tc-99m was done using ligand exchange via tartrate. Binding affinity and in vitro cellular uptake studies were performed. Gamma camera imaging study was performed in murine models with PC-3 tumors. The average counts per pixel within the ROIs were measured and target-to-non-target ratios were calculated. **Results:** After radiolabeling procedures with Tc-99m, Tc-99m labeled peptides were prepared in high yield (>96%). Tc-99m TAMRA-GHEG-ECG-GRP ($K_d = 7.9 \pm 2.7$ nM) showed highest binding affinity for PC-3 tumor cells and Tc-99m TAMRA-GHEG-ECG-GRP18-27 ($K_d = 12.6 \pm 3.6$ nM) showed relatively low binding affinity. Confocal microscopy images of PC-3 cells incubated with TAMRA-GHEG-ECG-GRP and TAMRA-GHEG-ECG-GRP21-27 showed strong fluorescence in the cytoplasm. Gamma camera imaging revealed substantial uptake of Tc-99m TAMRA-GHEG-ECG-GRP21-27 in tumors. **Conclusion:** We developed three Tc-99m and TAMRA labeled GRP analogues as a molecular imaging agent binding targeting tumor. In vitro studies demonstrated substantial binding affinity and cel-

lular uptake of TAMRA-GHEG-ECG-GRP and TAMRA-GHEG-ECG-GRP21-27. In contrast, in vivo gamma imaging study revealed that only Tc-99m TAMRA-GHEG-ECG-GRP21-27 was significantly accumulated in the tumor tissue. Taken together, the present study suggest that 7-mer peptide, GRP21-27 is the best surrogate as a targeting ligand for tumor imaging.

EP-0932

Tc-99m-labeled peptide-based N_3S_1 chelator with enhanced renal clearance for folate receptor imaging

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Peptide-based N_3S_1 chelator PXC, which are comprised of amino acids (Pro-X-Cys backbone, X are designated for some amino acids) for radiolabeling with $^{99\text{m}}\text{Tc}$ has been designed and evaluated for development of radiopharmaceuticals. However, the lipophilicity of the first core structure, Pro-Gly-Cys (PGC) in its RGD complex has resulted in substantial hepatobiliary excretion when administered in tumor-bearing mice. In this study, to improve biological behavior in the biodistribution with the intention of enhancing renal clearance, we describe the synthesis, evaluation of a novel lysine derivative, Pro-Lys-Cys (PKC) derived from PXC chelator system, and its application with $^{99\text{m}}\text{Tc}$ labeled folate derivative ($^{99\text{m}}\text{Tc}$ -PKC-fol) for *in vivo* imaging of FR-positive tumor. A novel tripeptide chelating sequence, PKC and its RGD conjugate were synthesized and evaluated in normal mice to explore the effect of chelator on the pharmacokinetic properties. Thereafter, a novel folate conjugate, PKC- $\epsilon\text{K}\gamma\text{E}$ -folate (PKC-fol), was radiolabeled with $^{99\text{m}}\text{Tc}$ and evaluated in FR-positive KB tumor bearing mice for *in vivo* biodistribution profile and *in vivo* SPECT image. Tissue distribution in normal mice demonstrated that PKC-conjugated peptide resulted in greater renal clearance and significantly less intestinal uptake than that of the PGC complex. $^{99\text{m}}\text{Tc}$ -PKC-fol exhibited specific uptake and retention in tumor tissues with high renal clearance and significantly reduced intestinal uptake. Tumor uptake was 2.96 ± 0.51 % ID/g at 1 h p.i. and 2.24 ± 0.27 % ID/g at 3 h p.i., respectively. SPECT images showed good tumor-to-normal tissue contrast of $^{99\text{m}}\text{Tc}$ -PKC-fol, and clearly confirmed the accumulation of the $^{99\text{m}}\text{Tc}$ -PKC-fol in KB tumor. This study demonstrated that the lipophilicity can be controlled and biodistribution profile of $^{99\text{m}}\text{Tc}$ -PXC complex can be altered through the design and synthesis of PXC chelator core, thus opening up application of novel peptide-based PXC chelator system for the development of radiopharmaceuticals.

EP-0933

^{131}I -labeled dendrimer-entrapped gold nanoparticles for single photon emission computed tomography/computed tomography (SPECT/CT) imaging and radionuclide therapy of gliomas

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Purpose/Introduction: Gliomas are the most common and fatal tumors in brain, which are difficult to be cured by conventional therapies. ^{131}I -labeled *Buthus martensii* Karsch chlorotoxin-

in (BmK CT) has been reported to be used for SPECT imaging and radiotherapy of gliomas. Meanwhile, dendrimer-entrapped gold nanoparticles (Au DENPs) are praised to enhance the biocompatibility for computed tomography (CT) imaging. Herein, in this study, we explored the synthesis, characterization, and utilization of ^{131}I -labeled BmK CT-modified Au DENPs for targeted Single Photon Emission Computed Tomography (SPECT)/CT imaging and radionuclide therapy of gliomas. **Subjects & Methods:** The new formed BmK CT-Au DENPs before and after ^{131}I labeling were characterized in vitro and in vivo. The binding affinity of BmK CT-Au DENPs to C6 glioma cells was evaluated by flow cytometry and confocal microscopy experiment. To explore the imaging ability of ^{131}I -BmK CT-Au DENPs, SPECT/CT was performed in C6 glioma cells and subcutaneous glioma-bearing nude mice at 0.5 h, 2 h, 4 h, 6 h, 8 h, and 16 h postinjection. The targeted radionuclide therapeutic effect of ^{131}I -BmK CT-Au DENPs was first assessed in C6 glioma cells via CCK8 assay and then further evaluated in subcutaneous glioma-bearing nude mice. **Results:** Flow cytometry and confocal microscopy experiment both proved that BmK CT-Au DENPs has a relatively high cellular uptake in C6 gliomas. ^{131}I -BmK CT-Au DENPs displayed excellent SPECT/CT imaging effect in C6 cells and subcutaneous glioma-bearing nude mice at 8 h postinjection. Moreover, CCK-8 assay showed that C6 glioma cells growth was obvious inhibited by ^{131}I -BmK CT-Au DENPs, which was further verified in glioma bearing nude mice. **Discussion/Conclusion:** The new designed radiolabeled multifunctional dendrimer, ^{131}I -BmK CT-Au DENPs, has a great potential to be used for SPECT/CT imaging and targeted radiotherapy of gliomas.

EP-0934

Developing Radiolabeled Neuropeptide Nanoconstructs as Potential Theranostic Agents

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Purpose/Introduction: The over-expression of neuropeptide Y_1 -receptors in human breast cancer leads to a potential application of selective neuropeptide Y (NPY) Y_1 -receptor ligands as a new generation of agents for cancer diagnosis and therapy. NPY-derived Y_1 -receptor ligands, e.g., $^{99\text{m}}\text{Tc}(\text{core})^{3+}$ -(N⁶His-ac)-labeled-[Phe⁷,Pro³⁴]NPY have been previously developed and investigated *in vitro* and *in vivo*. The preclinical and first clinical data by using these NPY derivatives in human breast cancer patients produced very promising results with remarkable peptide uptake in metastases spread in other organs, originating from the tumor. These novel findings clearly indicate that the overexpression of the Y_1 receptor in human breast cancers offers a unique possibility for tumor targeting by using NPY-derived Y_1 -receptor ligands. These excellent results prompted us to develop peptide-based gold and silver nanoparticles, thus ultimately, resulting highly specific radiolabeled nanoconstructs decorated with DOTA-NPY molecules to act as 'nanotheranostics'. **Subjects & Methods:** For this purpose, we produced highly stable gold and silver nanoparticles (NPs) using arabinoxylan (AX) from ispaghula (*Plantago ovata*) seed husk. The NPs were synthesized by stirring a mixture of AX and $\text{HAuCl}_4 \cdot \text{H}_2\text{O}$ or

AgNO_3 , separately, below 100°C for less than an hour, where AX worked as the reducing and the stabilizing agent. The synthesized NPs were characterized by various analytical techniques, and coupled with DOTA-NPY Y_1 -specific derivatives, thus resulting in "nanoconstructs". *In vivo* uptake of radiolabeled ^{198}Au -labeled nanoconstructs was studied in various organs of normal rabbits after regular time intervals. **Results:** The particle size was (for silver: 5–20 nm and gold: 8–30 nm) found to be dependent on pH, temperature, reaction time and concentrations of AX and the metal salts used. The biodistribution data showed a slower uptake with a significantly higher retention time, thus leading to sufficient renal excretion to allow absorption of the labeled compound into the tumor, with ultimately fast body clearance to avoid unspecific peptide accumulation. These potential features of NPY nanoconstructs make them strong candidates for theranostic applications after radiolabeling with ^{68}Ga for PET imaging studies and radionuclide therapy after labeling with beta or alpha-emitting radionuclides (study in progress). **Discussion/Conclusion:** This approach might be further extended to a tumor-specific targeting by using NPY derivatives for carrier of chemotherapeutic agents and might not be limited to breast cancer, because Y -receptor expression has been identified in other tumors, such as neuroblastoma, glioblastoma, ovarian adenocarcinoma, gastrointestinal stromal tumor, neuroblastomas, renal cell carcinoma, and pheochromocytoma, thus ultimately, used as a future tool for Peptide Receptor Radionuclide Therapy (PRRT).

EP-0935

Comparison Of "In Vitro" Chemotaxis Between Labelled Leucocytes With Non-Stabilized And Stabilized $^{99\text{m}}\text{Tc}$ -HMPAO

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Aim: The use of non-stabilized $^{99\text{m}}\text{Tc}$ -HMPAO is well established to label leucocytes, although the radiopharmaceutical short stability limits its optimal use. HMPAO stabilization with CoCl_2 could be an approach if leucocyte function is preserved. This study evaluated "in vitro" the chemotaxis using HMPAO stabilized. **Material and Method:** Three aliquots of leucocyte-rich plasma (LRP) from 45 mL of 14 blood donors were processed: 1) Unlabelled, 2) Labelled with $^{99\text{m}}\text{Tc}$ -HMPAO and 3) Labeled with $^{99\text{m}}\text{Tc}$ -HMPAO stabilized. A chemotaxis assay (Migrate[®]) was performed. The chemoattractant fMLP was placed into the wells of a multiwell plate in parallel with PBS as a negative control. Afterwards, cell-culture inserts with $3\mu\text{m}$ pores in their membranes were placed into these wells and LRP were added. The plate was incubated at 37°C . During the incubation period the leucocytes migrated through the pores. The inserts were removed and the cell suspension from each well was added

to tubes. In addition, part of the unstimulated, non-migrated cells from the LRP of the PBS-Insert (negative control) were dispensed in another tube (L-Selectin control). All cell suspensions were labelled with (FITC)-anti-L-Selectin-antibody and counting beads. Vital DNA staining was added. It was analysed using a flow cytometry the expression of the adhesion molecule L-Selectin as well as shape change. Once the leukocytes become activated, change its cellular shape, enlarge and shed L-Selectin. The percent of activated leucocytes was calculated and cell size measured as mean Forward Scatter signal (FSC) in migrated and not migrated cells of each aliquot. **Results:** The percent of activated leucocytes in negative, positive and L-Selectin controls were respectively: $62.0 \pm 16.9\%$, $85.2 \pm 6.7\%$ and $31.9 \pm 12.2\%$ (unlabelled); $66.5 \pm 7.8\%$, $85.5 \pm 5.2\%$ and $32.2 \pm 8.8\%$ (^{99m}Tc -HMPAO); $66.0 \pm 7.6\%$, $86.2 \pm 4.8\%$ and $33.8 \pm 14.4\%$ (^{99m}Tc -HMPAO stabilized). All three groups presented statistically significant differences between the negative and positive control (Wilcoxon test, $p < 0.01$). The FSC mean values in negative, positive and L-Selectin controls (leucocytes have not migrated so they are size control) were respectively: 360 ± 18 , 390 ± 43 and 341 ± 29 (unlabelled); 366 ± 17 , 393 ± 47 and 337 ± 29 (^{99m}Tc -HMPAO) and 365 ± 17 , 403 ± 62 and 327 ± 45 (^{99m}Tc -HMPAO stabilized). Comparing FSC in L-Selectin control with negative and positive control FSC values it is demonstrated that the leukocytes have migrated because of they have been activated so they enlarge. There are statistically significant differences between groups (Wilcoxon test, $p < 0.001$). **Conclusion:** All three samples have more activated leucocytes in the positive control, according to an increase of the percent of activated leucocytes. Using ^{99m}Tc -HMPAO stabilized with CoCl_2 for labelling leucocytes does not modify their chemotactic capacity.

EP-0936

In Vitro and In vivo evaluation of a lyophilized kit formulation for labeling of HER-2 Targeting peptide containing tripeptide sequence as N_3S with ^{99m}Tc

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Introduction: Recent years have witnessed an increasing interest in radiolabelled peptides for nuclear medicine applications. The high expression of the human epidermal growth factor receptor 2 (HER2) and the accessibility of its extracellular domain make it an ideal target for the targeted delivery of anti-tumor drugs as well as imaging agents. In this study, the heptapeptide leucine-threonine-valine-serine-proline-tryptophan-tyrosine (LTVSPWY) as a new small peptide for an anti-HER2 target was labeled by incorporating ^{99m}Tc to the cysteine-based CSSS (Cys-Ser-Ser-Ser) linked to this peptide. **Subjects & Methods:** Radiolabeling studies were performed using two-vial formulation. First, ^{99m}Tc was allowed to react with sodium gluconate as ligand exchange in the presence of SnCl_2 and bicarbonate buffer in 10 min at room temperature to afford the ^{99m}Tc -gluconate intermediate. An aliquot of this solution was added to an aqueous solution containing peptide and ammonium acetate buffer. The radiolabeled mixture was incubated at 37°C for 30

min. **Results:** Radiolabeled peptide was labeled with ^{99m}Tc with more than 99% efficiency and showed favorable stability in solution and serum. The HER2 binding affinities the radiolabeled peptides were inhibited up to 60% by the unlabeled peptide, as well as with trastuzumab antibody. We observed nanomolar binding affinities for radiolabeled peptide. high kidney uptake and subsequent rapid clearance resulted in a faster washout of the radiolabeled peptide from non-targeted organs, a critical parameter for high contrast in tumor imaging. **Discussion:** This small new peptide was selectively targeted to the HER2 receptor, and introduction of a serine residue into the chelator improved the pharmacokinetics of ^{99m}Tc labeled LTVSPWY for clear tumor imaging in animals.

EP-0937

Design and Synthesis of Polymer Coated Gold Nanoparticles, AuPEI-Glc- ^{99m}Tc , for Targeted in vivo Imaging

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Aim: The need to develop best targeted, disease suited and, also, accessible radiopharmaceuticals, rest a main permanent concern in nuclear imaging precision medicine. The present study (acknowledgements for financial support from the H2020 WIDESPREAD 2-2014: ERA Chairs Project no. 667387: SupraChem Lab, ERA Chair initiative) is a first step in a work that aims to develop a hybrid ^{99m}Tc SPECT-MRI radiotracer as molecular architecture assembled in a nanoparticle shape, comprising of a magnetic core, a region involved in radioisotope entrapment, the recognition molecule, and a polymeric sequence providing biocompatibility. Glucosamine (Glc) units, grafted onto the polymer surface, are expected to accumulate in high-glucose-consuming areas, due to the steric hindrance caused by the complex architectures, being a vector molecule for these areas. **Materials and Methods:** Gold nanoparticles (AuNPs) were synthesized and stabilized through thiol-terminated PEG. Both polyethylenimine (PEI) coating and Glc functionalization were performed using a bifunctional linker (PEG diglycidyl ether). The oxirane ring opening and primary amine substitution were established in FTIR spectroscopy by disappearance of 914, 1585 and 3300 cm^{-1} bands. The structure of intermediate compounds was confirmed by mass spectrometry, the m/z values indicating their molecular weight. The particle size and morphology were investigated using UV-Vis, DLS and TEM techniques. ^{99m}Tc was eluted from a $^{99}\text{Mo}/^{99m}\text{Tc}$ Drytec Generator system as $\text{Na}^{+99m}\text{TcO}_4^-$, then reduced with sodium borohydride (NaBH_4) or stannous chloride (SnCl_2), for radiolabeling. Radiolabeling efficiency was assessed using instant thin layer chromatography (ITLC). **Results:** Macromolecular structures exceeding positive charge

on their surface have been achieved, with particle size ranging between 20 and 30 nm. The radiolabeling took place varying the concentration of reducing agents (12.5 - 100 mg/mL) and the $\text{Na}^{99\text{m}}\text{TcO}_4^-$ activity (1-5 mCi). The complex between $[\text{TcO}_4^-]$ and the highly positive charged PEI was confirmed by decreasing the zeta potential from +4 mV up to -60 mV after 2h. A slightly particle aggregation subsequently occurred as TEM images revealed. The investigated systems $\text{AuPEI-}^{99\text{m}}\text{Tc}$ and $\text{AuPEI-Glc-}^{99\text{m}}\text{Tc}$ are stable longer than 6 hours, although the complexation was reversible after 24 hours, while zeta potential returned to the initial values. A 95% radiolabeling yield was achieved for 12.5% NaBH_4 ; SnCl_2 has been also considered for experiments due to its known higher biocompatibility. **Conclusions:** A macromolecular vector able of stably $^{99\text{m}}\text{Tc}$ binding was synthesized and characterized, $\text{AuPEI-Glc-}^{99\text{m}}\text{Tc}$ complex, with characteristics suited for tumor glucose metabolism visualization, intended to be a starting point for a structural-functional hybrid accessible radiopharmaceutical.

EP-0938

Synthesis And Evaluation Of Evans Blue Derived RGD Peptide as A Carcinoma Therapeutic Agent

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Cyclic peptides c(RGDfK) showed high binding affinity for integrin $\alpha\beta_3$. Radiolabeled RGD peptides that are integrin specific can be used for integrin-targeted radionuclide therapy. Thus, the problem is that the cyclic RGD Peptide are high radioactivity accumulation in liver and kidney, which may limit the imaging potential of cyclic RGD peptide tracers in tumors. Evans blue is an azo dye that has a very high affinity for serum albumin. To improve the pharmacodynamics profile of cRGDfK and molecular imaging agents by conjugated with truncated Evans blue. The conjugate was denoted as DOTA-EB-RGD. The DOTA-EB-RGD (from NIH Xiaoyuan Chen) were prepared by linking a truncated Evans blue to the lysine and attaching the DOTA chelator to the α -amine, attaching a maleimide to the ϵ -amine. Finally, attaching thiolated cRGDfK peptide to the maleimide. The DOTA-EB-RGD (30-40 μg) was labeled with $\sim 6\text{mCi}$ InCl_3 (from INER) in sodium acetate (NaOAc) with different pH values (5.0-6.0) at 95°C within 15mins. After labeling with In-111 , quality control was performed by RP-HPLC and radio thin layer chromatography. Radiochemical purity was analyzed in the radio-TLC scanner with a 0.1 N sodium citrate solution as the mobile phase. The R_f of free In-111 was approximately 0.95, and the R_f of $^{111}\text{In-DOTA-EB-RGD}$ was approximately 0.05. The Radiochemical purity of the $^{111}\text{In-DOTA-EB-RGD}$ was assayed by HPLC (95.59%) and TLC (98.68%). U87MG tumor bearing mice were intravenously injected with $^{111}\text{In-DOTA-EB-RGD}$. Scans were performed 1, 2, 4, 24, 48 and 72 h after the administration. $^{111}\text{In-DOTA-EB-RGD}$ showed high tumor uptake at all time points (13.00, 15.35, 20.58, 22.74, 23.48 and 22.20%ID/g at 1, 4, 24, 48 and 72h after injection). A truncated Evans blue that binds to albumin and prolongs half-life in the blood. DOTA-EB-RGD improving contrast with diagnostic imaging agents, improving effective radiotherapy of cRGDfK targeted tumors.

EP-0939

Labeling of a new bacterial peptide analogue by $^{99\text{m}}\text{Tc}$ as scintigraphic imaging agent for abdominal infection

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Introduction: Microcins are antimicrobial peptides that produce by *E. coli*. The present study focuses on the preparation a new peptide radiopharmaceutical derived from microcin for diagnosis of infection foci in animal model. **Subjects & Methods:** An antibacterial peptide microcin derivative was constructed by standard Fmoc solid phase method and purified by semi preparative HPLC. The purified peptide indirectly labeled with $^{99\text{m}}\text{Tc}$ thorough bifunctional chelating agent conjugated to N-terminal of peptide. Radiochemical purity of labeled microcin derivative peptide was performed by RP-HPLC on C-18 column and ITLC on silica gel strips. In vitro stability of labeled peptide in human serum and binding to bacterial cell were investigated. The biodistribution studies were carried out in infected mice by $5-6 \times 10^8$ cfu/ml of *E. coli*. The detection of infection foci in Swiss mice was performed using scintigraphic imaging up 4 h post injection. **Results:** Radiochemical analysis revealed 98% radiolabeling was performed during 30 min. The amount of non-peptide related $^{99\text{m}}\text{Tc}$ -impurities that measured by ITLC did not exceed 3% of the total radioactivity. The labeled peptide was extremely stable for 24 h in aqueous solution. 50-60% of protein binding was occurred after incubation of labeled peptide in diluted human serum at 37°C . In vitro studies of binding showed more than 40% radioactivity bound to bacterial cells. A large portion of the labeled peptide in mice was excreted through the kidneys. The induced infection sites into left thigh muscles of mice were visualized by gamma camera within 1 h with after intravenously injection of 100 μl labeled peptide. **Conclusion:** The results showed that $^{99\text{m}}\text{Tc}$ -microcin peptide derivative could be a promising candidate as a targeting radiopharmaceutical for *E. coli* infection imaging in mice model and further investigation is on the way.

EP-0940

Radiolabeling and biodistribution study of engineered antibody-mimetic protein repebody with $^{99\text{m}}\text{Tc}$ for EGFR-expressing tumor imaging

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Recently, antibody-like scaffold proteins have received a great deal of interest in diagnosis and therapy applications. Since antibody-like scaffold proteins possess intrinsic features that are often required for tumor imaging and therapy, they have potential to be used as platforms for integrating imaging and therapeutic

functions. Intrinsic issues that are associated with therapeutic application of antibody-like scaffold proteins, particularly in cancer treatment, include an efficient and straightforward radiolabeling for understanding in vivo biodistribution and excretion route, and monitoring therapeutic responses. Herein, to investigate the biodistribution and blood clearance, antibody-like scaffold protein, repebody, was successfully radiolabeled with the $^{99m}\text{Tc}(\text{OH})_2(\text{CO})_3]^+$ (^{99m}Tc -tricarboxyl) by using a site-specific direct labeling method via hexahistidine-tag, which is a widely used for general purification of proteins with His-affinity chromatography. Repebody is antibody-like scaffold that consist of highly diverse leucine-rich repeat (LRR) modules, it has been constructed to bind to epidermal growth receptor (EGFR) for cancer therapy. For ^{99m}Tc labeling to repebody, we first prepared ^{99m}Tc -tricarboxyl precursor. Synthesis of ^{99m}Tc -tricarboxyl precursor achieved more than 90% yields. The result of radio-TLC, the Rf value for ^{99m}Tc -tricarboxyl was 0.0 and 0.3~0.4 using a saline and solvent mixture (methanol 99%, HCl 1%) as the eluent, respectively. And then, the repebody was radiolabeled with ^{99m}Tc -tricarboxyl at 37°C for 1 h. After radiolabeling, for remove unconjugated ^{99m}Tc -tricarboxyl, simple purification step was performed using 10 kDa cut-off filter. Radiochemical purity was determined by radio-TLC. The radiochemical purity of radiolabeled repebody with ^{99m}Tc (^{99m}Tc -repebody) was estimated to be greater than 99% and the specific activity was 925 MBq/mg. ^{99m}Tc -repebody was highly stable up to 24 h for both in vivo SPECT/CT and in vitro histidine challenge study. When we examined the whole-body distribution of ^{99m}Tc -repebody via SPECT/CT image analyses, especially after intravenous administration, ^{99m}Tc -repebody was shown to be preferentially presented in the kidney at early time point. Even after 6 h, the radioactivity in the kidney remained high compared to the surrounding tissue. This result indicates the main excretion route of ^{99m}Tc -repebody was through renal clearance. These biodistribution studies of repebody will be useful for development of therapy strategy along with their systemic information.

EP-0941

A simple modification of radioactive labelling leukocytes with ^{99m}Tc -HMPAO

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Introduction: Scintigraphy with labelled autologous white blood cells is used to detect suspected sites of acute inflammation or infection including also inflammatory bowel disease and fever of unknown origin- the most frequent indications to leukocyte scintigraphy. Several methods for in vitro and in vivo labelling of leukocytes have been proposed from 1990 still now. The methods differ for the volume of blood withdrawn, for the kind of cells to label, for the isotope used, for the pharmaceuticals used to carry the isotope. Aim: Demonstrate the effects of saline as a medium to resuspend white blood cells in the in vitro labelling of mixed leukocytes procedure. **Materials and Methods:** Procedure of radioactive labelling leukocytes includes some phases: collection of blood, isolation of mixed leukocytes, isolation of cell free plasma, labelling of leukocytes with ^{99m}Tc -HMPAO, quality control and reinjection. We

used the auxiliary material supplied with the kits for labelling. Our modification of labelling white blood cells takes saline as a medium to resuspend leukocytes. We identified the labelling efficiency of the radiopharmaceutical, the yields of radiolabelled leukocytes, final activity of leukocytes end final activity injected for each patient. **Results:** These results are based on our study group of 20 patients of plasma group and 19 patients of saline group, who were administered autologous leukocytes labelled with ^{99m}Tc -HMPAO. In plasma group the labelling efficiency of the radiopharmaceutical was 86.41 % +/- 3.38 %, the yields of radiolabelled leukocytes were 71.20 % +/- 5.68 %, final activity of leukocytes was 700 +/- 3.45 MBq and final activity injected was 580 +/- 3.82 % MBq. In saline group the labelling efficiency of the radiopharmaceutical was 87.21 % +/- 3.24 %, the yields of radiolabelled leukocytes were 70.40 % +/- 5.66 %, final activity of leukocytes was 690 +/- 3.25 MBq and final activity injected was 562 +/- 3.48 % MBq. **Conclusion:** Saline is an efficient medium to suspend and wash leukocytes. The using saline to resuspend and wash the cells during multiple in vitro labelling we can avoid the risk to exchange the plasma of the patients. Our long experience has shown that this modification provides leukocyte labelling efficiency high above the limit values. The results of our method seem to be functional.

EP-0942

The Using Of Glucose Labeled With Technetium-99m For Visualization Of Breast Cancer And Myocardial Imaging

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Purpose: to study possibility of using 1-thio-D-glucose labeled with ^{99m}Tc for breast cancer and myocardial imaging. **Materials and Method:** the study included 11 patients with stage T₁₋₄N₀₋₁M₀ breast cancer who underwent SPECT with « ^{99m}Tc -1-thio-D-glucose» for visualization of primary tumor and regional metastases. SPECT was performed 20 minutes after intravenous injection of 500 MBq of « ^{99m}Tc -1-thio-D-glucose» into a cubital vein opposite from the tumor side. In addition, the tumor / background index was calculated. Myocardium visualization possibility with « ^{99m}Tc -1-thio-D-glucose» was studied in rat hearts (10 Wistar male rats, 250-300g): 10 minutes after radiopharmaceutical injection heart was extracted and was evaluated in gamma ray well detector. All rats had not been fed during 12 hours before study. **Results:** the primary breast tumor was visualized in all patients. Sensitivity of SPECT with « ^{99m}Tc -1-thio-D-glucose» in the diagnosis of breast cancer was 100%. Metastases in regional lymph nodes were detected in 8 patients out of 10. Thus, the sensitivity of SPECT with « ^{99m}Tc -1-thio-D-glucose» in detecting regional metastases in breast cancer was 80%. The mean values of the index tumor / background were 3.91±0.2. The counts of gamma rays from rat hearts (pulses/sec) was not

significantly higher than background radiation. **Conclusion:** the present study demonstrated that «99mTc-1-thio-D-glucose» is a prospective radiopharmaceutical for the breast cancer visualization and not prospective for myocardium visualization without any previous influence to heart. This study has shown that SPECT with «99mTc-1-thio-D-glucose» can be one of the supplementing methods in detection of primary breast tumors and regional metastases.

EP-0943

PLGA nanoparticles for combined SPECT and 19F MRI in vivo cell tracking

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Introduction: Nuclear imaging techniques are particularly well-suited for in vivo tracking of intravenously injected cells, due to its high sensitivity, quantitative nature and whole-body imaging capability. However, spatial resolution is limited in clinical setting. Previously, we have developed PLGA-based nanoparticle (PLGA-np), containing 19F for MR imaging and different fluorescent dyes for optical imaging, which are suitable for clinical use. Here we describe the modification of these PLGA-nps for labelling with 111In to include SPECT in the multimodal tracking of cells in vivo, in a single agent. **Methods:** The production of PLGA-np has been described previously. For this study, we modified the PLGA-np with a dihydrazide or diamine cap (PLGA-np-AA). Subsequently, both normal and PLGA-np-AA, were conjugated with excess p-SCN-Bn-DTPA in MilliQ. After washing, the NPs were labelled with 3 MBq/mg of [111In]InCl₃ in either 0.5 M HEPES, MES or NH₄Ac buffer. Radiochemical yield was measured using a dose calibrator and radiochemical purity with instant iTLC. Peripheral blood mononuclear cells (PBMC) were incubated with concentrations of 2 MBq/mg or 4 MBq/mg [111In]In-DTPA-PLGA-np-AA (4 mg) overnight at culture conditions. Cells were harvested, washed, and radionuclide labelling was measured in a dose calibrator. A trypan blue staining was carried out for viability assay. **Results:** The results show specific radiolabelling of DTPA-PLGA-np-AA with 111In. Labelling efficiency in HEPES, MES, and NH₄Ac was 83%, 65%, and 97%, respectively. Labelling of the non-modified PLGA-np, had <10% radiochemical yield. After washing, radiochemical yield for HEPES, MES, and NH₄Ac was 70%, 50%, and more than 90%, respectively. After the last wash, radiochemical purity of all the samples exceeded 99%. Although the total radioactivity in the pellet progressively decreased during washing, iTLC of the supernatant demonstrated that this was due to manual disruption of the pellet; and not disintegration of the particle nor its conjugation. Labelling of the PBMCs with [111In]In-DTPA-PLGA was 116 KBq/10⁶ cells for the 2 MBq dose and 443 KBq/10⁶ cells for the 4 MBq dose. The viability assay indicated 92% cell survival for the 2 MBq dose and 89% cell survival for the 4 MBq dose. **Conclusions:** We have shown a specific radiolabelling of amine capped PLGA-np compared to normal PLGA-np. Furthermore, NH₄Ac buffer showed highest la-

belling efficiency. Preliminary results on PBMC labelling indicates sufficient labelling of cells for *in vivo* imaging. Importantly, overnight incubation of the cells with high dosage of radioactivity did not result in higher cell death.

EP-68

e-Poster Area

Preclinical and translational aspects, including radiopharmacy, radiochemistry and drug development -> Radiopharmacy, radiochemistry, drug development -> Radiopharmacy -> Radiopharmaceuticals - Therapy

EP-0944

Molecular targeting of various human tumor cell lines with 177Lu-octreotate

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Introduction: Somatostatin receptors are overexpressed on the cell surface in several types of neuroendocrine tumors (NETs). This overexpression offers the possibility of targeted diagnostics and treatment with radiolabeled high-affinity somatostatin analogues. Systemic treatment with ¹⁷⁷Lu-octreotate has shown encouraging results in gastroenteropancreatic NETs. Its potential needs to be investigated also in other tumor types, such as breast cancer and neuroblastoma. The aim of this study was therefore to determine the specific uptake of ¹⁷⁷Lu-octreotate in human cancer cell lines of different origin. **Materials and Methods:** Lung adenocarcinoma (h1975, h2228), neuroblastoma (CLB-BAR, IMR-32) and invasive breast carcinoma (BT474, MCF-7, MDA-MB-231, MDA-MB-361, T47D, ZR-75-1) cell lines were studied. The cells were incubated with two concentrations of ¹⁷⁷Lu-octreotate and harvested after 24h and/or 48h. To study non-specific binding, control groups were incubated with ¹⁷⁷Lu-octreotate and excess octreotide. After incubation, the amount of unbound, membrane-bound and internalized ¹⁷⁷Lu was measured by a gamma counter. **Results:** The highest binding and internalization after 24h was found in the neuroblastoma cell lines IMR-32 (58% internalized, 9.4% membrane-bound) and CLB-BAR (26% internalized, 3.4% membrane-bound). A majority of the breast cancer cell lines also showed specific uptake after 24h (e.g. 3.1% internalized, 0.5% membrane-bound in MDA-MB-361). Specific uptake was also seen after 48h in neuroblastoma cell lines IMR-32 (47% internalized, 30% membrane-bound) and CLB-BAR (36% internalized and 10.8% membrane-bound). No specific binding was seen in lung adenocarcinoma cell lines. Corresponding values in primary cell culture from two gastrointestinal stromal tumors was 5.8-8.0% internalized and 0.45-

0.99% membrane-bound. The results suggest the potential of ^{177}Lu -octreotate as a treatment alternative for neuroblastoma and some breast cancer cell types. **Conclusions:** These encouraging results demonstrating a high specific binding and internalization of ^{177}Lu -octreotate in various tumor cell lines indicate that the use of molecular targeting with ^{177}Lu -octreotate for diagnostics and therapy could be applied for a broader range of tumor types than currently used.

EP-0945

PET Imaging Biomarkers of Anti-HER-1 therapy in Esophageal Squamous Cell Carcinoma Xenografted Model

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Purpose: Epidermal growth factor receptor (EGFR, HER-1) is overexpressed in esophageal squamous cell carcinoma (ESCC) patients and it is considered as a proper molecular target for diagnosis and targeted therapy. This study evaluated the usefulness of PET imaging biomarkers with ^{64}Cu -PCTA-cetuximab immuno-PET imaging for measuring of *in vivo* EGFR level and monitoring therapeutic efficacy, and ^{18}F FDG-PET imaging for determining glucose metabolism against anti-HER-1 immunotherapy in ESCC xenograft models. **Methods:** EGFR expressing TE-4 and TE-8 ESCC cells were implanted in BALB/c athymic female mice. *In vivo* EGFR status with ^{64}Cu -PCTA-cetuximab immuno-PET and glucose metabolism with ^{18}F FDG-PET were evaluated before and after cetuximab treatment. EGFR expression and therapeutic response by imaging biomarkers were analyzed and compared with western blot and immunohistochemical staining data. **Results:** EGFR expression on TE-8 cells is higher than that on TE-4 cells, evaluated by flow cytometry and western blot. TE-4 and TE-8 tumors were clearly visualized by ^{64}Cu -PCTA-cetuximab PET imaging, and the TE-8 tumors showed 2.6-fold higher uptake than the TE-4 tumors. Tumor volumes were markedly reduced by cetuximab treatment in TE-8 tumor ($92.5 \pm 5.9\%$ reduction), but TE-4 tumor refractory to cetuximab treatment. After cetuximab treatment, SUVs in ^{64}Cu -PCTA-cetuximab (65.7%) and ^{18}F FDG (62.4%) PET images were statistically significant reduced in TE-8 tumors, but not in TE-4 tumors. ^{64}Cu -PCTA-cetuximab immuno-PET images and FDG uptake patterns were well correlated with EGFR and pAkt western blot, and TUNEL and pAKT immunohistochemical staining results. **Conclusion:** ^{64}Cu -PCTA-cetuximab immuno-PET imaging has a potential for determining EGFR expression level and monitoring therapeutic response by anti-HER1 therapy. ^{18}F FDG-PET imaging is also attractive for monitoring efficacy of anti-HER1 therapy. Therefore, those PET imaging biomarkers may be useful for selecting patient that express target molecules and monitoring therapeutic efficacy of EGFR targeted therapy in ESCC patients.

EP-0946

Pharmacodynamic Immuno-PET imaging of HSP90 inhibitor on HER2 expression with ^{64}Cu -NOTA-Trastuzumab

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Purpose: Immuno-PET imaging could provide non-invasively whole body information on target expression. This study aimed to prepare ^{64}Cu labeled trastuzumab for evaluating HER2 expression on tumors and determining pharmacodynamic change of HER2 expression on breast tumors by heat shock protein 90 (HSP90) inhibitor treatment. **Methods:** Trastuzumab were conjugated with NOTA and radiolabeled with ^{64}Cu at room temperature. Serum stability and affinity of ^{64}Cu -NOTA-trastuzumab were performed. Change of HER2 expression by HSP90 inhibitor, 17-DMAG was evaluated by western blot, flow cytometry and *in vitro* cell binding assay of ^{64}Cu -NOTA-trastuzumab. Immuno-PET imaging and biodistribution of ^{64}Cu -NOTA-trastuzumab were done with BT-474 (HER2 positive) and MDA-MB-231 (HER2 negative) subcutaneous tumor models. HER2 expression by 17-DMAG treatment was evaluated by ^{64}Cu -NOTA-trastuzumab immuno-PET imaging in BT-474 xenograft model. Additionally, ^{18}F FDG-PET images also obtained at 1 and 8 day post treatment. **Results:** ^{64}Cu -NOTA-trastuzumab radiolabeling accomplished in high radiochemical yield (>99%) and specific activity with above 2 mCi/mg. *In vitro* assays demonstrated >99% radiochemical purity with a affinity of 1.95 ± 0.21 nM and a high serum stability of 99%. There was good correlation between flow cytometric data and cell binding assay of ^{64}Cu -NOTA-trastuzumab. PET imaging and biodistribution data showed ^{64}Cu -NOTA-trastuzumab selectively accumulated in BT-474 tumors, compared to MDA-MB-231 tumors. BT-474 tumor volumes were decreased by 17-DMAG treatment. ^{64}Cu -NOTA-trastuzumab uptake markedly reduced in BT-474 tumor at 1 day and 8 day post-treatment of 17-DMAG. ^{18}F FDG uptake in BT-474 tumor reduced at 1 day post-treatment, but it recovered to ^{18}F FDG uptake level of control tumors at 8 day post-treatment. **Conclusion:** These results indicate that ^{64}Cu -NOTA-trastuzumab provides non-invasive, quantitative information on HER2 expression on breast tumor model and also has the potential for evaluating pharmacodynamic change of HER2 expression by HSP90 inhibitor treatment.

EP-0948

Production and quality control of radioactive microspheres of resin-rhenium 186/188 for treatment of local tumors

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Introduction: Intravenous injection of radioactive microparticles is one of the effective methods of radiotherapy of tumors such as pulmonary. These microparticles can be polymers, resins or albumins that have compound with a suitable radionuclide. In this study, the construction of a microsphere complex of IRA-68 amberlite resin with rhenium 186/188 was investigated. **Methods:** For preparation the compound of resin and rhenium, first HReO_4 acid was prepared. Then the various amount parameter including reaction time and rhenium oxide concentration to achieve the maximum absorption of rhenium by microsphere resin were studied and analyzed by ICP and scanning electron microscopy. In all states, the pH of the compound was 7-6. After

preparation the compound was irradiated with thermal neutron flux of $3.5 \times 10^{13} \text{ n / s.cm}^2$ for 5 hours. Total activity and purity of radionuclide were evaluated using HPGe detector. Radiochemical purity was checked by ITLC system with normal saline as mobile phase. The stability of the compound in the human serum with ratio of 1:10 was also assessed. SEM and EDX analysis were also prepared from the irradiated compound after two half-life periods. **Results:** Rhenium adsorption by microsphere resin was investigated in different reaction times and different concentrations of rhenium oxide. The absorption percentage with the results obtained from ICP indicates that the highest adsorption rate is about 95% at the concentration of 20ppm of rhenium oxide and after 3 hours. The images produced by the scanning electron microscope show microspheres particles as uniform spheres. After irradiation of the compound, images of the electron microscope showed that the spherical structure of the particles does not change after exposure to the neutron flux and particles have a uniform shape. EDX analysis also shows the amount of rhenium per microsphere particle as atomic percent and weight percent. Radiochemical purity of the resin-rhenium microspheres composition by the ITLC system at room temperature and pH = 7 was about 93%. The stability of the compound at room temperature and in the human serum at 37°C were 92% and 93% after 24h and 85% and 76% after 72h respectively. **Conclusion:** The results of this project have indicated the successful preparation of compound IRA-68 amberlite resin with rhenium that retained uniformly after irradiation by thermal neutron and exhibited a high stability. These results promise an appropriate application of this compound for radiotherapy and imaging for local tumor. Keywords: Radioembolization, Microspheres, IRA-68 Amberlite Resin, Rhenium 186/188

EP-0949

Indium-111 afterloading of preformed EGF containing liposomes for molecularly targeted radionuclide delivery via ultrasound induced cavitation

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Introduction: The addition of nuclear localising sequence peptides to radiolabelled carrier molecules enhances nuclear uptake. However, Peptide or protein based drugs often have unfavourable circulation kinetics and are highly susceptible to degradation and elimination by local enzymes. Liposome nanoparticles consist of a phospholipid bilayer structure which can encapsulate a chemotherapeutic payload. Such encapsulation can improve the pharmacokinetic profile of a therapeutic. However, enhancing the circulation kinetics does not necessarily enhance tumour uptake of the therapeutic. One promising method for targeted therapeutic delivery is through the use of ultrasound, a longitudinal pressure wave of frequency >20 kHz. Ultrasound can be efficiently delivered through the body and localised to sub-millimetre tissue domains. Liposomes have been previously shown to crack and release their therapeutic

payload upon the application of ultrasound. **Aim:** The aim of this proposal is to develop a clinically relevant method of loading ¹¹¹In-DTPA-hEGF into liposomes which can be released at the target site via externally applied ultrasound. **Methods:** hEGF-DTPA was created and passively loaded into liposomes. Loading efficiency was analysed via High Pressure Liquid Chromatography (HPLC). Liposomes were then loaded with indium via incubation with indium chloride for 1 hour followed by loading efficiency analysis by thin layer chromatography. For therapeutic efficacy liposomes were incubated with an EGFR positive cell (468) and an EGFR negative cell line (MCF7) followed by application of ultrasound. Cells were then seeded in 6 well plates and colony formation was analysed 14 days later along with all controls. **Results:** Liposome size was approximately 200 nm. Protein loaded liposomes had a 93 % loading efficiency for Indium encapsulation whereas empty liposomes only loaded 34 % of the Indium. Clonogenesis results revealed that the greatest effect was on an EGFR expressing cell line after exposure to ¹¹¹In-hEGF-DTPA loaded liposomes, sonovue microbubbles and ultrasound were applied in combination relative to all controls. **Conclusion:** A protein loaded liposome has been developed which loaded Indium in an active process within one hour. The liposomes had high binding efficiency for indium imitating techniques currently used in radiopharmacies. The liposome is ultrasound sensitive and was shown to crack upon application of ultrasound. A biodistribution has been obtained and a therapeutic study has now been planned. This technology can be utilised for ultrasound targeted delivery of nano-encapsulated radiotherapeutics to tumours with site specific delivery and no side effects to healthy tissue.

EP-0950

Fabrication of bio-degradable chitosan microspheres containing Dy-166/HO-166 for an in vivo generator system

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Aim: Microspheres (MS) containing radioactive ¹⁶⁶Ho are promising radiopharmaceuticals as an alternative approach to ⁹⁰Y-glass microspheres to treat of liver malignancies owing to its high-β radiation energy. In this research, we will present here the preparation of Chitosan microsphere containing ¹⁶⁶Dy as parent nuclide for treatment of liver tumor through a ¹⁶⁶Dy/¹⁶⁶Ho *in vivo* generator system. We also present here separation of ¹⁶⁶Dy and ¹⁶⁶Ho and show the absorption and release profile of ¹⁶⁶Dy from microspheres. **Materials and Methods:** Chitosan MS were prepared by W/O emulsion technique. Chitosan solution dissolved in itaconic-acid were added into the paraffin oil with the addition of an emulsifier. After the W/O emulsion was formed, glutaraldehyde saturated toluene as a cross linking agent was slowly dropped into the mixture and stirred for 2.5 hr until a brown precipitate formed. The obtained MS were washed 3 times with D.W and hexane, consecutively. 30 μl of DyCl₃ solution was dropped into the MS and kept for 30 min. Then, the MS were washed with 1 ml of D.W. and separated by centrifugation at 1,500 rpm. The 500 μl of supernatant was diluted with 4.5 ml of D.W and Dy concentration in the supernatant was measured by

AAS. The MS absorbed Dy were dispersed in PBS and human serum for release test. The MS were incubated at 37 °C under constant shaking for 24, 48 and 168 h. The MS separated from the supernatant and the releasing percent were calculated using the Dy concentration in supernatant. **Results and Conclusion:** The synthetic MS have spherical shape and smooth surface. The average size of the MS is affected by stirring speed, concentration of emulsifier and crosslinking agent. Also, the size of the MS show an 8-fold increase in volume after absorption with water. The average absorption (%) of Dy into MS was $57.89\% \pm 2.41$ and the Dy in MS released about 6% in human serum and about 4% in PBS with a nearly similar value for each interval time. This would allow Dy in the MS to remain in the target tumor tissues and continuously induce tumor cell necrosis.

EP-0951

Comparative evaluation of carrier added and non carrier added Lu-177 for preparation of therapeutic doses of Lu-177 radiopharmaceuticals

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Aim: Targeted radionuclide therapy using Lu-177 radiopharmaceuticals has emerged as a potential modality for cancer treatment. The radiolabeling of the DOTA conjugates peptides with Lu-177 depends on the specific activity of the Lu-177 used, which further depends upon the route of production (direct vs indirect). The present study reflects upon the differences between the radiochemical yields, peptide to Lu-177 molar ratio, and stability of Lu-177-DOTA-peptides for carrier added and non-carrier added Lu-177. **Materials & Methods:** Carrier added Lu-177 was procured from BRIT, India and Non-Carrier added Lu-177 was imported in commercially available form. In-house manual radiolabeling of DOTA conjugated peptides including Octreotate, PSMA-617 and RGD (n= 10 batches for each) was done in the presence of acetate buffer containing gentisic acid at pH 5 (for carrier added Lu-177) and pH 4.5 for non carrier added Lu-177. Molar concentration of peptides was varied from 2:1 to 5:1 and reaction was allowed for 25 minutes (for carrier added Lu-177) and 60 minutes (for non carrier added Lu-177). Radiochemical yield and stability post purification (for radiochemical yield less than 90%) was assessed from radiochromatographs obtained from instant thin layer chromatography (ITLC). Whole-body gamma scintigraphy images were compared for both types of Lu-177-peptides to compare in-vivo stability. **Results:** Radiochemical yield (upto 99%) was obtained with carrier added Lu-177 having specific activity greater than 20 mCi/μg at peptide: Lu-177 molar ratio of 2.5:1, which accounted to using 200-250 μg DOTATATE for 200 mCi Lu-177 (SA: 20 mCi/ μg). PSMA could be radiolabeled with 99 % radiochemical yield at 2: 1 peptide:Lu-177, SA= 20 mCi/ μg which accounted to using 100μg DOTA-PSMA-617 for 150 mCi clinical dose preparation. DOTA-RGD (dimeric) could be radiolabeled at 5:1 peptide: Lu-177 ratio i.e 230 μg peptide for 100 mCi Lu-177. For Non-Carrier added Lu-177 (SA= 100 mCi/ μg), both DOTATATE and PSMA could be radiolabeled to achieve more than 95 % radiochemical

yield at peptide:Lu-177 molar ratio of 4:1 i.e 100 μg for 200 mCi of Lu-177, which is half the amount used to label same radioactivity of carrier added Lu-177. Lu-177 labeled peptides showed post preparation stability up to 6 hours with RCP 95% and above. **Conclusion:** Relatively similar radiochemical yield and in-vitro/in-vivo stability was observed for both carrier added and non-carrier added Lu-177. The peptide requirement however reduces to half with non carrier added Lu-177.

EP-69

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Data analysis -> Cardiology: data analysis and imaging systems

EP-0952

Quantifying the extent of abnormality in myocardial perfusion scans: intra-observer repeatability of a trainee and an experienced physician

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Aim: In myocardial perfusion scintigraphy the severity of ischemic heart disease is commonly expressed quantitatively as "small-moderate-large" or as summed stress score (SSS) or as percentage of the myocardium. This work investigates the intra-observer repeatability of a trainee and an experienced operator in the determination of the severity of ischemia. **Method:** Fifty consecutive stress myocardial perfusion scans were assessed twice, allowing a few days between the readings, and independently by a trainee and an experienced physician. Using an automated software program (Toolbox, Emory University), ischemia severity was expressed quantitatively as " SSS_{dev} " and also as percentage of abnormal myocardium (%myo). A 17-segment model was used to visually grade ischemia with " SSS_{obs} " and as "no ischemia" (<1), "small" (1-2 segments), "moderate" (3-4) and "large" (≥5) ischemic area. **Results:** In the trainee, Pearson's coefficient of correlation (r_s) and the Bland-Altman statistic (Mean(diff)±2SD) showed: SSS_{dev} $r_s=0.933$, $p<0.001$, -0.6 ± 6.2 , SSS_{obs} $r_s=0.924$, $p<0.001$, -0.8 ± 6.5 , %myo $r_s=0.968$, $p<0.001$, -0.8 ± 7.4 . In the experienced physician; SSS_{dev} $r_s=0.969$, $p<0.001$, -0.2 ± 4.2 , SSS_{obs} $r_s=0.984$, $p<0.001$, 0.0 ± 3.0 , %myo $r_s=0.981$, $p<0.001$, 0.7 ± 5.9 . In the clinically important zone of 10% extent of ischemia, the differences in measurements between the trainee and the experienced physician were up to 67% and 59% of the mean value, respectively, and the coefficient of variation was 47% and 42%, respectively. In grading visually ischemia in a semiquantitative manner: **Conclusion:** (1) The repeatability in quantifying ischemia with an automated software program is not superior to visual semiquantitative assessment, it offers no advantage in a trainee as compared with an experienced physician and it is very problematic in the clinically important zone of 10% extent of ischemia. (2) The standard semiquantitative grading system visually with a 17-segment model offers a high repeatability in both a trainee and an experienced physician.

EP-0953

Quantifying the extent of abnormality in myocardial perfusion scans: the agreement between a trainee and an experienced observer

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Aim: In myocardial perfusion scintigraphy the severity of ischemia can be expressed as “small-moderate-large abnormality” or as summed stress score (SSS) or as percentage of abnormal myocardium. This work investigates the agreement between a trainee and an experienced observer in grading the severity of ischemia.

Method: Fifty consecutive stress myocardial perfusion scans were assessed twice, allowing a few days between the readings, and independently by a trainee and an experienced physician. Using an automated software program (Toolbox, Emory University), ischemia severity was expressed quantitatively as “SSS_{dev}” and also as percentage of abnormal myocardium (%myo). A 17-segment model was used to visually grade ischemia with “SSS_{obs}” and as “no ischemia” (<1), “small” (1-2 segments), “moderate” (3-4) and “large” (≥5) ischemic area. The average of the two measurements or assessments of every variable (or observer as indicated) was entered in analysis. **Results:** Pearson's coefficient of variation (r_s) and the Bland-Altman statistic (Mean(diff)±2SD) showed: SSS_{dev} $r_s=0.960$, $p<0.001$, 1.1 ± 4.6 SSS_{obs} $r_s=0.933$, $p<0.001$, 1.8 ± 5.8 %myo $r_s=0.968$, $p<0.001$, 0.4 ± 7.5 . In the clinically critical zone of extent of ischemia 5-15%, the differences of measurements was up to 96% of the mean value and the coefficient of variation 67%. Kappa statistic of the semiquantitative assessment of ischemia visually: Among cases with no or small area of ischemia in visual semiquantitative assessment, 38% and 100%, respectively, had >10% extent of ischemia in automated software analysis (average of observers). **Conclusion:** (1) In assessing the severity of ischemia, although the inter-observer agreement appears to improve by automated software analysis, this is largely due to a systematic overestimation of ischemia on trainee's visual assessment. (2) The measurement of the percentage of ischemia with automated software analysis results in overestimation of the abnormality in cases with no or limited findings on visual assessment, whereas in the clinically important zone of 10% extent of ischemia the inter-observer agreement is highly problematic.

EP-70

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Data analysis -> Data analysis and management

EP-0954

Development of new dedicated SPECT image analysis software

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Purpose: In this study, our final aim is to design a practical and reproducible technique for measuring volume and absorbed

dose of different organs and tumors. In the current study 3 different thresholding methods were applied for object extraction.

Subjects& Methods: The proposed technique follows different schemes to determine threshold. The first one consisted of different steps as follows: 1. Defining ROI by user from a 2D slice. 2. Object's border extraction using an optimal threshold. A threshold K was selected for each slice based on the between class variance maximization. 3. Attribute the pixels higher than threshold to the object and ignore the remaining pixels. The second one considers a complete range of [0-100] percent of maximum intensity as threshold. In the last scheme, the threshold was selected by user. After object's border extraction, object's volume and absorbed dose were determined. The technique was tested for two different activity ranges. **Results:** Obtained accuracies for activities lower than 2 mCi were 60.2%, 44.7% and 42.4% for 3 different previously mentioned schemes respectively. For activities higher than 2 mCi accuracies were 96%, 92.8% and 92.8% respectively. **Conclusion:** Based on the obtained results it can be concluded that accuracy greatly improved for activities higher than 2 mCi. On the other hand first technique which aims to maximize between class variance provided the best result. This technique can be extended for clinical study in order to measure volume and absorbed dose for different organs such as renal, thyroid, spleen and etc. **Keywords:** SPECT, activity measurement, volume measurement

EP-0955

Assessment of the Change in Normal Tissue Distribution of the (68)Ga-PSMA in Normal Tissues in Patients Underwent PET/CT for Metastatic Prostate Cancer.

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Aim: The prostate-specific membrane antigen(PSMA) is not specific to the prostate gland and accumulation of PSMA-ligands is also observed in non-tumorous normal tissues, such as lacrimal gland, salivary glands, mediastinal blood pool, liver, spleen, kidneys, intestines, bone marrow and urinary bladder. The purpose of the study; we retrospectively evaluated change of distribution of the radiolabeled PSMA-ligand Ga-68-PSMA-11 in normal tissues in relation to tumor load in patients who underwent PET/CT for metastatic prostate cancer(PC). **Methods:** A total of 187 consecutive patients with PC who underwent (68)Ga-PSMA-PET/CT between July 2017 and March 2018 were evaluated retrospectively. Mean patient age was 70.3 ± 8.4 years, mean administered activity was 150.2 ± 39.6 MBq. 68Ga-PSMA-11 was prepared using a fully automated radiopharmaceutical synthesis device based on a modular concept. Radiochemical purity, as determined by high performance liquid chromatography, exceeded 95% in all cases. Circular regions of interest(ROI) was drawn for lacrimal gland, parotid gland, submandibular gland, mediastinal blood pool, liver, spleen, kidneys, bone marrow, intestine, urinary bladder and prostate gland. SUVmax was calculated by measuring the maximal concentration of the labeled tracer in the ROI. Patients were examined in 3 groups according to (68)Ga-PSMA expression. 1-Normal(68Ga PSMA negative),

2-Local (prostate gland and/or pelvic lymph node involvement), 3-Metastatic (disseminated metastases). Distribution of PSMA in between groups was evaluated by t-test in independent groups **Results:** (68)Ga-PSMA-PET/CT imaging showed normal PSMA distribution in 51 patients, local disease in 80 patients and metastatic disease in 56 patients. Mean SUV max values of lacrimal gland, parotid gland, submandibular gland, mediastinal blood pool, liver, spleen, kidneys, urinary bladder, intestine, bone marrow, and prostate gland were 11.7, 21.5, 20.8, 3.5, 8.1, 9.4, 57.1, 22.9, 11.4, 3.5 and 4.4 respectively in normal group (PSMA negative); 11.2, 20.05, 20.4, 3.79, 8.3, 9.45, 59.7, 17.9, 13.6, 2.9 and 15.7 respectively in local disease group and 9.8, 16.7, 16.4, 3.5, 7.5, 8.5, 48.4, 20.6, 10.8, 2.7, 16.2 and 17.7 respectively in metastatic disease group. Mean SUVmax values of lacrimal glands, parotis, submandibular glands and kidney were significantly reduced in PSMA positive metastatic group compared to PSMA negative normal group. **Conclusion:** In our study, the mean SUVmax value of (68)Ga-PSMA in metastatic PC showed a significant decrease in the lacrimal glands, parotid, submandibular glands and kidney in relation to tumor burden. Thus, it is predicted that the radiation exposure of these organs, which have high SUV value during the lutetium treatment, will be reduced.

EP-0956

A method for determining pharmacokinetic population parameters

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Aim: Prior knowledge about the pharmacokinetics of a patient population is of great importance, e.g. for therapy optimization in nuclear medicine. For the identification of representative parameters and their variation within the patient population, there are various approaches, such as the “Standard Two-Stage” (STS) method (individual fitting with a subsequent averaging of the parameters). However, such methods, which are still often used in pharmaceutical industry, is not simply transferable to nuclear medicine data as these data sets generally consist of a low number of data points. Therefore, a method was developed where the number of adjustable parameters can be reduced by simultaneously fitting parameters to all data sets **Methods:** Population parameters were determined based on kidney time-activity data (In-111-DOTATATE) of 5 patients with neuroendocrine tumours (NETs). Firstly, the STS method was compared with the new method using shared adjusted parameters by taking a bi-exponential function as an example. The corrected Akaike information criterion (AICc) was used as model selection criterion. Subsequently, bi- and tri-exponential functions with different parameterisations were simultaneously fitted to the biokinetic data and the calculated AICc weights were compared. The AICc weight is the probability that the model is best supported by the data among all investigated models. **Results:** For the bi-exponential function, the method using shared adjusted parameters was best supported by the data with an AICc weight of 100% (STS method 0%). The ratio of measured data points to adjust-

able parameters increased from 25/20 (STS method) to 25/12. Analyses revealed that tri-exponential functions with shared adjusted parameters (e.g. transfer rates) are preferred compared to bi-exponential functions (AICc weight of 100% to 0%) in all investigated cases. **Conclusion:** The described method for the determination of population values reduces the number of adjustable parameters by suitable parameterisations, which are enabled by simultaneous regression. Furthermore, the new method offers the possibility to analyse more complex models, which cannot be implemented in the STS method (number of data points < number of parameters to be adjusted). The potential to calculate and take into account intra- and interindividual covariances of the patient's fit parameters can also be of advantage.

EP-0957

Prediction of metastasis in Osteosarcoma Using ¹⁸F-FDG PET image deep learning

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Objectives: Osteosarcoma is the most common malignant bone tumor. It is known that about 15-20% of patients metastasis into the lung mostly, and its prognosis remains poor with an event free survival rate of only 20% in five years approximately. Therefore, the prediction of metastasis is very important approaches before the neoadjuvant chemotherapy. The aim of this study was to predict the metastasis of osteosarcoma patients using ¹⁸F-FDG PET image machine learning approaches. **Methods:** The retrospective study was a conducted in a cohort of fifty nine osteosarcoma patients. They were categorized two groups (metastasis patient and non-metastasis patients). ¹⁸F-FDG PET data were acquired in PET/CT scanner (Biograph 6 PET/CT scanner, Siemens, Malvern, Pennsylvania) before the chemotherapy. PET scan was performed the 3.5 min per frame 3-dimensional (3D) mode 60 min after the intravenous injection of ¹⁸F-FDG (7.4 MBq/kg). Machine learning approach was consist of random forest (RF) and convolution neural network (CNN) in order to predict the metastasis in osteosarcoma patients. Quantitative image texture features were used for RF and tumor PET images were used for CNN. Feature selection was used logistic regression for RF method. RF was performed k-fold validation (k = 10). To avoid the overfitting the CNN for prediction, we selected the 2 convolution layer CNN method. Each of convolution layers was included max pooling layer. The metastasis and statistical significance of quantitative features were assessed using receiver operating characteristic (ROC) curve and logistic regression analysis. Cox regression analysis was performed to investigate each image texture feature was the effective parameter in osteosarcoma patients ¹⁸F-FDG PET image. **Results:** Logistic regression was show that the predictable quantitative image feature was SUVmin (minimum). Likewise, Cox analysis show that SUVmin was the effective parameter in osteosarcoma patients ¹⁸F-FDG PET image ($p = 0.007$, 95% confidence interval: 0.046 - 0.608). According to the ROC area under the curve (AUC) was 0.739. To multivariable analysis in machine learning, we selected features that are SUVmin and tumor volume. The predict accuracies of 10 fold validation accuracy of RF and 2 con-

volution layer CNN were 85 and 90%, respectively. **Conclusions:** The results of this study show that 2 convolution CNN model can predict the metastasis using ^{18}F -FDG PET image before chemotherapy response more accurately when comparing to 10 fold cross validated RF and AUC values. ^{18}F -FDG PET image machine learning method provide more accurate and useful prediction of metastasis in cancer patients.

EP-0958

Human Brown Adipose Tissue Activity Assessed via Positron Emission Tomography/Computed Tomography is Inversely Associated with Environmental Temperature

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Purpose/Introduction: Cold exposure increases brown adipose tissue (BAT) activity, which may lead to increased resting energy expenditure (REE) with beneficial effects on body composition. However, evidence on the impact of normal daily living environmental temperature (Tenv) on BAT activity is limited. In this study, we examined the impact of Tenv on BAT activity of healthy men. **Subjects & Methods:** Twenty-two healthy men [age (years): 36.68 ± 5.22 , body mass index (BMI): 29.29 ± 6 (kg/m²)] were assessed for: (i) Tenv, recorded via a wireless temperature sensor which was carried by the participants for one week prior to BAT measurements and (ii) BAT activity, via ^{18}F -fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (^{18}F -FDG PET/CT) scan, following a REE measurement and a 2-hour mild cooling protocol (temperature: $16.7 \pm 0.55^\circ\text{C}$; humidity: $49.02 \pm 11.08\%$), based on recent guidelines. Body composition was assessed via Dual energy x-ray absorptiometry (DEXA) prior to the ^{18}F -FDG PET/CT scans. **Results:** Ten out of the 22 participants displayed no BAT activity [i.e., standard uptake value (SUV) equal to background], while 12 participants revealed BAT activity (SUV corrected via DEXA lean body mass = 2.85 ± 0.78). Individuals who displayed BAT activity showed reduced Tenv, age, BMI, and fat mass, as well as increased REE compared to individuals who did not display BAT activity, yet these differences did not reach statistical significance ($P > 0.05$). However, small to moderate Cohen's d effect sizes were detected between the two groups (Tenv: $d = 0.29$; age: $d = 0.80$; BMI: $d = 0.38$; REE: $d = 0.27$). Within the group who displayed BAT activity ($n = 12$), BAT activity was inversely correlated with Tenv ($r = -0.62$, $P = 0.03$). Linear regression analysis confirmed the association ($R^2 = 0.39$, $P = 0.03$), while Cohen's f^2 effect size analysis revealed a moderate effect size ($f^2 = 0.64$) between BAT activity and Tenv. We also found a strong positive correlation between BAT activity and REE ($r = 0.62$, $P = 0.05$), which was further confirmed by Linear regression analysis ($R^2 = 0.39$, $P = 0.05$) and a Cohen's small effect size ($f^2 = 0.22$). Finally, we found no relationship between BAT activity with

BMI, lean body mass and fat mass of the participants ($P > 0.05$). **Discussion/Conclusion:** In healthy individuals who display BAT activity following a mild cooling protocol, BAT activation is inversely associated with Tenv and positively with REE. This indicates that the Tenv humans are exposed to during daily living may affect body weight management. Nevertheless, the current evidence should be treated with caution, given that the Tenv, REE and fat mass characteristics were not significantly different between individuals who did or did not display BAT activity.

EP-0959

Optimized scatter correction of J-123 Meta-Iodobenzylguanidin (MIBG) szintigraphy using factor analysis

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Purpose: The aim of the study was to investigate if the quantitative assessment of Heart/Mediastinum (H/M) ratio could be improved by implementing Factor Analysis (FA) during the process of scatter correction of 123I-MIBG scintigraphy. The FA results were compared with Dual- and Triple Energy Window (DEW, TEW) scatter correction methods. **Subject & Methods:** Monte Carlo (MC) simulations and phantoms were measured using the SPECT-CT gamma camera. Subsequently, MC simulations were separately calculated using one point- and two point sources. Jaszczak cardiac insert phantom and planar 123I-MIBG phantom were filled with 123I. Then, static anterior planar and single-photon emission computed tomography were acquired using Low Energy High Resolution (LEHR) and Medium Energy General Purpose (MEGP) collimators respectively. FA was applied to separate photopeak- and compton scatter in both MC simulation and phantom measurements. **Results:** The H/M ratio of the planar images 123I-MIBG phantom produce similar results compared with the FA (2.4 H/M), DEW-Method (2.5-2.8 H/M) and MEGP collimator (2.8 H/M). Interestingly, TEW-Method shows the much higher value (3.8 H/M) than FA, DEW, and MEGP. The planar images of the Jaszczak phantom indicated significant deviation ($\geq 80\%$) from the reference values 44 H/M and 22 H/M. The FA (20.5 H/M) tomographic data showed a slight deviation with 7% less than the expected value 22 H/M. Taken together, the point sources results show a correlation between the simulated and FA calculated data. **Discussion & Conclusion:** Based on the results, SPECT-CT imaging using a LEHR collimator and either applying Attenuation- and Scatter-correction with FA or by using TEW-Method, is recommended for the quantitative analysis of 123I-MIBG scintigraphy.

EP-0960

Determining the influence of patient's positioning in PET/CT breast examination on the selection of the contouring algorithm

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Aim: PET/CT study in standard clinical routine is performed in supine position. This is also true for breast examination but the supine position impedes comparison of PET/CT study with MRI scan of the breast which is executed in prone position with a special breast coil to improve signal to noise ratio. In this study we have compared the outcome of PET/CT scan done in supine and in prone position. For both positions a metabolic parameters of the lesion were determined using three different contouring algorithms. Our question was how the selection of the algorithm influences the metabolic parameters and how the situation changes in both positions. **Materials and Methods:** 33 patients with lesions in breast were selected and double PET/CT series were performed in two positions: standard supine and additional prone. Mean age of analysed women was 52 years $\pm$ 12 (with range of 30 to 74 years). Prone position was achieved using a homemade special pad, with the shape of breast coil in MRI. Regions of interest including lesions were contoured using three segmentation methods: adaptive contouring, 41% maximum value and 2.5 SUV implemented in Philips IntelliSpace station. The following metabolic parameters in ROI were determined: SUVmin, SUVmax, SUVmean, SUVstd, metabolic tumour volume (MTV), TLG. Data analysis was performed using Matlab Statistics Toolbox to compare above mentioned parameters if they differ significantly regarding the algorithm used. Tests were performed for each position separately. Statistical significance was determined using Friedman's non-parametric test with p-value less than 0.05 considered as significant. **Results:** For each metabolic parameter Friedman's resulted in p-values: SUVmin $p=6e-08$, SUVmean $p=0.1633$, SUVstd $p=0.006$, MTV $p=0.2496$, TLG $p=0.1622$ in supine position and SUVmin $p=8e-05$, SUVmean $p=0.1281$, SUVstd $p=0.1281$, MTV $p=0.0835$, TLG $p=0.1812$ in prone position. SUVmax was the same in each algorithm. Only SUVmin was different in both positions as p-value is below 0.05 level and SUVstd in supine position. **Conclusions:** Statistical significant differences were observed in tested methods for SUVmin value in both positions. In supine only SUVstd was different in those contouring methods but after changing position to prone changes in standard deviation was insignificant. This lead us to the conclusion that in prone position the choice of the contouring algorithm has less impact on SUV values. Surprisingly, this test did not indicate to relation between the algorithm choice and MTV values. **Acknowledgment:** Grant No. STRATEGMED2/267398/4/NCBR/2015.

EP-0961

Differences of quantitative indexes for PET/CT between analysis software using modified DRO

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Aim: To investigate differences of quantitative indexes among commercial analysis software using modified digital reference object (DRO) published by Quantitative Imaging Biomarkers Alliance (QIBA). **Methods:** Noise-less DRO was smoothed using a Gaussian function with 10mm in full width at half-maximum. The modified DRO was imported 8 commercial analysis software for PET/CT (Virtual Place, Xeleris, MIM Encore, OsiriX, GLPET, Vox-Base II, EQPET and PMOD). Mean, peak and maximum standardized uptake values (SUVmean, SUVpeak, SUVmax), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) at thresholds with 60% and fixed value of 2.5 were evaluated in hot spheres (10, 13, 17, 22, 28, 37mm in diameters) except for SUVpeak at 10mm and SUVmean, MTV, TLG at threshold with 2.5. Differences between analysis software were evaluated by coefficient of variation (CV) for each index. **Results:** Although a CV in SUVmax was nearly negligible, CVs in other indexes were considerable depending on sphere diameter. Average CVs for SUVmax, SUVpeak, SUV60%, SUV2.5, MTV60%, MTV2.5, TLG60% and TLG2.5 were 0.00 (all spheres <0.01), 0.05 (0.01-0.09), 0.04 (0.01-0.08), 0.04 (0.02-0.07), 0.15 (0.03-0.38), 0.01 (0.00-0.02), 0.12 (0.01-0.37) and 0.01 (0.00-0.02), respectively. **Conclusion:** Modified DRO was successfully applied various commercial analysis software to validate differences in several quantitative indexes. SUVmax showed the best consistency in noise-less condition. Differences between analysis software may be considered for most quantitative indexes in PET/CT (includes SUVpeak).

EP-0962

Metabolic volume thresholding method comparison in patients suspected for LVAD driveline infection in 18F-FDG-PET/CT

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Metabolic volume (MV) has been speculated to be useful in monitoring some oncological diseases with various success rates. The key to using MV correctly is the selection of an appropriate thresholding method. The purpose of this study was to analyze and compare different thresholding methods in calculating the MV in patients suspected for implantable continuous flow left ventricular assist device (CF-LVAD) driveline infection. A total of 41 (35 male) patients with CF-LVAD from July 2009 until April 2016 that were suspected for LVAD related infection were evaluated in this study. A single large volume of interest (VOI) was placed over the entire intracorporeal length of the driveline. Thereafter, different thresholding methods were used on the same VOI: fixed threshold, SUVmax dependent threshold and SUVmean (liver) dependent threshold. The standard of reference was the final clinical diagnosis at the end of clinically recorded follow-up that included microbiological samples obtained during surgery and recurrence of clinical symptoms on follow-up. The SUVmax dependent thresholding resulted in very low sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) below 60% with an area under the curve (AUC) of 0.406. The fixed threshold performed

somewhat better with Se, Sp, PPV and NPV of 87%, 83%, 87% and 83%, respectively, with an AUC of 0.877. The SUVmean(liver) dependent thresholding showed a very high and balanced Se, Sp, PPV and NPV of 91%, 89%, 91% and 89%, respectively, with an AUC of 0.971. Finally, only the volumes resulting from the SUVmean(liver) dependent thresholding were statistically different between patients with and without ascertained driveline infection. A lesion independent thresholding based on a reference organ or tissue (in this case liver) has proven to be the most accurate MV thresholding method over the other previously known methods in patients suspected for CF-LVAD driveline infection, indicating the importance of standardization of thresholding criteria for the calculation of the metabolic volume.

EP-0963

Does measuring ^{18}F -FDG PET-CT tumour metrics by altering thresholds affect prognosis and response assessment in oesophageal Cancer?

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Purpose/Introduction: The purpose of this study was to evaluate whether measuring PET-CT derived tumour parameters SUVmax, SUVmean, MTV & TLG by different threshold methodologies affects a) prognosis and b) the assessment of treatment response (metabolic versus pathological response) in oesophageal AC. **Subjects & Methods:** 155 patients with AC of the oesophagus or oesophagogastric junction were separately analysed in Surgery (n=100) and Multimodal (n=55) treatment groups. Surgery group patients had a PET-CT study prior to surgery and Multimodal group patients had a pre-treatment and post-treatment PET-CT study. The SUVmean, MTV and TLG were calculated using five common tumour delineation methodologies (thresholding by percentage 42% and 50%; thresholding by a fixed background SUV cut-off 2.5, 3.5, or variable depending on SUVmax). The SUVmax which is independent of threshold methodology was also recorded. **Results:** Metabolic tumour metrics according to different threshold methodologies were strongly correlated with each other. The metabolic parameters according to each threshold methodology were not significant predictors of tumour location, tumour differentiation, depth of tumour invasion (T stage), nodal disease (N stage) or overall pathological stage in either the Surgery or Multimodal group. The study also did not demonstrate that any threshold methodology was better in terms of predicting DFS or OS in either treatment group or predicting treatment response in the Multimodal group. **Discussion/Conclusion:** This study did not demonstrate that any metabolic parameter had a better association with tumour characteristics, cancer recurrence or patient mortality than metabolic parameters measured with the other threshold methodologies. Metabolic tumour metrics (SUVmean, MTV and TLG) were not affected by the choice of threshold methodology. This provides an assurance that metabolic tumor metrics generated using different threshold methodologies can be compared with confidence in oesophageal AC.

EP-0964

A novel daily routine method of denoising and quantification in $^{99\text{m}}\text{Tc}$ -Mag3 renography.

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Aim: To overcome the presence of high level of Poisson noise in fast dynamic renal acquisition which hinders images analysis and interpretation. **Material and Methods:** To subdue the noise problem, a method based on fitting and filtering time activity curves (TAC) in Legendre space is proposed. The signal in time domain is transformed to a space domain where noise and signal are mapped into different subspaces. A "cut off" is applied onto the set and an inverse Legendre transform lead to a denoised TAC. This method was used to extract the usual functional information in $^{99\text{m}}\text{Tc}$ -Mag3 renography. We used a renal database (<http://www.dynamicrenalstudy.org>) which contains Monte-Carlo (MC) simulated studies and real patients' data for a total of 70 different studies. The MC studies provided Gold Standard with different levels of injected activity, renal clearance and noise in the anterior and posterior views. The relative kidney function (integral method), time to maximum of uptake (TM) and half emptying time (T1/2) were computed using a homemade software written in Python. The results were compared to the ground-truth (MC data) and to the values obtained with a state-of-the-art commercial software (Hermes) currently used in clinical practice for nuclear image analysis. For each parameter (TM, T1/2) a parametric image at voxel level was also obtained. **Results:** When pooling all data, slope (R^2) of the linear regression between Hermes and Legendre was: 0.97 (0.99) for uptake, 0.92 (0.78) for TM, 0.26 (0.10) for T1/2. Furthermore Mean (SD) for the Bland-Altman analysis was: 0.23 (0.93) for uptake, 0.09 (1.11) for TM, -2.05 (2.30) for T1/2. In case of high level of noise, the Legendre method held up performing and remained accurate (to the 10s frame temporal resolution) while the commercial software delivered TM and T1/2 values with sometimes difference exceeding the minute. The same analysis has been performed at pixel level and led to the generation of TM and T1/2 parametric images that reflected the regional dependence of each parameter. **Conclusions:** The Legendre method revealed not only to be accurate, routinely applicable and very robust in presence of high level of noise but a major breakthrough is the possibility to also generate parametric image at pixel level thanks to a fast and congruent fitting and a considerable noise removal.

EP-71

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Data analysis -> Image reconstruction

EP-0965

Q.Clear reconstruction optimization for digital PET: finding optimal balance between patient comfort, received dose and image quality

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Purpose: During ^{18}F -FDG Whole Body PET/CT examinations short total acquisition times would be preferable for both patient comfort and the reduction of several motion artifacts, while image quality could be degraded. Furthermore, low-dose imaging protocols are possible with the improved SNR performance of new digital PET/CT systems. Bayesian penalized likelihood image reconstructions (e.g. Q.Clear) include noise control implemented within the iteration process, and theoretically lead to image convergence. These advancements can compensate for image quality degradation in case of short total acquisition times if optimal regulatory reconstruction settings (e.g. β value) are used. **Materials and Methods:** Aiming to find the optimal β value in case of low-dose patient protocols, patient examinations and a phantom scan were performed on a GE Discovery MI digital PET/CT system. A NEMA IEC Image Quality phantom was filled with ^{18}F -FDG according to the EARL protocol and image dataset was acquired in two axial frames 5 min each. Several Q.Clear reconstructions with β value varied between 500–2100 were performed. Patient scans including wide range of BMIs (19.7–44.8) were acquired with 1.5 min/bed positions. Two groups with injected activity of ^{18}F -FDG was investigated: 5 patients with 3.0, 3.5, 4.0 MBq/kg, while for low dose protocol 5 patients with 2.0, 2.5, 3.0 MBq/kg for BMIs ≤ 20 , between 20 and 30, >30 respectively. For all patient scans Q.Clear reconstructions with β value of 500, 1000, 1500 and 2000 were performed, and analyzed qualitatively by nuclear medicine physicians and quantitatively by 40 mm liver VOI analysis. **Results:** Standard Deviation of the background VOI for the IQ phantom was decreasing monotonously while β value increased. This measure saturated over 1500 and was not decreasing significantly over 1000. Medical reading revealed that β value 1000 resulted excellent image quality for all BMI categories, and showed the same qualitative result both for both injected activity protocols. Liver VOI analysis revealed that SUV mean ranged between 2.19–2.88, and (St.Dev./Mean)² values were significantly lower compared to conventional TOF reconstructions for both injected activity protocols. **Conclusion:** Q.Clear image reconstruction could provide good image quality performance when using β value 1000 at short total acquisition times for better patient comfort, even in case of low injected activity protocols.

EP-0966

The effect of reconstruction algorithms on metabolic parameters in patients affected by oncological disease: a preliminary experience

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Introduction: the aim of this study was to evaluate the effect of resolution recovery with Point Spread Function (PSF) correction and smooth on both metabolic parameters and image noise for the list-mode reconstruction algorithm of the Ingenuity TF PET/CT scanner. **Subjects & Methods:** Ten ^{18}F -FDG PET/CT exams acquired on the Ingenuity TF PET/CT scanner were included in this study. Each image was acquired in list-mode, with 1.5 minutes for field of view. Images were reconstructed with the TOF

list-mode algorithm, without sinogram interpolation. This algorithm allows to activate the PSF corrections and to change the image smooth. Resolution recovery is achieved by modelling and correcting for the effects of the scanner's PSF with the iterative Richardson-Lucy maximum-likelihood algorithm. Smooth is the relaxation parameters, meaning the weight factor used for every iterations. The standard clinical reconstruction was performed with 3 iterations, 33 subsets and relaxation parameter (relax) equal to 1. Six different reconstructions were compared: 1) standard for clinical use; 2) no PSF with relax 0.7; 3) no PSF with relax 0.5; 4) PSF with relax 1; 5) PSF with relax 0.7 and 6) PSF with relax 0.5. A total of 22 lesions were evaluated in terms of SUV_{max} , SUV_{mean} , metabolic tumor volume (MTV), total lesion glycolysis (TLG) and image noise (by means of a 7 cm diameter ROI placed inside the liver). All the parameters were compared to the standard clinical reconstruction. **Results:** PSF correction improved lesion quantification, with an average recovery of about 30% both for SUV_{max} and SUV_{mean} . Decreasing the relaxation parameters caused a reduction of less than 5% both for SUV_{max} and SUV_{mean} . MTV and TLG were both affected by PSF introduction and smooth. PSF with relax 0.5 reconstruction showed a larger MTV variation (-34%) than the standard clinical image, while the largest TLG variation was observed for no PSF with relax 0.5 reconstruction (-20%). Image noise was sensitive both to PSF introduction and image smooth. In particular, PSF caused an increase of 20% in image noise, while decreasing the relaxation parameter reduced noise even to -30%. PSF with relax 0.7 reconstruction had the same noise of the standard clinical image with a lesion quantification recovery of +30%. **Conclusion:** PSF introduction increases quantification but also image noise. Tuning the reconstruction parameters in order to improve lesion quantification keeping image noise at an acceptable level is possible. MTV and TLG are both affected by reconstruction parameters.

EP-0967

A Phantom and Patient Based Quantitative Comparison of PET/CT and SPECT/CT, for post 90Y SIRT Imaging

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Aims: The aim of this work was to quantitatively compare PET/CT and SPECT/CT for imaging of ^{90}Y (post-Selective Internal Radiation Therapy (SIRT)) through the use of phantom and patient datasets. This was investigated with the view of carrying out individualised patient dosimetry. **Methods:** A NEMA IQ phantom (8:1 sphere-to-background ratio) and an anthropomorphic liver phantom (AbdoMan™, 4:1 sphere-to-background ratio) were scanned on both a GE D710 PET/CT scanner and GE D670 SPECT/CT scanner. SPECT/CT datasets were reconstructed using an optimised OSEM algorithm (5 iterations, 15 subsets, CT attenuation correction, Monte Carlo collimator modelling) using Hermes Hybrid Recon (Hermes Medical Solutions AB)^[1]. PET/CT datasets were reconstructed using a quantitatively optimised BPL algorithm (Q.Clear, GE Healthcare) with a penalty weighting factor of 1000. Contrast recovery (CR), background

variability (BV) and recovered activity percentage (RAP) were calculated and compared for both modalities. The AbdoMan™ phantom contained a sphere with a solid core representing a necrotic tumour. Line profiles through this sphere were taken on both the SPECT and PET images to compare how effectively each modality could recover the true activity distribution. Twenty patients that had had both SPECT/CT and PET/CT post-SIRT were retrospectively reconstructed using these optimised algorithms. Voxel-based dosimetry was carried out using Hermes Internal Radionuclide Dosimetry (HIRD) to compare differences in liver doses for both modalities. **Results:** CR and RAP values for the spheres in the NEMA phantom were significantly higher ($P<0.05$) for PET/CT compared to SPECT/CT. For the 30mm & 20mm spheres in the AbdoMan™ Phantom, there was a significant increase ($P<0.05$) in CR and RAP for PET/CT. Furthermore the line profile through the 'necrotic' sphere in the AbdoMan™ phantom showed better conformance to the true activity distribution when imaged with PET/CT. For voxel based dosimetry, PET/CT imaging produced, on average, a 7% higher mean liver dose compared to SPECT/CT. **Conclusions:** Results indicate that optimised PET/CT appears to be superior to SPECT/CT for the purposes of quantitative imaging of ^{90}Y , and therefore better suited as a basis from which to carry out individualised patient dosimetry. **References:** [1] Porter CA, Bradley KM, Hippeläinen ET, Walker MD, McGowan DR. 'Phantom and clinical evaluation of the effect of full Monte Carlo collimator modelling in post-SIRT yttrium-90 Bremsstrahlung SPECT imaging'. EJNMMI Res. EJNMMI Research; 8(1):7. (2018)

EP-0968

Motion deblurring versus full motion correction in wholebody PET/CT

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Introduction: Physiological respiratory motion during PET data acquisition degrades PET image quality and accuracy which may influence clinical decision making. Therefore, motion-compensated image reconstruction (MCIR) has been recommended to prevent image blurring and artifacts. In this study, a fast elastic motion compensation approach based on motion deblurring (EMC) is evaluated on patient data and compared to state of the art MCIR technique using different gating methods.

Methods: CT and whole-body PET data (6-8 bed positions, duration 120s or 360s) were acquired on an integrated PET/CT (Siemens Biograph mCT), 1 h after injection of ^{18}F -FDG (4MBq/kg body weight). During PET data acquisition the respiratory signal was recorded using the Anzai belt system (Anzai Medical Co.). Motion compensated images were reconstructed using both correction techniques, EMC and MCIR and also different gating methods (Anzai based and data-driven gating). Within EMC, motion is corrected using a deblurring kernel during iterative image reconstruction, where the motion between the reference image (optimal gate) and all data is estimated using mass-pre-

serving optical flow. Within MCIR, 10 respiratory gated images were reconstructed using the Anzai or data-driven gating signal. Motion vector fields between each respiratory gate and a predefined reference image were calculated using optical flow methods. Finally, a motion corrected image was reconstructed using a standard EM-based image reconstruction that incorporates elastic motion correction. To evaluate the effect of motion correction on quantitative data analysis, regions-of-interest defined on lesions were analyzed and changes in SUV_{max} and metabolic ^{18}F -FDG volume (defined on an adaptive threshold of SUV_{max}) were reported. **Results:** Data of 32 patients (57 ± 13.4 y) with a total of 66 identified lesions were included in the comparative analysis. SUV_{max} of all lesions increases for MCIR-ANZAI from 10.25 ± 7.34 to 11.18 ± 7.74 (mean $\pm$ std), for MCIR-DDG similar from 10.25 ± 7.34 to 11.11 ± 7.62 (mean $\pm$ std) and for EMC-ANZAI from 10.32 ± 7.85 to 11.48 ± 8.90 (mean $\pm$ std). The metabolic volumes of the lesions after EMC-ANZAI motion compensation decreased from 1.85 to 1.36 (median), for MCIR-ANZAI from 1.68 to 1.43 (median) and for MCIR-DDG from 1.66 to 1.48 (median). **Conclusion:** Both motion compensation methods (EMC and MCIR) show a clear quantitative improvement on PET images with an increase of SUVs and a decrease of metabolic volumes. Based on our study, both techniques are equally applicable to clinical data.

EP-0969

Comparison of MR Based Attenuation Correction Methods with CT Based Attenuation Correction in Dynamic Brain PET imaging

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Introduction: In PET imaging, radiation emitted from the radioactivity administered to the subject is attenuated due to scatter and absorption when traveling through different tissue structures in the body. In a combined PET/CT scanner, a low dose CT scan is acquired to create an attenuation map (μ -map) to correct this bias in PET measurement. This approach is not available in state-of-the-art PET/MR scanners and MR-based attenuation correction methods are used instead. Attenuation correction (AC) using MR data is not straightforward and is particularly challenging for brain imaging, where the skull makes a significant contribution to the attenuation but does not produce a strong signal in conventional MR imaging. In this abstract, we present a comparison between the CT- and MR-based AC methods for dynamic brain PET imaging. **Materials and Methods:** Four subjects taking part in a study evaluating the role of GABA_A using ^{11}C -Ro15-4513 provided informed consent to take part in this methodology study. Following a 90 min dynamic PET-CT scan on a Siemens Biograph 6 HiRez PET/CT scanner, subjects underwent a 30 min PET-MR scan on the GE SIGNA PET/MR scanner. Three different μ -maps were generated: based on a low dose CT from PET/CT (CT-AC); based on a Dixon-type LAVA-Flex MR sequence, using an anatomical atlas to estimate the skull (Atlas-AC); based on a zero echo time (ZTE) MR sequence, capable of detecting cortical bone tissue (ZTE-AC). The reconstructed PET images from all the above mentioned AC methods were

compared using both static and dynamic PET analysis outcome measures. Regional standard uptake values (SUVR), estimated for 60–90 min p.i. scan window, was considered as static outcome measure and binding potential (BP_{ND}) estimated from kinetic modelling of ^{11}C -Ro15-4513 over the full 90 min scan as dynamic outcome measure, both with respect to cerebellum.

Results: The results show that the average percentage SUVR value difference between the CT-AC and Atlas-AC methods is ~15% and for ZTE-AC is ~5% for the majority of brain regions. The average percentage BP_{ND} value difference between the CT-AC and Atlas-AC methods is ~25% and for ZTE-AC is ~10% for the majority of brain regions. **Conclusion:** The results so far on a limited number of subjects suggest that the ZTE-AC method performs better than the Atlas-based method in terms of PET quantitative outcome measures in comparison to CT-based AC. Further investigation is required with more number of subjects to confirm this finding.

EP-0970

Image Reconstruction Robustness of Radiomic Features in Lymphoma FDG PET/CT studies

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Purpose: Before PET radiomics can be implemented in multicenter lymphoma studies, it is essential to identify its robustness against variations in image reconstruction methods. The aim of this study was to evaluate the sensitivity of radiomic features derived from 18F-FDG PET/CT scans in lymphoma patients on variations in reconstruction protocols. **Methods:** Whole-body 18F-FDG PET/CT images from 10 lymphoma patients at staging were reanalyzed. Each scan was reconstructed using: (1) an EARL compliant protocol (144x144 matrix, 4 mm voxel size); (2) a high resolution protocol (HR, 288x288 matrix, 2 mm voxel size) and (3,4) these protocols with point spread function (PSF) reconstruction. Radiomic features were extracted for each lesion (162 in total) and for each reconstruction protocol after delineation based on 50% of SUVpeak with local background correction. Features were categorized as descriptors of texture (n=334) applied with and without a fixed bin size of SUV=0.25 (FXD), intensity (n=33) and shape (n=17). Based on the maximum percentage difference in the mean value of each parameter over the four reconstructions, features were classified as robust (<10%), low sensitive (10–30%), moderate sensitive (30–40%), sensitive (40–50%) and highly sensitive (>50%). **Results:** The 384 features were classified as robust in 14%, low-sensitive in 12%, moderate sensitive and sensitive in 9%, and highly sensitive in 56% of the cases. Features related to intensity are classified as robust in only 5%, whereas 29% are noted as highly sensitive. 45% of all features showed to be highly sensitive to the applied reconstruction protocol when comparing EARL to HR+PSF (changing voxel size and using PSF), this effect was mainly seen for the FXD features of which 66% are highly sensitive. When studying the effect of

PSF reconstruction only, 41% of the features were classified as robust to a change in reconstruction protocol from EARL to EARL+PSF and 46% to a change from HR to HR+PSF. Shape features were least sensitive to the use of PSF reconstructions; 94% of the shape features are robust against a change from EARL to the EARL+PSF protocol and 100% when changing from HR to HR+PSF. **Conclusion:** Image reconstruction protocols have a high overall impact on the values obtained for most radiomic PET features in lymphoma patients. Discarding features not robust to image reconstruction protocols could exclude features with potential high clinical value. Therefore, rigorous standardization of PET/CT imaging procedures is warranted for reliable use of PET radiomics in multicenter lymphoma 18F-FDG PET/CT studies.

EP-0971

Comparison of recovery coefficient in different reconstruction algorithm in state-of-the-art non digital PET/CT scanners

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Purpose/Introduction: recent advancements in PET image reconstruction algorithms comprise modelling of the point spread function (PSF) and noise statistics modelling (NSM). Within this work we compare different reconstruction algorithms implemented in 3 state-of-the-art non-digital PET/CT scanners with and without time-of-flight (TOF) technique. **Subjects & Methods:** the same 68Ge-phantom based on a standard IQ body phantom filled with a 68Ge epoxy resin was used. The activity concentrations in the spheres (internal diameter-ID = 6,10,13,17,22,28,37 mm) and in the background were measured with a radionuclide calibrator tested against a NIST traceable source and were respectively 40.67kBq/ml and 10.58kBq/ml at reference time (uncertainty $\pm 3\%$). Nominal sphere-to-background ratio was 3.84. Acquisition time was adjusted according to the age of the phantom to meet 1.5 min per frame at the reference date on each PET scanner and reconstructed with variable reconstruction parameters (iterations: 48,72; amplitude of Gaussian filter: 5, 6.4, 8mm) with traditional iterative technique (IT) and by combining advanced modalities, when present: PSF, TOF, TOF+PSF, NSM. For each PET scanner and each reconstruction modality maximum Recovery Coefficient (RCmax) values were evaluated for each visible sphere. RCmax were normalised to 37 mm ID sphere result. **Results:** For each reconstructed modality, RCmax (mean $\pm$ sd) were averaged on different reconstruction parameters and PET scanners and for increasing sphere ID respectively 6,10,13,17,22,28,37 mm resulted: - IT: (0.31 $\pm$ 0.03),(0.51 $\pm$ 0.05),(0.63 $\pm$ 0.03),(0.82 $\pm$ 0.03),(0.89 $\pm$ 0.03),(0.95 $\pm$ 0.04),(1 $\pm$ 0) - IT+TOF: (0.32 $\pm$ 0.01),(0.56 $\pm$ 0.08),(0.64 $\pm$ 0.07),(0.84 $\pm$ 0.03),(0.91 $\pm$ 0.00),(0.97 $\pm$ 0.04),(1 $\pm$ 0) - IT+PSF: (0.30 $\pm$ 0.01),

(0.50 ± 0.04), (0.65 ± 0.05), (0.88 ± 0.04), (0.93 ± 0.02), (0.95 ± 0.04), (1 ± 0) - IT+PSF+TOF: (0.30 ± 0.01), (0.56 ± 0.08), (0.70 ± 0.11), (0.91 ± 0.03), (0.94 ± 0.00), (0.97 ± 0.04), (1 ± 0) - NSM: (0.30 ± 0.02), (0.67 ± 0.19), (0.84 ± 0.14), (0.94 ± 0.05), (0.98 ± 0.03), (0.98 ± 0.06), (1 ± 0) **Discussion/Conclusion:** the RC obtained with the 3 state-of-the-art scanners demonstrate clearly that, independently of the reconstruction method used, modern PET/CT scanner outperforms respect to older one described by EARL curve. Higher differences are recorded for smaller spheres. Moreover, applying more advanced reconstruction techniques progressively enhances RC, NSM reconstruction being the most promising algorithm. Even if RCmax of different scanners converge at larger (>22 mm) and smaller (10mm) spheres, the overestimations observed in the size between 1 and 2 cm are currently under investigation.

EP-0972

Impact of a Commercial Resolution Recovery Algorithm on the Image Quality of Brain Dopamine Transport SPECT Imaging

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Purpose/Introduction: The Evolution Package (GE Healthcare) is a resolution recovery (RR) algorithm which can potentially improve the image quality of SPECT images by including accurate 3D physical models of the collimator-detector response functions into the iterative reconstruction process. The aim of this study was to evaluate the impact of the RR algorithm in the image quality of DaTscan SPECT images when reduced acquisition times were used. **Subject & Methods:** Ten DaTscan SPECT patient data sets were reconstructed with the usual clinical protocol of our institution: OSEM, 2 iterations, 10 subsets and Butterworth filter, with a critical frequency of 0.48 and power of 10. Poisson resampling was then used to simulate data sets with 50, 70, 85 and 100% of original counts and then reconstructed with Evolution. The images were compared with the original OSEM reconstruction by three independent nuclear medicine physicians, who blindly assessed for noise, contrast and resolution using the following scale: -2, significantly worse; -1, slightly worse; 0, equivalent; +1, slightly better; +2, significantly better. In addition, the physicians were asked to assess changes in their clinical decision following this scoring system: 0, no change; +1, no change but improved confidence; -1, change in clinical decision. Image quality was calculated as the average of noise, resolution and contrast for every patient and reconstruction method. All the images were evaluated in the same Xeleris (GE Healthcare) workstation. **Results:** Mean image quality scores of RR reconstruction showed a positive value in the 100 (+0.17), 85 (+0.12) and 70% (+0.20) images. Only the 50% reconstruction was evaluated with a negative score for the mean image quality (-0.06). On the other hand, the scoring of the clinical confidence showed positive values for all the RR images: +0.28 (100%), +0.36 (85%), +0.39 (70%) and +0.33 (50%). The differences in scores between physicians were always statistically non-signifi-

cant ($p > 0.05$). **Discussion/Conclusion:** The number of patients included in this study was limited due to large number of reconstructions involved. Despite this, the study of the images reconstructed suggest that it could be possible to reduce the injected activity or the acquisition time up to 30% compared with the reference clinical OSEM protocol. This would benefit the patient in terms of reduced exposure or less scanning time. Even in the case where the mean image quality score was negative, the physicians showed an increased confidence in the clinical decision when using RR images.

EP-0973

Investigation of a simplified quantitative yttrium-90 bremsstrahlung SPECT reconstruction by usage of background compensation and patient-specific calibration factors for yttrium-90 SIRT dosimetry

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Purpose: Yttrium-90 bremsstrahlung SPECT reconstruction is challenging due to the continuous energy spectrum and the lack of a discrete photo peak with related complex energy-dependent scatter and attenuation correction. Nevertheless clinical dosimetry requires quantitative post-SIRT-therapeutic imaging. For this purpose a simplified quantitative reconstruction with background compensation was investigated. In consequence of the assumptions made during yttrium-90 bremsstrahlung SPECT acquisition and reconstruction, an object-dependency of a global calibration factor is assumed and the need of a patient-specific calibration was evaluated. **Methods:** A calibration measurement was carried out with a cylindrical phantom, homogeneously filled with activity so that a global calibration factor (CF) could be determined. This global CF was compared to individual CFs of 5 SIRT patients, determined via the applied activity and the total amount of image counts. For the analysis of image quality and activity recovery, a phantom with three inserts was filled with yttrium-90 at a foreground-to-background ratio of 10:1 and scanned at a Siemens Symbia T2 SPECT-CT with energy windows of 86-130keV and 306-414keV. The bremsstrahlung SPECT was reconstructed with an in-house rotation-based penalized one-step-late OSEM with and without implemented background compensation (BC). The effect of the BC was analyzed with recovery coefficients (RC) and signal-to-noise ratio (SNR). **Results:** The deviation of the patient-individual CFs from the global CF was on average 35% (29-48%) for SPECT images reconstructed without BC and on average 30% (24-42%) when reconstructed with BC. The RCs without BC were 53% for 249ml, 37% for 52ml, 22% for 16ml and 103% for the phantom background in contrast to 59% for 249ml, 41% for 52ml, 24% for 16ml and 112% for the phantom background for with BC SPECT reconstruction. Without BC show a lower SNR of 7 to 27 in comparison to 8 to 30 of with BC SPECT images. **Conclusion:** A simplified quantitative yttrium-90 bremsstrahlung SPECT reconstruction containing a background compensation proved to be superior to a reconstruction without BC regarding at on average 9% higher recovery and 8% better signal-to-noise

ratio. Both is of advantage for yttrium-90 SIRT dosimetry. The expected object-dependency of the global calibration factor was found and reconstructions with BC showed a lower deviation of the patient-individual CFs from the global CF than reconstructions without BC. Therefore, we recommend a patient-individual calibration for clinical dosimetry.

EP-0974

Optimization of radiation dose and acquisition time with reconstruction method incorporating resolution recovery: A phantom study

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Aim: SPECT imaging is widely recommended for the diagnosis and prognosis of various diseases. Advanced reconstruction methods incorporating resolution recovery attempt to achieve comparable or even superior image quality to the standard protocol while shortening scan time or reducing the administered dose. This phantom study investigates the effects of reduced administered dose and/or scan time on SPECT image quality using GE's Evolution™ software, which includes iterative reconstruction incorporating resolution recovery. **Materials and Methods:** The Jaszczak Deluxe phantom was imaged on a GE Discovery NM SPECT scanner using LEHR collimators. The phantom was filled with 99mTc water solution; 10mCi for full dose and 5mCi for half dose acquisition. For each dose level, variable acquisition times were also used. The acquired data have been reconstructed using the filtered back-projection (FBP), the ordered-subset expectation maximization (OSEM) and the OSEM with incorporating resolution recovery (OSEM-RR). Therefore, datasets with all possible combinations of algorithms and acquisition options were generated. Image quality was assessed qualitatively and quantitatively by measuring mean counts and signal to noise ratios of various annular Regions of Interest (ROIs) drawn on different positions. **Results:** Irrespective of the number of counts, the OSEM-RR and OSEM resulted in better contrast and less noise than FBP. The image reconstruction with OSEM-RR with reduced counts, either due to shorter time or due to lower administered dose, is shown not to deteriorate the image quality compared to full counts reconstructed with OSEM. However, the quality between the two reduced count approaches is shown to vary. For the same acquired counts, the half time acquisition yields better quality images than the half dose acquisition. The advantage of using resolution recovery with less counts is shown to be only applicable in uniform areas or hot lesions in a cold field. In cold lesions in a hot field reducing counts resulted in reduced diagnostic accuracy which could not be enhanced with resolution recovery. **Conclusion:** This phantom study suggests that for SPECT imaging, OSEM-RR can offset the impact of less counts, thereby achieving comparable or even better-quality images compared to full counts data reconstructed with standard OSEM. Less counts due to half dose reconstructed with OSEM-RR produces images of comparable quality to those with full counts reconstructed with OSEM. Less

counts due to half time reconstructed with OSEM-RR is actually shown to produce even superior images than full counts reconstructed with OSEM.

EP-0975

Impact of respiratory-gated attenuation correction by 2-point Dixon MR sequence and PET reconstruction algorithm on F-18 FDG PET/MR

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Purpose: The purpose was to compare the difference in standardized uptake value (SUV) of physiological and pathological uptakes between free-breathing and respiratory-gated MR sequence for attenuation correction (FB-MRAC and RG-MRAC, respectively) and to assess the influence of PET reconstruction algorithm on MRAC error by respiratory motion. **Materials & Methods:** Twenty-nine normal subjects and 67 lesions in 38 patients with malignancy in the lower thorax and/or upper-abdomen who underwent F-18 FDG PET/MR with FB-MRAC and RG-MRAC were retrospectively analyzed. MRAC is comprised of 2-point Dixon based 3D fast spoiled gradient echo (FSPGR) by free-breathing and respiratory-gated acquisition with respiratory bellows. PET images were acquired with the same respiratory-gating windows and then reconstructed by ordered subsets expectations maximization (OSEM) and time-of-flight (TOF)-OSEM (iterations, 2; subsets, 16; gaussian filter, 4mm). Degree of misregistration between non-attenuation corrected (NAC) images and MRAC was evaluated by measuring the longest distance between the surfaces of the liver (dist-Liver). Voxels of interests (VOI) were semi-automatically placed on physiological uptake of the upper abdomen and pathological uptakes on NAC images with the fixed threshold value. To assess the relationship between misregistration of MRAC and SUVs, the correlation between dist-Liver and difference in mean physiological and pathological uptakes (phys-SUVdiff and patho-SUVdiff, respectively) were statistically evaluated by the regression analysis. To analyze the difference in pathological uptakes between FB-MRAC and RG-MRAC, maximum SUV (SUVmax) was statistically compared by the Wilcoxon's signed rank test. To evaluate the impact of reconstruction algorithm on SUV, phys-SUVdiff and patho-SUVdiff was statistically compared between OSEM and TOF-OSEM by the Wilcoxon's signed rank test. **Results:** The difference in dist-Liver between NAC and MRAC statistically correlated with mean phys-SUVdiff and mean patho-SUVdiff in both OSEM ($r=0.45$ and $r=0.52$, $p=0.015$ and <0.001 , respectively) and TOF-OSEM ($r=0.38$ and 0.50 , $p=0.043$ and <0.001 , respectively). SUVmax of the lesions with RG-MRAC by OSEM (4.80 ± 2.95) and TOF-OSEM (6.24 ± 3.39) were slightly higher than that with FB-MRAC (4.79 ± 2.93 and 6.22 ± 3.37 , respectively) without statistically significant difference ($p>0.05$). The maximum phys-SUVdiff and patho-SUVdiff on TOF reconstruction (0.08 ± 0.07 and 0.04 ± 0.10) were significantly smaller than those on non-TOF reconstruction (0.13 ± 0.10 and 0.05 ± 0.12 , respectively) ($p<0.0001$ and $p=0.013$, respectively). **Conclusions:** The difference in accu-

racy of registration between non-gated and respiratory-gated MRAC affects the physiological and pathological uptakes in the lower thorax and upper abdomen although the difference may not be clinically significant. TOF reconstruction is more robust to respiratory-related misregistration on MRAC than conventional OSEM.

EP-0976

Optimizing iterative reconstruction settings for ^{89}Zr -immuno-PET to improve image quality

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Objectives: Due to the long half-life of Zr-89 (~3 days) and late imaging time (4-6 days post-injection), radiation exposure limitations are an important concern with ^{89}Zr -immuno-PET imaging (~0.5 mSv/MBq). This results in low-activity injections and extremely low count-rates. At present, the number of subsets and iterations used for iterative reconstruction is not optimized for these low-count situations. The objective of this study was to optimize these reconstruction parameters using clinical ^{89}Zr -immuno-PET data to improve image quality. **Methods:** Four ^{89}Zr -antiCD20 patient datasets were acquired 6 days post-injection on either Philips Gemini-TF or Ingenuity-TF PET/CT scanners. Each list-mode dataset was binned into 3 doses: full dose (74 MBq), simulated standard clinical dose (37 MBq), and ICRP62 category IIb compliant dose (18.5 MBq). Data were then reconstructed using the 3D TOF blob-based OSEM algorithm with different combinations of subsets and iterations for a selection of OSEM updates (iterations $\times$ subsets: 20, 40, 60, 80, 100). Image quality was assessed using the average bias for max and peak tumor SUV with the full dose value as reference for each combination, the coefficient-of-variation (COV) for the background surrounding the tumor, and the contrast-to-noise ratio (CNR). Based on the optimum subset number, the optimum number of OSEM updates was determined (range: 5-300) considering average tumor convergence (max and peak SUV), COV and CNR. **Results:** Manually delineated volumes of the included tumors (n=31) ranged from 1.5-261 mL (mean 24.3 mL) with tumor-to-background ratios ranging from 1.6-13.5 (mean 4.8). Optimization subsets: Across all OSEM updates and doses, SUV bias was stable until 5 subsets, deteriorating for higher subsets. COV and CNR values remained stable until 20 subsets and then rapidly deteriorated for higher subsets. Optimization OSEM updates with 5 subsets: Tumor SUV reached convergence after 50 (SUVmax) and 30 (SUVpeak) updates for all doses. For 18.5, 37, 74 MBq, tumor background COVs were 62%, 60%, 56% (50 updates) and 56%, 54%, 51% (30 updates), respectively, with CNR values of 4.1, 5.4, 6.3 (50 updates) and 4.4, 5.7, 6.6 (30 updates). Corresponding COV and CNR values for the default reconstruction setting (3 iterations, 33 subsets) were: 79%, 72%, 64%, and 3.4, 4.8, 5.8,

respectively. **Conclusions:** Over all doses, quantitative results were reliable up to 5 subsets, defining the optimum number. The minimum number of required OSEM updates for full convergence were 30 for SUVpeak and 50 for SUVmax, resulting in large improvements in COV and CNR over all doses with respect to default reconstruction settings, indicating a significant improvement in ^{89}Zr -immuno-PET image quality.

EP-0977

Optimization Of MR-Based Attenuation Correction For Cardiac PET/MR

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Introduction: Cardiac PET/MR has recently gained attention, but technical obstacles remain before its widespread adoption. For imaging the heart, optimal MR-based attenuation correction (MRAC) is required to compensate for cardiac motion and to segment sufficient tissues for accurate PET reconstruction. Recently, it was demonstrated that MR acquisition during free-breathing allows for better PET co-registration. However, MRAC inaccuracies arise from thresholding image intensity into only 2 tissue classes (all soft tissue and background air-plus-lungs). Our purpose is to compare cardiac PET images reconstructed with 4 different MRAC maps using different combinations of tissue classes. **Subjects and Methods:** Nine patients underwent PET/MR 30min after administration of 10mCi 18F-FDG and data were acquired for 60min (Biograph mMR, Siemens, Erlangen). A multi-echo stack-of-stars sequence (DIXON-radial-VIBE) was used to acquire 4 different MRAC's comprising: the standard 2-component map (2C); a 3-component map with soft tissue, fat and background (3CF); a 3-component map with soft tissue, lung and background (3CL); and a 4-component map with soft tissue, fat, lung and background air (4C). Seventeen myocardial segments were manually drawn on short axis MR images. PET images reconstructed with each MRAC map were then superimposed and SUVmean, SUVmax and TBR (normalized to SUVmean of left-ventricular blood) were recorded for each segment. SUVmean, SUVmax and TBR values were compared with a paired t-test between standard MRAC (2C) and new MRAC types. The primary analysis was performed on all 17 heart segments. A secondary analysis was performed on base, mid-ventricle, apex, lateral wall, septum. **Results:** No difference was visually appreciated among PET images reconstructed with the 4 different maps. SUV and TBR values of the 17 myocardial segments were significantly lower (higher) when PET was reconstructed with 3CF and 4C maps (3CL map) compared to 2C map (p<0.0001). Differences in SUV were significantly greater than differences in TBR (p<0.0001). Sub-analysis of specific heart segments confirmed the effect of different MRAC types on SUV measurement, with the exception of basal and lateral segments, where SUV values in 2C and 4C maps were comparable. TBR differences became less evident and even lost significance. **Con-**

clusion: MRAC maps that use different combinations of tissue classes affect measurement of myocardial FDG uptake (SUV), but not qualitative assessment. Therefore, MRAC optimization is likely to be critical in research, when accurate quantification of PET data is needed. At present, it may have only a marginal role in the clinical setting, where PET interpretation is largely qualitative.

EP-0978

Cardiac Time Of Flight Pet For Evaluating Myocardial Perfusion

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Background: ¹³N-ammonia (¹³N-NH₃) PET is being used for diagnosis of ischemic heart disease. The dynamic acquisition capacity of myocardial perfusion imaging with PET may allow for absolute quantitative assessments and available for its higher accuracy in detecting flow-limiting coronary artery narrowing with more improved temporal and spatial resolution. Recently new time-of-flight (TOF) PET camera has become available. Reconstruction is an essential step in the processing of cardiac PET imaging. Commonly used reconstruction algorithms for PET are filtered back projection (FBP) and ordered subsets expectation maximization (OSEM) methods. New PET cameras recently have three-dimensional (3D) mode acquisition and OSEM reconstruction with TOF and point spread function (PSF) correction technology. In clinical setting, patients' prognosis is often strongly related with the amount of perfusion defects. However there is few basic technical data on this new technology regarding defect detectability and image quality using ¹³N-NH₃ cardiac PET. Therefore, the purpose of this phantom study was to elucidate the effect of OSEM reconstruction, to assess the effects of TOF and PSF on the estimation of myocardial perfusion abnormalities. **Method:** PET imaging was performed using a lung-heart torso phantom with myocardial perfusion defects. The indices of defect contrast, the coefficient of variation (CV) and the index of homogeneity were analyzed by using four reconstruction schemes, including OSEM, OSEM+TOF, OSEM+PSF, and TOF+PSF correction methods. **Results:** The phantom study showed that TOF resulted in improvements to defect lesion detectability with low statistical noise. The defect contrast index of TOF+PSF was significantly larger than that of OSEM only ($p=0.048$). The cardiac percent root mean square uncertainty (RMSU) with PSF was 25.9 % in OSEM+PSF and 20.9 % in TOF+PSF. In contrast cardiac % RMSU without PSF correction was 14.8 % in OSEM and 15.3 % in TOF, which was lower than that with PSF correction. The average wall counts were homogeneous in four reconstruction methods in ¹³N-NH₃. The value of % CV on the profile curve of ¹³N-NH₃ images was confirmed to be smaller than 5% in all reconstruction methods. **Conclusions:** The new PET/CT camera employing 3D PET/CT with 3D OSEM, TOF and PSF algorithms broadened the possibility of precise analysis of abnormal perfusion. The novel ¹³N-NH₃ myocardial PET using TOF and PSF information might have the potential for better quantification of the absolute value

of myocardial flow. Both diagnostic and prognostic studies using new technology should be performed with many patients of coronary artery disease.

EP-0979

Impact of time-of-flight PET on PET/CT standardized uptake values measurements in lymphoma patients

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Objectives: PET/CT is an effective tool in staging, detection of recurrence, and monitoring of treatment response in patients with Hodgkin's disease and NHL. In the last decade time-of-flight (TOF) positron emission tomography (PET) has become a standard technology in almost all commercial systems and is used routinely in clinical oncology. However, the time-of-flight (TOF) reconstructed images may potentially affect the standardized uptake values (SUV) measurements in treatment response evaluations. The purpose of this study is to determine the direct impact of SUV quantitation between TOF and conventional non-TOF reconstructions. **Methods:** Fifty five consecutive lymphoma patients (DLBCL and nodular sclerosis Hodgkin lymphoma) confirmed by histological examination were investigated with [¹⁸F]-Fluorodeoxyglucose ([¹⁸F] FDG) and a GE Discovery PET/CT 710 scanner with TOF capability. All patients underwent PET/CT interim or end-of-treatment. All datasets were reconstructed using a 3D OSEM algorithm without, and with the inclusion of TOF information. Attenuation correction data were gathered from the CT low-dose images. Identical and matched volumes of interest (VOIs) were placed on the target lesions, aortic arch (blood pool), hepatic parenchyma and L4 vertebral body. The maximum standardized uptake value normalised with body weight (SUVmax-bw) was measured inside each VOI. Changes in SUVmax values (Δ SUVmax-bw) between the two reconstruction methods were calculated. The visual response to therapy assessment was carried out according to the Deauville 5-point scale (DS). Student's t-test was used to test for the significance of continuous data with Pearson's r as a measure of the linear correlation. Non parametric Mann-Whitney U test assessed the discrete distribution of DS. **Results:** The SUVmax-bw values were significantly higher in 3D OSEM TOF reconstructed images with a Δ SUVmax-bw in target lesions of 16% (from 8.64 to 10.02 g/ml, $P<0.001$), bone marrow of 9% (from 2.70 to 2.94 g/ml, $P<0.001$) and bloodpool of 6% (from 2.23 to 2.37 g/ml, $P<0.05$). There was an upward trend at the level of the hepatic parenchyma (Δ SUVmax-bw = 0.07 g/ml, $P=0.25$). A strong positive linear relationship was found between SUVmax-bw values in the target lesion ($r=0.99$), bone marrow ($r=0.91$), hepatic parenchyma ($r=0.75$) and only a moderate positive linear relationship for bloodpool ($r=0.65$). Visual assessment of target lesion based on DS indicate no difference between scores obtained with each reconstruction method ($P=0.64$). **Conclusions:** TOF based reconstruction significantly increased SUVmax-bw in target lesions, bloodpool and bone marrow, but not in hepatic parenchyma. Deauville scores were not influenced by the choice of PET reconstruction.

EP-0980**Robustness of iterative reconstruction resolution recovery in reducing time of myocardial perfusion SPECT data acquisition.**

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Objective: Recently, our group demonstrated the role of iterative image reconstruction with resolution recovery in minimizing the acquisition time in myocardial perfusion SPECT imaging (Khalil et al, 2016-S-1176-EANM) and (Taher et al, 2016-S-159-EANM). The aim of the current study was to evaluate the impact of acquisition time on the performance of state-of-art iterative reconstruction resolution recovery algorithm versus filter back projection applied in myocardial perfusion SPECT scan. **Methods:** Cardiac insert of standard volume 110 ml and two defects one solid located in the anterior wall and fillable insert placed in the inferior wall. The insert was positioned inside available cylindrical phantom filled with water to simulate image degrading factors (i.e. attenuation and scatter). Activity concentration was calculated using data of 10 random patients relating the injected activity to the system sensitivity. Thus, activity concentration of 8 uCi/ml and 2 uCi/ml was injected in the cardiac walls and background respectively. Two SPECT/CT scans were performed as in table 1. The CT attenuation map was created applying 20 mA tube current and 120 kV and helical scan over the whole length of the phantom. Two reconstruction algorithms FBP and iterative reconstruction corrected for collimator depth dependent, attenuation and scatter (IRACSCRR). Figures of merit used to evaluate the image quality of the reconstruction algorithms were slice count uniformity, Coefficient of Variation (CoV), SNR and CNR calculated for normally perfused myocardium walls while percentage defect contrast was used to evaluate hypo-perfused segments represented by cold defects. **Results:** IRR demonstrated a better performance in comparison to analytical method while reducing the acquisition time to one fourth of the conventional scheme. The SNR and CNR was better for normally perfused apical and basal slices. Furthermore, defect contrast percentage showed significant improvement for hypo-perfused segments. However, relatively high noise level in the image of IRR when compared to conventional method. **Conclusion:** The acquisition time reduction of iterative reconstruction with resolution recovery is superior to full time filter back projection. The slightly high level of noise has limited impact on the IRR with reduced acquisition time and could be negligible considering the improvement on other parameters. An extensive validation studies in comparison to gold standard technique is warranted.

EP-0981**Impact of different iterative metal artifact reduction (iMAR) algorithms on PET/CT attenuation correction in artifacts after port implantation**

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Purpose: To evaluate the impact of iterative metal artifact reduction (iMAR) algorithms on Hounsfield units (HU) and standardized uptake values (SUV) in bright-band artefacts caused by port catheter systems. **Material and methods:** In this prospective study, 30 oncological patients (12 female, 18 male, mean age 59.6±10.5y) with port chambers undergoing clinical indicated PET/CT on a Biograph mCT were included. An additional phantom scan was performed, consisted of a 25-L container containing a standard port catheter system in a solution of 18F-fluorodeoxyglucose (18F-FDG) and water. CT datasets were reconstructed on a dedicated workstation using standard weighted filtered back projection (WFBP) CT and three different iMAR algorithms (algorithm for dental filling (DF), hip and pacemaker (PM)). PET attenuation correction was performed with all four datasets. SUVmean and HU measurements were performed in fat and muscle tissue in the vicinity of the port chamber at the location with the most prominent bright band artifacts. Differences between HU and SUVmean values across all CT and PET-images were investigated using paired t-tests. Bonferroni correction was used to prevent alpha-error accumulation ($p < 0.008$). **Results:** In Comparison to WFBP (fat: 94.2 ± 53.9 HU, muscle: 197.6 ± 49.2 HU) all three iMAR algorithms led to a decrease of HU in bright band artifacts. iMAR-DF led to a decrease of 159.2% (fat: -51.9 ± 58.5 HU, muscle: 94.5 ± 55.3 HU), iMAR-hip of 138.3% (fat: -30.3 ± 58.5 , muscle: 70.4 ± 28.8) and iMAR-PM of 122.3% (fat: -21.2 ± 47.2 HU, muscle: 72.5 ± 25.1 HU; for all $p < 0.008$). There was no significant effect on SUVmean in bright band artifacts (SUVmean 0.48 ± 0.23 with WFBP, 0.43 ± 0.21 with iMAR-DF, 0.46 ± 0.22 with iMAR-hip and 0.47 ± 0.22 with iMAR-PM). Similar results were shown for HU and SUVmean measurements in the phantom scan. **Conclusion:** Using iMAR-CT images for attenuation correction of PET-datasets led to a significant change of HU values in artifacts caused by port catheter chambers in comparison to WFBP, which might impact the evaluation of adjacent tumorous lesions. However, these findings did not translate to significant differences in attenuation correction and consecutive changes in SUV.

EP-0982**Comparison of different metal artifact reduction (MAR) techniques in 18F-FDG PET/CT examinations: How do they impact attenuation correction in metal implants?**

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Purpose: To evaluate the impact of metal artifact reduction (MAR) algorithms on Hounsfield units (HU) and standardized uptake values (SUV) in bright band artefacts caused by metal implants. **Material and methods:** In this prospective study, 25 oncological patients (13 female, 12 male, mean age 70.3±13.0y) undergoing clinical indicated PET/CT on a Biograph mCT with 32

different metal implants were included. An additional phantom scan was performed, consisted of a 25-L container containing a standard port catheter system in a solution of 18F-fluorodeoxyglucose (18F-FDG) and water. CT datasets were reconstructed on a dedicated workstation using standard weighted filtered back projection (WFBP), metal artifact reduction in image space (MARIS) and iterative MAR (iMAR, using hip algorithm). PET attenuation correction was performed with all three datasets. SUVmean and HU measurements were performed in fatty tissue at the site of the most prominent bright band artifacts. Differences between HU and SUVmean values across all different reconstructions were investigated using paired t-tests. Bonferroni correction was used to prevent alpha-error accumulation ($p < 0.017$). **Results:** In the phantom scan, in comparison to WFBP (261.4 ± 98.8 HU), MARIS led to a non-significant mean decrease of 25.8% (197.4 ± 74.1 HU, $p > 0.017$), whereas iMAR-hip led to a significant decrease of 82% (48.0 ± 26.4 HU, $p < 0.017$). For SUVmean measurements in WFBP (1.147 ± 0.035), MARIS showed no significant effect (1.102 ± 0.090), while iMAR-hip led to a significant decrease of 16.4% (0.990 ± 0.075 , $p < 0.017$). Similar results were observed in the patient scans: MARIS led to a non-significant mean decrease of 8.1% (378.0 ± 331.0 HU) in comparison to WFBP (411.4 ± 309.2 HU), whereas iMAR-hip led to a significant decrease of 66.4% (138.4 ± 195.3 HU, $p < 0.017$). For SUVmean, MARIS showed no significant effect in comparison to WFBP (WFBP: 0.965 ± 0.380 , MARIS: 0.942 ± 0.372), while iMAR-hip led to a significant decrease of 11.3% (0.856 ± 0.321 , $p < 0.017$). **Conclusion:** iMAR significantly reduces bright band artifacts caused by metal implants in CT and thus leads to a significant decrease of SUVmean in bright band artifacts comparison to WFBP and MARIS. This has a direct effect on PET quantification if malignant tracer uptake is adjacent to metal implants.

EP-0983

Quantifying Lesions in Prostate Cancer Patients with PET/MRI: A Study on Impact of the Attenuation Map Generation Scheme

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Introduction: Both in clinical diagnostics and research, the whole-body MR-PET system Siemens Biograph mMR is a well-known imaging system. Several solutions for PET attenuation correction (AC) have been provided since its introduction in 2010, starting with a four-compartment (air, fat, water, soft tissue) AC scheme, initially based on a two-point DIXON-VIBE, which was gradually improved with each system upgrade. The most recent upgrade included a fifth compartment (major bones) and the MR field-of-view extension with HUGE, to compensate for truncations in the arms. We compared the impact of four AC methods, namely DIXON-VIBE, HUGE with bones, HUGE without bones, and MLAA, on lesion quantification in prostate cancer patients using [18F]-PSMA. **Methods:** This study was based on 48 prostate cancer patients, injected with (321.2 ± 44.4) MBq of [18F]-PSMA, subjected to a 30-minute PET/MR scan. The acquired images were reconstructed with the four AC methods using 3 iterations, 21 subsets, filtered with a 4 mm FWHM Gauss-

ian kernel. The results were assessed both qualitatively, employing visual analysis, and quantitatively, by examining SUVmean and SUVmax of 85 detected pelvic lesions (62 in soft tissue, 23 in bones) and their respective backgrounds. Having no absolute ground truth data, the results were compared using linear regression against DIXON-VIBE methodology. The significance in the differences between the four evaluated methods was analysed using the Wilcoxon rank-sum tests. **Results:** Between the four reconstruction methods, no significant visual differences were observed. For 62 soft-tissue lesions, with DIXON-VIBE as reference, the average bias in SUVmean for [HUGE with bones, HUGE without bones, MLAA] was [$3.34 \pm 1.81\%$, $1.57 \pm 1.42\%$, $4.34 \pm 2.52\%$], and in SUVmax [$3.37 \pm 1.67\%$, $1.53 \pm 1.20\%$, $4.32 \pm 2.49\%$]. For 23 bone lesions, we calculated average biases [$11.25 \pm 4.79\%$ ($R^2 = 0.955$), $3.32 \pm 2.79\%$, $4.99 \pm 2.75\%$] for SUVmean and [$10.64 \pm 4.49\%$ ($R^2 = 0.957$), $3.20 \pm 2.32\%$, $5.01 \pm 2.62\%$] for SUVmax. All remaining R^2 correlation coefficients were in the range 0.988–0.999. The Wilcoxon rank-sum tests showed no statistical significance. **Conclusion:** Deducing from these results, although the tracer uptake quantification in the less frequent bone lesions manifested, as expected, a noteworthy difference between DIXON-VIBE and HUGE with bones, for more common lesions, occurring in the soft tissue, no substantial difference was found between DIXON-VIBE and any of the other three evaluated AC methods. We therefore conclude including major bones and compensating for truncations in the arms did not significantly change tracer uptake quantification in pelvic soft-tissue lesions. Especially for serial studies, this finding suggests that stable MR-based whole-body AC does not depend on the actual degree of refinement.

EP-72

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Data analysis -> Neurology: data analysis and quantification

EP-0984

[¹²³I]-MIBG Turnover Estimated by Dynamic Planar Myocardial Scintigraphy

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Introduction: Despite the usefulness of [¹²³I]-MIBG myocardial scintigraphy in diagnosing Parkinson's disease and Lewy body dementia, performing two scans approximately three hours apart is burdensome. So, we aimed at omitting the second scan. Instead, we replaced the first one with a dynamic planar imaging procedure of 30 min, and analyzed the finely sampled TACs using a pharmacokinetic model similar to a [¹⁸F]-FDOPA inlet-and-outlet model (Kumakura et al., 2007). Then, we investigated the relationship between the conventional semi-quantitative indices and the new kinetic indices representing [¹²³I]-MIBG loss from myocardium as well as unidirectional uptake to catecholamine storage vesicles. **Subjects and Methods:** A

total of consecutive 67 subjects diagnosed/suspected of having symptoms of the aforementioned disorders were enrolled. We used a conventional two-detector SPECT camera (GE Discovery NM 630) equipped with ELEG collimators. The dynamic imaging was started immediately after a bolus injection of 111 MBq of [^{123}I]-MIBG. To obtain TAC-based “input functions”, we used a three-phase exponential decay function for smoothing mediastinum TACs, a population-based blood-to-plasma ratio (BPR) curve, and a population-based metabolite correction (PBMC) curve. The two correction curves were published by another group. (Wu et al., 2016). Besides, we used the smoothed mTACs for subtraction of cardiac blood pool radioactivity from heart TACs. We calculated magnitudes of the kinetic indices based on the FDOPA model by means of non-linear least squares optimization. Three indices representing unidirectional uptake (iUp), loss rate (iLoss), and fractional distribution equilibrated with the myocardial interstitial space were estimated. **Results:** The mean (SD) magnitudes of iUp, iLoss and iUp/iLoss were 0.139 (0.073), 0.051 (0.019) and 3.33 (2.22), respectively. The mean magnitudes of early HMR, delayed HMR and WR were 2.06 (0.61), 2.06 (0.84) and 0.38 (0.28), respectively. Linear regression analysis revealed that iUp/iLoss (an index of vesicular storage) was a significant predictor of early HMR (slope: 0.27, $P < 0.0001$, R^2 : 0.98). Likewise, 1/iLoss (min: an index for the pharmacological half-life of trapped [^{123}I]-MIBG) was a significant predictor of WR (slope: -0.0346, $P < 0.0001$, R^2 : 0.67) and the ratio of delayed HMR to early HMR (slope: 0.0167, $P < 0.0001$, R^2 : 0.58). **Discussion and Conclusion:** Although the absolute tomographic quantation is impossible, the 30 min planar dynamic imaging procedure is suited to estimate the kinetic indices of [^{123}I]-MIBG turnover in the cardiac sympathetic nerve terminals. In addition to keeping early HMR available, if necessary, delayed HMR and WR can be predicted from the new indices.

EP-0985

Generation of Oxygen Extraction Fraction like image from H_2^{15}O PET scan on the basis of Machine Learning

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Objectives: PET with ^{15}O -labeled tracers is capable of providing unique and essential information in patients with cerebro-vascular disorders, by means of quantitative images of cerebral blood flow (CBF), oxygen extraction fraction (OEF), and metabolic rate of oxygen. We have recently developed a novel DBFM method, allowing extremely short examination period of <10 min scan for CBF and OEF [1]. Also a computation method for appearance time of blood (ATB) on arterial territories was developed [2], suggesting that ATB delayed regions were similar to those of OEF elevated. It would be of interest to generate a similar image to OEF as OEF-like image from ATB image, namely only from a scan for CBF. This study was intended to generate an OEF-like image using CBF and ATB images applying the machine learning. **Methods:** PET measurement applying DBFM scan [1], was performed for patients with suspected disorders ($n=318$), involving ICA or MCA occlusion/stenosis, aneurism, and Moy-

moya disease. From the PET data, OEF, CBF and ATB images were obtained. Brain regions were separated into 64 segments using Free Surfer Program [3]. For each segment, OEF, CBF and ATB values were extracted. Then, the machine learning was applied to predict OEF difference between hemispheres, from segment information, CBF values and ATB differences between hemispheres. The data was separated to learning part with 80% and 20% for testing score of OEF prediction. Using the obtained machine learning weight data, OEF-like image was generated from CBF and ATB images, and that was compared to measured OEF image. **Results:** The correlation coefficient between differences of OEF and predicted OEF values in test was 0.65. The generated OEF-like images from CBF and ATB were similar distribution to that by PET measurement. Between the OEF and OEF-like images, correlation of differences between hemispheres was 0.55. **Conclusion:** The present results suggest that OEF-like image could provide similar information as the measured OEF. [1] Kudomi et al JCBFM (2013) 33; 440-448 [2] Kudomi et al EJNMMI Res (2013) 3; 41 [3] <https://surfer.nmr.mgh.harvard.edu/>

EP-0986

A method for automatic semi-quantification of DaTScan images using RBV correction

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Purpose: Clinical imaging with ^{123}I -FP-CIT SPECT (DaTScanTM) suffers from poor spatial resolution resulting in partial-volume effect in the striatal regions, which affects the subsequent semi-quantification. Definition of regions of interest for semi-quantification is further subject to user's experience and inter-observer variability. The results also depend on the number of slices taken into evaluation. The aim of this work has been to develop an automatic method for definition of volumes of interest using patient-specific MRI, to correct for partial-volume effect, and to optimize its parameters. **Method:** The procedure consists of three steps: (1) spatial pre-processing (MRI and SPECT/CT image registration and segmentation), (2) partial-volume correction in SPECT images, and (3) calculation of uptake indices in striatal regions. All image processing was performed using FMRIB software library. Partial-volume correction was performed by region-based voxel-wise (RBV) technique provided by PETPVC tool. Expected spatial resolution, as the key parameter for RBV correction, was determined using Jaszczak phantom. Uptake indices were calculated in the volumes-of-interest defined upon MRI data. Accuracy of the proposed method was verified using digital phantom. **Results:** It was possible to find a value of expected spatial resolution which provided complete uptake recovery in digital phantom simulation. This value was similar to result of Jaszczak phantom experiment. Testing the method with patient data showed strong influence of spatial (mis)alignment between SPECT and MRI on striatal uptake indices and suggested using hybrid SPECT/MRI imaging or SPECT/CT imaging with CT to MRI registration. The method fairly correlated with routine clinical assessment. Due to its nature, it did not exhibit any inter-observer variability. **Conclusion:** The pro-

posed method provides complete recovery of striatal uptake. It has a potential to reduce inter-observer variability, to completely avoid errors resulting from measurements in selected slices, to accurately define and localize volumes of interest, and to effectively suppress partial-volume effect. Its results can be used for research purposes. The method can be reproduced using publicly available software.

EP-0987

Investigation of Proper Evaluation Method of Effectiveness of Intravenous Immunoglobulin Therapy for Cerebellar Ataxia using Technetium-99m ECD-SPECT

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Purpose/Introduction: Positive effects of intravenous (IV) immunoglobulin (Ig) therapy for autoantibody-positive cerebellar ataxia from a viewpoint of cerebellar blood flow were previously reported. Some patients, however, had no improvements of cerebellar blood flow in visibility after the IV-Ig therapy, even some patients of them showed increased quantitative values of cerebellar blood flow after the therapy. The aim of this study is to examine the reason why this discrepancy between no improvement in visibility and increased quantitative values of cerebellar blood flow after IV-Ig therapy in patients with cerebellar ataxia arises. Appropriate evaluation methods of comparing cerebellar blood flow by single photon emission computed tomography (SPECT) were also examined. Subjects and **Methods:** Thirteen spinocerebellar degeneration (SCD) patients with cerebellar ataxia were included in this study. IV-Ig therapy for 5 days at 400 mg/kg/day was administered to all the patients. Six patients of them showed elevated anti-Glutamic Acid Decarboxylase (GAD) antibodies in cerebrospinal fluid (CSF). Values of brain blood flow in mL/100g/min of these patients before IV-Ig therapy (pre-IV-Ig) and after IV-Ig therapy (post-IV-Ig) were measured by Technetium-99m ethyl cysteinate dimer (ECD) SPECT using semi-quantitative Patlak-plot method with regions of interest (ROIs) placed on cerebellar hemispheres. The average blood flow values of ROIs on bilateral cerebellar hemispheres were utilized to compare cerebellar blood flow between pre-IV-Ig and post-IV-Ig. Two methods of evaluation were applied; Method 1, direct comparison of values of cerebellar blood flow between pre-IV-Ig and post-IV-Ig as previously reported, and Method 2, comparison of values of ratios of cerebellar blood flow to cerebral blood flow (Cerebellar/CBF ratio) between pre-IV-Ig and post-IV-Ig. The statistical difference was evaluated by Wilcoxon t-test. **Results:** Values of cerebellar blood flow increased in 6 cases (54%) using Method 1, i.e., direct comparison between pre-IV-Ig and post-IV-Ig. Values of ratios of Cerebellar/CBF ratio using Method 2, on the contrary, showed no statistically significant differences between pre-IV-Ig and post-IV-Ig in grouped comparison by Wilcoxon t-test ($P=0.256$). Only two cases (15%) showed prominent increased values of Cerebellar/CBF ratio after IV-Ig therapy using Method 2. **Conclusion:** The apparent improvement of cerebellar blood flow values after IV-Ig therapy was due to improvement of values of whole brain blood flow,

not only cerebellar blood flow. Two cases showed true improvement of values of cerebellar blood flow after IV-Ig therapy, properly judging from methods using Cerebellar/CBF ratios.

EP-0988

SPM analysis of FP-CIT SPECT scans: do we need optimization of preprocessing parameters?

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Purpose: To investigate the best parameters to apply during the preprocessing phase of a Statistical Parametric Mapping (SPM) analysis of FP-CIT SPECT images, in order to obtain the most statistically significant results in the comparison between Parkinson's Disease (PD) patients and controls. **Methods:** We selected a group of 75 patients with clinically confirmed diagnosis of PD, and a group of 100 controls, with a clinical follow-up of at least 2 years confirming no neurodegenerative disease. All subjects underwent FP-CIT SPECT imaging, according to the EANM guidelines, reconstructed using OSEM algorithm (4 iterations; 10 subsets). PD scans were flipped according to the most affected side, so that all PD scans demonstrated prevalent left-sided degeneration. All scans were spatially normalized using a dedicated FP-CIT template and applying different "source image smoothing" FWHM of 4mm (w4), 6mm (w6), 8mm (w8), 10mm (w10) and 12mm (w12). All normalized images were then smoothed applying different FWHM Gaussian kernels, from 4mm (s4) to 12mm (s12). For all the 25 different combinations, a two-sample t-test PD vs controls, (FWE-corrected $p<0.05$, age and gender as nuisance variables) was performed. **Results:** All SPM8 analyses PD<controls showed three different clusters of significantly reduced uptake in left striatum (putamen and caudate), right striatum (putamen and caudate) and midbrain. T-values ranged from 16.76 (w12s4) to 18.82 (w8s10) in most affected striatum, from 16.13 (w12s4) to 17.46 (w6s8 and w6s10) in less affected striatum and from 3.93 (w12s10) to 4.85 (w4s4) in midbrain. **Discussion:** The optimal combination of normalization and smoothing parameters appears to be different depending on the regional uptake difference between patients and controls. These results could be taken into account when performing group or single-patient SPM analyses with FP-CIT scans, in order to optimize the results.

EP-0989

Usefulness of Classification of Amyloid PET Images by Use of Textural Features

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Purpose/Introduction: The purpose of this study is to investigate the usefulness of classification of amyloid PET images between Alzheimer's disease (AD) and normal control (NC)

groups by use of textural features such as gray level co-occurrence matrix (GLCM) and gray level run length matrix. Subjects & **Methods:** We used Alzheimer's Disease Neuroimaging Initiative (ADNI) database (NC, 100; AD, 100) and a basal ganglion slice of ^{18}F -florbetapir PET images. Then, image textural features obtained from GLCM and GLRLM. PET images were classifying to AD and NC groups by support vector machine. Classification accuracy was tested by cross validation test and ROC analysis, and compare to standardized uptake value ratio (SUVR). **Results:** The classification accuracy of using textural features between AD and NC were as follows; sensitivity, 93.0%; specificity, 89.5%; AUC, 0.92. Furthermore, classification accuracy of SUVR was lower than that of textural features. **Discussion & Conclusion:** Textural features obtained from amyloid PET images could be useful for classifying AD and NC groups.

EP-0990

Evaluation of Different Methods for SUVR Calculations to Classify Subjects in [^{11}C]PiB PET Imaging

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Purpose/Introduction: The use of biomarkers in research diagnostic criteria for Alzheimer's disease, such as amyloid PET imaging, requires that individuals are categorized as either normal or abnormal. Several methods and cutoff values can be found in literature to define positive and negative subjects. Under these circumstances, standardization and quantitative accuracy of PET studies are mandatory. The aim of this work was to evaluate the application of different methods for standardized uptake value ratio (SUVR) calculations to classify subjects in [^{11}C]PiB PET imaging. **Subjects & Methods:** Ten healthy older adults (3 males and 7 females, mean age = 70 ± 14 y; range = 51–91 y) underwent dynamic PET imaging with [^{11}C]PiB for 90 minutes using list mode data acquisition. Mean injected activity was (388 ± 210) MBq. Reconstruction included corrections for attenuation, scatter, random coincidences and dead time. Static images were generated at two time frames (30–60 and 50–70 minutes, post-injection), coregistered with volumetric MRI and normalized to MNI space, using PVELab (v.2016). Volumes of Interest (VOIs) were delineated based on atlas provided by the software (modified Tailarach). Three PVC methods were tested: Meltzer, Müller-Gartner and Müller-Gartner-Rousset. The regions analyzed for SUVR were: frontal, parietal, temporal, anterior cingulate and posterior cingulate cortex. Two methods were used for SUVR calculation: (a) using volume weighted average of the median uptake in 30–60 min time frame and a cutoff value of 1.42; (b) using mean uptake of 50–70 min time frame and a cutoff value of 1.51. Both methods use cerebellum gray matter as reference region. Medical history of neurologic/psychiatric condition was considered an exclusion criterion. Individuals were required to perform within average for age and education in RAVLT and MMSE tests. **Results:** All methods showed that SUVR increases with age. Average SUVR, without PVC, for (a) and (b) were (1.20 ± 0.21) and (1.24 ± 0.22) and Pearson's correlation co-

efficient was 0.99 ($p < 0.05$). Only one healthy subject was above cutoff value for both methods. When performing PVC, average SUVR presented higher values and significant differences ($p < 0.05$). Then, two previously PIB-negative subjects were then classified above cutoff, for both time frames. **Conclusion:** We highlight the importance of a standardized method for [^{11}C]PiB processing in research settings. SUVR is affected by time frame and PVC choices, over or underestimating amyloid burden. Misclassification of individuals may ultimately impact in biased conclusions and ethical issues. Further studies should include larger sample in order to establish a reliable method for [^{11}C]PiB quantification and subjects' classification.

EP-0991

Visual and semiquantitative analysis of FDG PET brain images of patients with dementia

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Purpose: F-18 FDG PET brain imaging is commonly used in the early detection and differential diagnosis of various subtypes of dementias. In addition to visual assessment of the images various commercially available semiquantitative (SQ) analysis programs are also used to find regions with metabolic abnormality. In this retrospective study, we aimed to determine the certain limitations of SQ analysis programs in detecting regional metabolic changes in patients with dementia. **Subjects and Methods:** FDG PET/CT brain images of 39 patients with history of dementia were analyzed both visually and semiquantitatively. Using the visually markedly abnormal FDG PET images as standard, we wanted to test the accuracy of 2 commercially available SQ analysis programs. Gray and color scales were used to assess PET images visually. SQ analysis results were classified as matching, partially matching and non-matching with visually markedly abnormal studies. **Results:** On visual analysis, FDG PET showed marked regional hypometabolism in 19 patients. SQ analysis-1 results matched with visual analysis in 8 patients (42.1 %) and partially matched in 11. SQ analysis-2 findings were matched with visual analysis in 11 patients (57.8%) and partially matched in 7 and did not match in 1. Both SQ programs also showed additional areas of various degree of abnormalities in all patients which were not seen visually. PET showed mild abnormalities in 12 and was normal in 8 patients on visual analysis in which SQ analysis showed various degree of regional abnormalities in all of these patients. Visual inspection of image registration and automated selection of areas by SQ analysis programs showed varying degree of suboptimal results in all patients. Overall, reviewing images in color scale better demonstrated the hypometabolic regions as compared to gray scale. MIP image was helpful in displaying regional abnormalities in 3D presentation. Of note, marked regional hypometabolism was either on the left side of the brain or was more significant on the left than the right in 63% of patients. **Conclusion:** FDG PET brain imaging is useful in patients with dementia. When there is visu-

ally obvious regional hypometabolism, SQ analysis may not be needed. Due to suboptimal image registration and selection of brain areas, SQ analysis with commercially available programs may provide inaccurate results for regional changes in certain areas. When reporting SQ analysis results, image registration and selection of areas with these programs should be checked carefully to provide accurate results.

EP-73

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Data analysis -> Quality control, performance and standardization

EP-0992

Development of a New Method for the Microbiological Analysis of Iodine-131

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Purpose: The main aim of this study is to develop a new microbiological control method for the solution of iodine 131 in a closed system for radiopharmacy services not equipped with a class A Hot Cell dedicated to perform microbiological analysis according to GMP requirements. **Subjects & Methods:** The method is based on the preparation of perforated petri dishes containing three culture media. The perforation of the Petri dishes was realized under a class A laminar flow hood using a heated metal cylindrical rod. A sterile magnetic stir bar was then placed in each Petri dish before closing the hole and sealing Petri dishes with autoclaving adhesive. First, the method was tested inside a class C room then inside an unclassified area by perforating the adhesive with a sterile syringe and injecting a volume of sterile water before the perforation was closed by a second sterile adhesive. Seeding was performed by moving each Petri dish on a magnet. Then the Petri dishes were incubated inside the Hot Cell at room temperature for Yeast and Mold and at 32.5 °C for Total Aerobic Microbial and Total Coliform. A positive control (bacterial suspension) and a negative control (sterile water) were performed for each culture medium. Finally, the method was tested inside a class C Hot Cell for three production batches of sterile iodine-131 following the same protocol. **Results:** After 5 days incubation at 32.5°C and 7 days at room temperature, The Petri dishes were sterile for both tests performed in class C room and for the unclassified room. The same result was obtained with the solution of iodine-131 in the three production batches. **Conclusion:** This new method has shown good efficiency to keep the sterility of culture medium during the microbiological analysis independently of the environmental class. It could be adopted by radiopharmacy services to perform the microbiological quality control of the solution of iodine-131 and other radiopharmaceuticals. This method would make it possible to carry out the microbiological analysis of radiopharmaceuticals quickly without waiting for the decay. Moreover, it allows to minimize the risk of exposure of the laboratory technicians by iodine inhalation.

EP-0993

Justification For A Quadratic FDG-dose Regimen With Digital PET Imaging

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Introduction: Recently, digital PET systems were introduced with timing resolutions near 300 picoseconds (ps). In particular, PET image quality of obese patients may improve with this higher TR. We evaluated the impact of a digital PET system on image quality when using a quadratic bodyweight-dependent FDG-dose regimen. **Subjects & Methods:** We performed 41 PET/CT scans on a digital PET system (Vereos, Philips Healthcare) with a measured TR of 307 ps. As prescribed by European guidelines, we used a quadratic relation between administered FDG-dose and patient's body weight $A = 4.4 \cdot w^2 \cdot t$ with A the administered dose (MBq), w the patient's bodyweight (kilogram) and t the scan time per bed position (sec). For all patients, PET data were reconstructed using three protocols: a protocol with $4 \times 4 \times 4$ mm³ voxels that fulfils EANM accreditation specifications, a high-resolution protocol with $2 \times 2 \times 2$ mm³ voxels and an ultra-high resolution protocol with $1 \times 1 \times 1$ mm³ voxels. On each reconstruction, we determined the signal-to-noise ratio (SNR) in the liver as a measure of image quality. The SNR was defined as the ratio between the mean pixel value and the standard deviation, in a ROI of 1800 mm² in three axial slices in a homogenous area of the liver. **Results:** Average bodyweight across all patients was 79 kg (range 50-137 kg). The use of a quadratic FDG-dose regimen resulted in a SNR that was independent of the patient body weight ($p > 0.05$), for all three reconstructions. Meanwhile, the SNR in the liver decreased when using smaller voxels. SNR decreased from 12.8 ($4 \times 4 \times 4$ mm³ voxels) to 6.2 ($2 \times 2 \times 2$ mm³ voxels) to 5.7 ($1 \times 1 \times 1$ mm³ voxels). **Conclusion:** To obtain a constant image quality on digital PET scans with a timing resolution near 300 ps, it is justified to use a quadratic FDG-dose regimen that takes into account patient's bodyweight.

EP-0994

Phantom study of the relationship between the signal-to-noise-ratio and the patient noise equivalent count for a BSMR algorithm

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Aim: To study the relationship between patient Noise Equivalent Count (pNEC) and image quality for a commercial BSMR algorithm, in order to optimize image quality by means of the optimum penalization factor. **Methods:** A NEMA Body IEC phantom was used on a 5 rings Discovery IQ PET/CT. All spheres were

filled with a background concentration of 20 kBq/ml at acquisition time, and a lesion-to-background activity of 8:1. The phantom was acquired during 4.5 hours, until a background concentration of 3.4 kBq/ml was achieved. The phantom was acquired in list mode, and reconstructed in 27 frames at intervals of 10 min. Acquisition time was 33 s for the first frame, and the subsequent frames were corrected by decay to have similar counts per frame, until 2.52 min in the last frame. Images were reconstructed in a 256x256 matrix, using the commercial algorithm Q.Clear with penalized factors of 50, 200, 350, 500 and 1000. Total true counts ratio and pNEC values were calculated from the image DICOM header. Mean values and standard deviation were computed from an homogeneous zone of a phantom using 200 non-adjacent pixels in a volume of interest of 3000 pixels. The Signal-to-Noise ratios (SNR) were computed as the mean pixel value divided by the standard deviation. The squared values of SNR were plotted vs. the pNEC. **Results:** Linear response of the SNR² vs the pNEC decreased as the penalized factor increased. R squared values were 0.87, 0.78, 0.74, 0.70, 0.4 for the penalized factors of 50, 200, 350, 500 and 1000, respectively. In On the other hand, the slope of the regression increased from 304, 1741, 3226, and 5377 for the same range of penalized factor, in units of SNR² gain per kcps. These results suggest that there is a gain in the computed SNR as pNEC increase, which increases as the penalized factor increase, although the relation loses its linearity for higher penalizations. **Conclusions:** For the scanner and reconstructions used, the relation between SNR and the pNEC depends on the penalization factor. However, the reliability of predicting image quality from pNEC depends on the penalization factors, implying that there could be an image quality gain modifying the penalization factor depending on the pNEC.

EP-0995

Improving the accuracy of image evaluation in clinical positron emission tomography/computed tomography examination by using Monte Carlo simulation

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As quantification using positron emission tomography/computed tomography (PET/CT) has become commonplace, concerns about standardization have been raised. Noise equivalent count density (NECd) is an indicator of image evaluation. NECd represents the count contributing to image quality, per unit volume of the patient, taking into account scatter and random coincidences. A scatter fraction (SF) is necessary to calculate the

NECd; however, it cannot be measured in clinical PET/CT examination. In this study, we estimated the SF for each patient using Monte Carlo (MC) simulation. We used the Geant4 as an MC code and simulated Discovery ST Elite (DSTE) and Biograph mCT/PET devices. Clinical images included in this study were acquired from 15 patients without tumors, between November 2016 and January 2017. An anthropomorphic phantom was constructed from the CT images, and the radioactive source was arranged based on the PET images. To verify the validity of the calculation geometry, the SF was calculated by MC simulation based on the National Electrical Manufacturers Association (NEMA) method using a phantom cylinder phantom, and compared to device-fixed SF. We calculated SFs using clinical data in each table position and compared them to SFs written in Digital Imaging and Communications in Medicine (DICOM) header in DSTE. In addition to this, we calculated NECds using device-fixed SFs and estimated SFs, and two one-sided tests were performed. SFs calculated using a phantom cylinder in both devices coincided exactly with the device-fixed SF (36% and 34%). The SFs of the clinical data calculated using DSTE and mCT were 36±2.4% and 35±2.3%, respectively. The correlations in the DSTE data between body mass index and SFs, and between patient volume and SFs were 0.55 and 0.54, respectively. The SFs estimated by MC simulation were approximately 2% lower than those written in the DICOM header, and the correlation between both values was 0.67. There were no differences between NECds using device-fixed SF and estimated SFs, with the margin being 0.15. Calculation geometry was validated by SFs that matched the device-fixed SF. Estimated SFs were distributed around a device-fixed SF. The effect of difference of SFs on NECd was small. We could reliably estimate SFs for each patient from the PET/CT images, using MC simulation. Based on these data, we postulate that the use of device-fixed SF to calculate NECd is feasible and reliable.

EP-0996

Design of reference material for image unit of positron emission tomography

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Harmonization of quantification parameters of positron emission tomography (PET) is important for longitudinal therapy monitoring and multi-center trials. The reference material is required for calibration and testing. The most commonly used quantity of PET is standard uptake value (SUV), and SUV is based on the unit of image voxels; Bq/ml (or kBq/ml). In this study, we designed Bq/ml reference material using fluorine-18-FDG. Dose calibrator, electric balance, weight set, thermometer and barometer those were used in this study were calibrated by Korea research institute of standards and science. To obtain uncertainty of radioactivity measurement linearity, about 370 MBq FDG were continuously measured during 30 hours. To obtain uncertainty of volume effect of radioactive solution in dose calibrator, 2, 3, 5 and 10 ml volume in vial were measured. Using measured temperature and air pressure, weight (g) of FDG solution was converted to volume (ml) under the assumption of FDG solu-

tion has equal density with water because volume of FDG in FDG solution was meaningless. Evaporation rate of FDG solution also measured during 24 hours on electric balance to acquire uncertainty of evaporation effect of solution in vial. Precisely measured Bq/ml of FDG solution was filled in 2 type of reference material of disk type phantom, 80 mm diameter with 20 mm thickness and 56 mm diameter with 20 mm thickness. The relative standard uncertainty of radioactivity measurement (dose calibrator), linearity of radioactivity, volume effect of radioactive solution measurement, decay correction and measurement statistics were 1.5%, 0.02%, 0.5%, 0.05 and 0.02%, respectively. The relative standard uncertainty of mass measurement (electric balance), volume of solution and solution evaporation were 0.5%, 0.1% and 0.2% respectively. Finally, extended uncertainty was calculated as 3.4% ($k=2$). The extended uncertainty of our Bq/ml reference material is sufficient for calibration and testing of PET systems. This reference material can contribute to harmonization of PET systems and finally, improve diagnostic accuracy.

EP-0997

Personalized radioiodine uptake measurement with g-camera planar images using 3D realistic thyroid phantoms in a multi-centre study

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Purpose: According to the EANM recommendations for benign thyroid diseases therapy, the absorbed dose should be personalized. Consequently, the iodine thyroid uptake should be accurately measured with γ -camera or NaI probe. Calibration phantoms are quite crude representations of neck anatomy. Therefore a set of realistic thyroid phantoms with varying volumes (3.2 - 30 cm³) representative of pediatric and adult patients were developed and 3D printed to investigate the precision of a standard calibration procedure when assessing thyroid uptakes. Additionally, a new calibration procedure that reduces the volume effect and the user-dependent choice of ROI was developed.

Materials and Methods: For measurements, the thyroid phantoms were filled with ¹²³I and ¹³¹I liquid solutions. The multi-centre study has been realized with 4 gamma-cameras at 3 French nuclear medicine departments. For ¹²³I measurements, Siemens Symbia T2 and S γ -cameras with LEHR collimators were used. The ¹³¹I measurements were realized using a Siemens Symbia T2 and a GE Discovery NMCT670 with HE collimators. The phantoms were imaged for three distances between the γ -camera and the table (10, 20 and 30 cm), in order to check the standard uptake measurements. Furthermore, a new calibration procedure simply consisting in defining an optimum threshold for image processing was developed. **Results:** The standard calibration procedure was found to often underestimate thyroid activity when compared to the realistic phantom calibration. More precisely for ¹²³I, the difference in activity was between +5% and -21%,

depending on the distance between the γ -camera and the table, the thyroid volume and the γ -camera model. The threshold is distance dependent but volume- independent and makes it possible to measure the uptake with an uncertainty limited to 7% for ¹²³I. Contrary to some literature claims, the present experiments show limited (<6%) impact of thyroid volume on uptake assessment. **Conclusion:** In current routine clinical practice, thyroid uptake is often underestimated indicating that the therapeutic activity given to patient could be reduced by at least 30% should the new calibration protocol based on realistic thyroid phantoms be used. A proper and simple image processing adapted to the clinical practice could also improve the calibration of gamma-cameras. ¹³¹I data require further analysis. A retrospective study is underway to estimate the difference between planned doses and delivered thyroid doses when patient uptake is measured according to the developed protocol.

EP-0998

Measurement of Red Cell Mass: Development of new software for standardization of results

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Objective: To develop and validate a software tool for red cell mass calculation (RCM) and standardize practices. **Material and Methods:** Local protocols and local Excel spreadsheet of two French centers (Toulouse, Dijon) have been reviewed to identify protocols differences needed to be taken account in the software tool. A free and open source software tool (GPL License - petctviewer.org project) has been developed in JAVA language for red-cell mass calculation using the counting results of the etalon and blood samples of both centers. The software has been retrospectively validated using dataset of patients from these two centers and one additional French center for external validation (Besancon). In all centers, erythrocytes were labeled in vitro with ⁵¹-Cr and injected to patients. Blood samples were collected at different time after Injection and measurement was made according to each local protocol. Recorded values were used to calculate RCM with the developed new software. **Results:** The software is provided as a standalone package with no installation process and was used by the radiopharmacists of each three centers following the provided quick user guide. The software was able to run on any operating system. For 46 patients (22 from Toulouse, 12 from Dijon and 11 from Besancon) the new software was compared to local Excel-based calculation for each hospital (using their own protocol for radiolabeling erythrocyte). The mean absolute difference of calculated red cell mass and plasma volume was 2.11% and 1.97% (Toulouse: 2.79%; 2.60% / Dijon: 1.04%; 1.06% / Besancon: 1.91%; 1.68%). The final conclusion was never modified for any patient. **Conclusion:** We provide a validated, free open source software taking account of the diversity of RCM measurement protocols. This new software is made for standardization of the determination and result report of RCM.

EP-0999

Clinical experience of ^{18}F -FDG-PET/CT performed with the low-dose injection of ^{18}F -FDG

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Aim: In Japanese clinical center without cyclotron, ^{18}F -FDG-PET/CT examinations are performed using commercial ^{18}F -FDG delivery. ^{18}F -FDG delivery may be delayed due to the traffic condition mainly under the influence of natural disasters. We experienced cases underwent ^{18}F -FDG-PET/CT with the low-dose injection of ^{18}F -FDG in such situations. The aim of this study was to evaluate the image quality of ^{18}F -FDG-PET/CT performed with the low-dose injection of ^{18}F -FDG (<2 MBq/kg). **Materials and Methods:** This retrospective study population consisted of consecutive 28 patients (22 males and 6 females; mean 65.6; range 20-91 years) who underwent ^{18}F -FDG-PET/CT with low-dose ^{18}F -FDG injection (mean 1.77 ± 0.22 ; range 1.19-1.99 MBq/kg) because of delay in ^{18}F -FDG delivery due to traffic conditions from January 2016 to December 2017. The image acquisition time was extended (mean 1.26 ± 0.19 ; range 1.0-1.6 times/bed) sometimes. The image quality was evaluated by visual analysis using a 5-point scale (5:excellent, 4:good, 3:acceptable, 2:poor, 1:unreadable) and quantitative analysis using the liver signal to noise ratio ($\text{SNR}_{\text{liver}}$). Spearman rank correlation was used to assess the relationship between image quality and the following factors; injected ^{18}F -FDG dose (MBq/kg), body mass index (BMI), acquisition time and blood sugar level. Among 28 patients, 13 patients also underwent ^{18}F -FDG-PET/CT with the routine ^{18}F -FDG dose injection (2 to 5 MBq/kg) on another occasion. For these 13 patients, the difference of image quality between low-dose and routine-dose ^{18}F -FDG was assessed using Wilcoxon signed-rank test. **Results:** In visual analysis, only 2 cases were rated as poor while the remaining 26 cases were above acceptable (visual score: mean 3.32 ± 0.60 ; range 2-4). As for the visual score, no significant correlation was observed with injected ^{18}F -FDG dose nor acquisition time while a significant correlation was observed with BMI ($P < 0.001$, $\rho = -0.748$). As for the $\text{SNR}_{\text{liver}}$, significant correlations were observed with injected ^{18}F -FDG dose ($P = 0.006$, $\rho = 0.504$), acquisition time ($P = 0.005$, $\rho = 0.520$) and BMI ($P = 0.004$, $\rho = -0.523$). Neither the visual score nor the $\text{SNR}_{\text{liver}}$ was significantly correlated with blood glucose level. In the 13 patients who underwent both low-dose and routine-dose scans, both visual score and $\text{SNR}_{\text{liver}}$ with low-dose ^{18}F -FDG-PET/CT were significantly lower than those of routine-dose ^{18}F -FDG-PET/CT ($P = 0.035$ and $P = 0.001$, respectively). **Conclusion:** The image quality was degraded in examinations with low-dose ^{18}F -FDG injection compared to routine examinations despite the extending acquisition time. The degradation of image quality tended to be seen in patients with high BMI. Nevertheless, the image quality with low-dose ^{18}F -FDG injection was almost acceptable for interpretation of the ^{18}F -FDG-PET/CT image.

EP-1000

Management of Brown Fat Tissue activation during oncological ^{18}F -FDG PET/CT in Northern Greece

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Purpose/Introduction: Cold activated brown fat tissue (aBFT) appearance on ^{18}F -FDG PET/CT, may potentially hamper diagnosis. aBFT frequency varies widely with climate and patient preparation. Minimization of aBFT appearance is primarily based on proper patient preparation, although pharmacological intervention with β -blockers or benzodiazepines has also been proposed. As Northern Greece (NG) including Thessaloniki, is the colder district of the country, the frequency of aBFT appearance would be expected substantial. The purpose of the study is to explore the frequency and seasonal distribution of BFT appearance in NG on ^{18}F -FDG PET/CT and the assess the need for pharmacological intervention. **Patients and Methods:** The monthly average minimum temperature (AmT) in Thessaloniki, Athens and Crete were obtained from the of the Hellenic National Meteorological Service records. Three thousand sequential ^{18}F -FDG PET/CT studies, performed in our center in children and adults NG patients from January 2016 to April 2018, were enrolled. All patients had previously receive oral, detailed, seasonally modified instructions for cold exposure avoidance the day before and the day of the test and rested calm in a $26\text{--}28^\circ\text{C}$ environment for 1 hour after ^{18}F -FDG administration. Patients were divided in two groups, with (aBFT+) and without (aBFT-) visible aBFT. Female sex (F), age, Body Mass Index (BMI), blood glucose level (GL) and frequency of mainly nodal pathology (lymphomas, sarcoidosis, lymphadenopathy) were determined for both aBFT groups. **Results:** Thessaloniki (40.6401°N , 22.9444°E), compared to Athens and Crete has permanently lower AmT , being lowest during January (1.3 vs 5.2 και 9.0°C , respectively). Thirty-six aBFT+ patients (1.2% of the total) were identified, with 3 monthly maxima, at January (2.8%), November (2.1%) and March (2.1%). BFT+ and BFT- groups significantly differed ($p < 0.05$) in F sex (75 vs 39%), age (33.1 ± 15.9 vs 58.6 ± 16.3 years), BMI (23.2 ± 6.0 vs 27.6 ± 6.0 kg/m^2), GL (96.8 ± 11.9 vs 107.0 ± 21.5 mg/dL) και nodal disease frequency (69 vs 22%). **Conclusion:** After proper patient preparation, the average frequency of aBFT appearance on ^{18}F -FDG PET/CT in the colder area of Greece is low. Accordingly, generalized use of pharmacological intervention for suppression of aBFT appearance is not justified both in Greece as well as in countries with similar climate. Moreover, as the risk factors for aBFT appearance (coldest month, season change, younger age, female sex, lower BMI, nodal disease) are easily recognizable, individualized, seasonally modified, instructions to the patients could also further reduce the seasonal peaks of aBFT appearance on ^{18}F -FDG PET/CT.

EP-74

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Instrumentation -> General aspects

EP-1001

Dose optimization of pediatric renography using simplified automated dynamic phantom

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Objective: Renography is used for diagnostic evaluation of pediatric patients with suspected obstruction of the urinary tract or impaired renal function. Pediatric dose guidelines including the recommended administered doses have been published by major nuclear medicine societies. As the acquisition counts in dynamic scintigraphy are affected by the administered doses and sensitivity of the scintillation camera, the scan procedure should be determined individually. In this study, we evaluated the feasibility of simplified automated dynamic phantom for the dose optimization in the pediatric renography. **Methods:** The simplified automated dynamic phantom was consisted of three components (infusion, kidney-simulation, and drainage sections). The infusion parameters on the syringe pump were optimized by comparing the time activity curves so that they can match the normal clinical model. For dose optimization, the administered dose was fixed as 3 MBq and the effect of attenuation was also evaluated by applying the equivalent solid phantom. The time-points of the maximum counts (T_{max}), those of two-thirds and one-half from the maximum counts ($T_{2/3}$ and $T_{1/2}$) were compared between the normal and the optimized model. **Results:** The infusion rates were optimized as 42, 1.0, 0.60 and 0.30 mL/min in the arterial (0-10 seconds), secretory (10-430 seconds), early-excretory (430-550 seconds), and late-excretory phase (550-1200 seconds), respectively. T_{max} , $T_{2/3}$ and $T_{1/2}$ of normal model were 242 ± 15.3 , 220 ± 10.0 and 317 ± 25.2 seconds, respectively. For optimized model, the T_{max} , $T_{2/3}$ and $T_{1/2}$ values were 242 ± 5.8 , 213 ± 11.5 and 310 ± 17.3 sec, respectively. There was no significant difference of these parameters. **Conclusions:** A simplified automated dynamic phantom for pediatric renography was constructed by several commonly products. We also demonstrated the dose optimization under the guidelines for pediatric renography. Our phantom can be widely used to determine the appropriate scan protocol and the dose optimization.

EP-1002

Initial Experience in Children Using Solid State SPECT/CT Gamma Camera for I-123 mIBG Imaging

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Purpose: To share the initial experience of planar and SPECT/CT imaging using full-field of view solid state detector general purpose SPECT/CT gamma camera for I-123 mIBG imaging

in children. **Subjects and Methods:** Since November 2017 we have utilized full-field of view cadmium zinc telluride (CZT) detector gamma camera to image children with neuroblastoma who have required I-123 mIBG imaging for staging and response assessment. Whole-body planar, SPECT, and SPECT/CT studies were performed in 24 patients with a total of 39 scans performed. There were 28 males and 11 females ranging in age from 1.6-18.4 years. For all these initial studies, we did not vary the dose of I-123 mIBG administered compared to our previous imaging with standard sodium iodide detector gamma camera. Initial acquisition parameters were similar to what was previously performed on prior equipment and then modified as required with change in acquisition time for planar whole-body or SPECT imaging. **Results:** All obtained scans were able to be interpreted. Improved in-plane resolution was noted for focal structures and lesions compared to prior studies in some of our patients on conventional sodium iodide crystal detector gamma cameras. There was an inherent increase in background activity noted with CZT imaging due to the low energy high resolution collimator utilized. Improvement in resolution was noted by changes to imaging times for planar and SPECT imaging. Acquisition in LIST mode allowed multiple processing options post acquiring of the studies including optimizing the energy window selection to benefit from the improvement in CZT energy resolution. **Conclusion:** Full-field of view solid state detector general purpose SPECT/CT camera can be utilized for planar and SPECT imaging of I-123 mIBG in children. Further modifications to hardware, acquisition parameters, and processing may further optimize images obtained with this technology.

EP-75

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Instrumentation -> Imaging guided surgery

EP-1003

PET/CT guided biopsy in lymphoma patients

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Biopsy of affected tissue is required for lymphoma diagnosis at onset and relapse and to plan adequate treatment. Open incisional biopsy (OIB) is traditionally the method of choice, providing an accuracy of approximately 100%. OIB is very expensive and is associated with several drawbacks (morbidity, surgical complications, tumor contamination of surrounding tissues). The development of imaging-guided biopsies (ultrasound, computed tomography) has almost overcome these disadvantages. However, in recent literature a variable amount of non-diagnostic procedures is reported, leading to an accuracy ranging between 50%-80%. FDG PET/CT is a functional imaging technique highlighting areas of active malignancy/infection with a

very high sensitivity in comparison to conventional imaging. It detects abnormal signals even before cancer-related morphological changes occur, and can accurately discriminate between fibrous residual tissue after therapy and disease persistence or relapse. It can potentially be used to drive the biopsy to the most active lymph node or to the most active area within a suspect mass, without increasing the risk related to the procedure for the patients. One hundred patients with suspect lymphoma at onset or relapse are expected to be enrolled in 3 years, provided they show FDG-avid findings. Patients are excluded if pregnant, breastfeeding or in case PET/CT guided biopsy is contraindicated. Diagnostic accuracy will be compared to published data concerning conventional imaging. Specimen adequacy will also be evaluated. The trial is supported by the Italian Association for Cancer Research (Progetto AIRC IG 2015 Id 177781). Data are available for the first 65 procedures. 3 procedures have been interrupted because of pain but could be successfully repeated in 2 cases. Biopsy target was lymph node in 42 and extra-nodal site in 23 (bone, soft tissues, liver and kidney). Median SUV max of target lesions was (10.8 ± 5.6). Insufficient samples were obtained in 4 (6%), while in all the other instances the sample was considered adequate to formulate a diagnosis. Mean sample length was (11.0 ± 5.4) mm. The mean amount of affected tissue in collected samples was 75%. No severe adverse events were reported during or after each procedure. These preliminary results prove that FDG PET/CT guided biopsy is feasible in the clinical practice. Furthermore it positively impacted on the time to treatment onset in those pts who presented with a previous non diagnostic biopsy.

EP-1004

FreehandSPECT with ^{99m}Tc -HDP can be used to guide percutaneous biopsy of skeletal lesions detected on bone scintigraphy

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Purpose: To assess the feasibility of using freehand Single Photon Emission Computed Tomography (freehandSPECT) for the identification of technetium-99m-hydroxydiphosphonate (^{99m}Tc -HDP) positive bone lesions and to evaluate the possibility of using these imaging data-sets for augmented- and virtual-reality based navigation approaches. **Methods:** In 20 consecutive patients referred for scintigraphy with ^{99m}Tc -HDP, 21 three-dimensional freehand-SPECT-images were generated using a handheld gamma camera. Concordance of the scintigraphic and freehandSPECT data sets was ranked as good, intermediate or poor. Signal to background ratio's (SBR) were determined from the scintigraphic images and the ability to automatically segment a navigation target from the freehandSPECT images was assessed. **Results:** In 86% of the cases freehandSPECT images showed good concordance with the corresponding part of the scintigraphic images (average SBR > 4.27). These lesions all were automatically segmented and could act as navigation target. In the remaining 14% of the cases (SBR 1.82, range 1.0–3.4) freehandSPECT images showed intermediate concordance due to difficult anatomical areas or negative bone

scintigraphy. **Conclusion:** In patients with a distinct focal ^{99m}Tc -HDP uptake freehandSPECT demonstrates good concordance with traditional scintigraphy. These high-quality freehandSPECT images supported the future exploration navigation strategies for e.g. guided needle biopsies.

EP-1005

Particle counting autoradiography of radioactive biopsy specimens

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Purpose: Measuring the distribution of metabolic activity along biopsy specimens promises benefits for interventional radiology (determining specimen diagnostic and genomic profiling adequacy), nuclear medicine (in situ high resolution validation of radiopharmaceuticals), histopathology and for tumor border verification for localized therapies. Autoradiography (ARG) of biopsy specimens extracted under ^{18}F -FDG PET/CT guidance or from patients injected with beta or alpha particle emitting radiopharmaceuticals provides such opportunity. Fast, quantitative and high-resolution measurements are desirable. **Methods:** We test and calibrate the response of two particle counting devices: the ionizing-radiation Quantum Imaging Detector (iQID) and a commercial device for digital autoradiography of small animal sections and compare their responses to digital autoradiography (imaging) plates. Autoradiography of gelatin based surrogate biopsy specimens loaded with ^{18}F , ^{89}Zr , and ^{124}I activity in concentrations varying between about 0.5 and 350 kBq/g and extracted with 18G core needles were performed for acquisition times between 1 and 10 min. iQID measurements were performed with three different scintillators with different event selection parameters. The mean number of counts under a mask of the samples was used to determine sensitivity and build calibration curves. The iQID and imaging plate responses were also compared for a sample containing ^{225}Ac . **Results:** The ARG images obtained with the three types of detectors exhibit similar resolution. For the ^{89}Zr loaded samples, the calibration lines for all types of detectors had slopes between 0.6 to 3.5 counts/(min mm²) per kBq/g and had an intercept close to zero. Using a 150 micron thick CsI(Tl) scintillator supplied with a fiber optic plate (Hamamatsu Co.) with the iQID provided the highest sensitivity for ^{89}Zr . The accuracy in quantifying the concentration of activity in the specimens can be significantly affected (up to ~ 50% or more) by their thickness. **Conclusions:** Particle counting devices exhibit high resolution, linear response with dose and sensitivities comparable to that of imaging plates. They have the advantage of real time display of the ARG image and the ability to provide quantitative results immediately after acquisition. Measurement times under 10 min are sufficient for quantifying the activity concentration in biopsy specimens with the above parameters.

EP-1006**Improved 3D printed designed Lead Shields for Breast Cancer Lymphoscintigraphy**

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Objective: Scatter from the point of injection (SPI) can hinder the detection of sentinel lymph node (SLN) in breast cancer lymphoscintigraphy. Most Nuclear Medicine Departments in Spain use a flat round lead shield (FLS) to reduce the SPI. However, the remaining scatter is still extensive. Furthermore, repositioning FLS to obtain the image with less SPI increases the acquisition time. This study aimed to design a lead shield that could reduce the SPI and diminish the acquisition time. **Material and**

Methods: For this study, two different concave lead shields geometries were designed, a semioval lead shield (OLS) and a semispherical lead shield (SLS), in order to introduce the PI inside the lead shield and reduce the scatter. A SICNOVA JCR 1000 3D printer was used to achieve the shield geometry polymeric pattern. Sand molds were then manufactured according to the reference patterns and pure lead alloy was casted. Both casted lead shields were properly surface finished. 20 breast cancer patients were examined after 111 MBq nanocolloid intratumoral or periareolar single injection, making early (5 minutes p.i.) and delayed (2 hours p.i.) studies in anterior oblique and anterior projections, achieving 2 minute images with each lead shield, obtaining a total of 225 valid images. The absolute and normalised subtracted background corrected scatter counts (CSC) as well as the percentage of scatter reduction (%SR) related to the FLS in early and delayed studies were calculated. Additionally the need of repositioning the LS in each projection and with each LS was estimated. **Result:** A mean %SR of 91.8% with OLS and 92% using SLS in early images and 87.2%SR in OLS and 88.5% in late images were obtained. There were statistically significant differences between CSC using FLS and OLS ($p < 0.001$) and between FLS and ELS ($p < 0.001$), but no differences between OLS and ELS ($p = 0.17$) in early images, with the same results observed in delayed studies ($p < 0.001$ in relation to FLS, and $p = 0.1$ between both curve shields). Also, repositioning the lead shield in anterior oblique projection 6/10 times was necessary with FLS, 2/10 times with OLS and 1/10 times with ELS. In anterior projection, 8/10 times with FLS, 2/10 using OLS and 1/10 in ELS. **Conclusion:** Two concave lead shields that significantly reduce the scatter from the point of injection and diminish the need of centring were created, optimising the sentinel lymph node lymphoscintigraphy in breast cancer patients, with slightly better results from semispherical geometry.

EP-1007**Radioguided surgery with beta radiation: a novel application with Ga⁶⁸**

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Aim: A novel approach to radio-guided surgery (RGS), based on β^- radiation, has been recently proposed, and has been proved to be effective in first ex-vivo trials. The technique relies on the detection of beta particles with a dedicated instrument ("beta-probe"). The number of application cases of this technique are today limited by the availability of Beta- emitting radiotracers. Thus, to evaluate the possibility to extend its application cases to Ga⁶⁸, a retrospective study on Ga⁶⁸-PSMA PET images was performed. This beta+ emitting tracer could indeed significantly enlarge the application scope of beta-RGS. **Materials and Methods:** A retrospective study on 68Ga-PSMA PET images of 45 patients with prostate cancer was performed. All of them gave written informed consent to participate in the clinical trial, already approved by the Ethics Committee. From PET images, SUV and TNR were acquired for tumor and healthy tissue, and Monte Carlo simulations of the detector were used to evaluate the expected counts on both tissues, and thus to infer the time the surgeon should spend on the sample to discriminate it during surgical interventions. **Results:** Median SUV on prostatic tumors was found to be 4.1 (IQR 3.0-6.1), and median TNR was found to be 9.4 (IQR 5.2-14.6). Median probing time was 3.7s (IQR 1.6-6.9s). **Conclusions:** Despite the expected variability among patients, the majority of cases have been found to be compatible with beta RGS within a reasonable scenario of injected activity and sampling time (5s).

EP-76**e-Poster Area**

Technical aspects -> Instrumentation and data analysis
-> Instrumentation -> PET and PET/CT

EP-1008**Image Quality Evaluation of SiPM-Based and Standard PMT-based Time-Of-Flight Systems for Yttrium-90 PET/CT imaging**

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This study evaluated the image quality of a next-generation SiPM-based (GE Discovery MI) and a PMT-based PET/CT (Siemens Biograph mCT Flow) for ⁹⁰Y using NEMA NU 2-2012 measurements. **Methods:** A NEMA IEC phantom (6 fillable spheres: 10–37 mm) with a ⁹⁰Y background concentration of 201 kBq/ml and a sphere to background ratio of ~ 8:1 was measured on both systems (Ghent University Hospital, Belgium) during a 14h single bed scan. Both the full 14h data and a 25 min time window (representative for clinical count statistics) were corrected for scatter and attenuation and reconstructed using time-of-flight ordered subset expectation maximization (TOF-OSEM GE:5i/17s-Siemens:4i/21s) including resolution modeling and a Gaussian post-filter (FWHM:4.5–10 mm). For the GE system, data were also reconstructed with a block sequential regularized expectation maximization (Q.Clear) for different penalization factors (β :300–3000) allowing full convergence and edge preservation. All reconstruction schemes were compared using recovery coefficients (RC) of the 14h data and background noise levels (coefficient of variation, CoV) of both the 14h and 25 min data with the aim to determine optimal reconstruction settings for clinical use of ⁹⁰Y-PET. **Results:** RCs were as expected with higher RCs for lower β and post-filter FWHM values. For TOF-OSEM reconstructions, GE and Siemens RCs were similar with slightly higher GE RCs for the same post-filter settings. In terms RC mapping, a Q.Clear β of 1500 corresponded to 6–7 mm and 5–6 mm post-filter for GE and Siemens TOF-OSEM respectively. Noise characteristics of GE and Siemens TOF-OSEM reconstructions were again similar with a slightly higher background CoV for Siemens TOF-OSEM compared to GE. For the 14h data, Q.Clear outperformed TOF-OSEM reconstructions in terms of noise levels with a 1.5 times lower background CoV. However, for the 25 min data, Q.Clear noise reduction was limited compared to TOF-OSEM with a highly non-linear penalization effect, revealing an optimal β value of at least 1000 to reach equivalent noise levels. **Conclusion:** Based on phantom measurements, the SiPM-based TOF PET/CT system demonstrated better bias-noise characteristics for ⁹⁰Y. Q.Clear reconstructions substantially improved bias-noise characteristics for longer ⁹⁰Y measurements with better count statistics. For clinically relevant count statistics, Q.Clear reconstructions had limited impact on noise levels of ⁹⁰Y-PET. However, these findings need to be confirmed by clinical data and the performance for the corresponding quantification or detection task.

EP-1009

⁶⁸Ga-PSMA-11 Imaging for Biochemical Relapse of Prostate Cancer Using Dual-Time LYSO and SiPM-Based Detectors PET/CT

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Objectives: ⁶⁸Ga-labeled prostate-specific membrane antigen (PSMA-11) is a highly specific tracer for biochemically recurrent

prostate cancer at low PSA levels. In this study we aim to compare the diagnostic performance of a new PET/CT scanner (Discovery Molecular Insights - DMI) using silicon photomultipliers (SiPM) detectors vs standard LYSO detectors PET/CT (Discovery 690 - D690) in patients with biochemical relapse following a single injection of radiopharmaceutical. **Methods:** Forty-four patients were prospectively recruited to undergo imaging on the D690 and DMI scanners, in randomized order. Images from the DMI PET/CT were reconstructed using ToF and a Bayesian penalized likelihood algorithm (Q.Clear®) whereas images from the D690 PET/CT were reconstructed using time-of-flight (ToF) and an ordered subset expectation maximization (OSEM) protocol. Two experienced nuclear medicine physicians reviewed both scans for each patient in random order, recorded the number and location of each lesion, and acquired standardized uptake value (SUV) measurements. **Results:** Twenty-three patients underwent imaging on the D690 PET/CT first followed by the DMI scanner, and twenty-one underwent scanning in the reverse order. The median PSA was 4.33 ng/mL with one outlier of 1170 ng/mL. PSMA PET detected sites of recurrence in 32/44 (73 %) patients, including 6/12 (50 %) patients with PSA below 1 ng/mL with the lowest PSA and a positive scan at 0.05 ng/mL. The mean lesion SUVmax measurements were higher on DMI than D690 regardless of the timely order of the scan (6.5 vs. 5.7 in D690 scan first and 4.6 vs. 4.2 for DMI performed first). However, the difference in mean lesion SUVmax was only significant for patients scanned on the D690 first ($p < 0.018$). Although the performance of the two scanners was equivalent on a per-patient basis, the DMI identified additional sites of metastases in 2 patients. **Conclusions:** These preliminary results suggest that the SiPM-based DMI PET/CT system offers better performance and superior detector technology and image quality compared to conventional LYSO-based D690 PET/CT. These results need to be confirmed in larger studies.

EP-1010

FDG-uptake in adrenal glands; Comparison between new-generation Silicon Photomultiplier (SiPM) -based PET/CT with respiratory synchronization and conventional PET/CT

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Purpose: Prior studies have documented increased physiological FDG-uptake in adrenal glands along with the development of the PET camera. Furthermore, the spatial resolution of the upper abdomen has improved due to the appearance of the respiratory synchronization. The purpose of this study was to determine whether the SiPM-PET/CT performs better than the conventional PET/CT and investigate the contribution of the respiratory synchronization to the physiological FDG-uptake in adrenal glands. **Methods:** 63 patients, who underwent both SiPM-based and conventional FDG-PET/CT for the follow up after acute treatment were investigated. We excluded the cases with adrenal mass, and with differences in FDG dose per body weight or blood sugar level between SiPM-based and conventional PET/CT. In 24 right adrenal glands and 43 left adrenal glands, we measured the SUVmax in the adrenal gland and compared

this with liver SUVmean to calculate the adrenal-to-liver ratio (AL ratio). **Results:** In both side of adrenal glands, SiPM-based PET/CT with respiratory synchronization group had a higher SUVmax than conventional PET/CT (2.50 ± 0.57 vs. 2.40 ± 0.35 on the right side, 2.46 ± 0.63 vs. 2.31 ± 0.45 on the left side: $p = 0.035$), and a higher AL ratio (1.08 ± 0.24 vs. 1.03 ± 0.16 on the right side: $p = 0.004$, 1.06 ± 0.27 vs. 0.99 ± 0.20 on the left side: $p < 0.0001$). SUVmean of liver were no significant difference among the three groups. SUVmax were improved about 14% with respiratory synchronization. **Conclusions:** Compared with conventional PET/CT, new-generation SiPM-based PET/CT with respiratory synchronization provides higher SUVmax in the adrenal glands, and AL ratio. Furthermore, using respiratory synchronization, the SUVmax in the adrenal glands were improved about 14%.

EP-1011

Monte Carlo simulation of MAMMI PET system and performance evaluation using GATE toolkit

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Aim: Molecular imaging, particularly positron emission tomography (PET) scanning, has become an important cancer diagnostic tool recently. Whole body PET are not effective for local staging of the breast because of declining their efficiency in detecting small lesions. MAMMI is a dedicated PET based on high resolution detectors placed close to the breast. In this study, we presented a GATE model for the simulation of MAMMI scanner and model its performance of the MAMMI (Dual and Quad Rings) based on an adaptation of the NU 4-2008 NEMA standard. **Materials and Methods:** A detailed of geometry MAMMI system that uses scintillation crystals coupled to position sensitive photomultipliers (PSPMT). The detector ring consists of 12 LYSO detector modules with a scanner aperture of 186 mm. Then we validated the model against experimental measurement, including spatial resolution, sensitivity, counting rates, noise equivalent count rate (NECR) and contrast. **Results:** Overall results showed reasonable agreement between simulation and experimental data. In the simulated measurements, the addition of the second two rings of detectors lead to a rise of the sensitivity from 2.81% to 4.8% with an energy window of

250-750 keV. For a breast phantom with a capillary source, the SF reaches 50.9 and NECR is 45 kcps with an activity of 11 MBq, 18F in quad rings. The spatial resolution at the axial FOV of dual rings (2.5 mm axial, 2 mm tangential, 2.3 mm radial) is slightly better than that measured at the axial center of quad rings (2.9 mm axial, 2.5 mm tangential and 2.5 mm radial). Two cylinders (4 mm diameter) in the PET phantom were filled with activity concentration ratios of 6:1, and 3:1 relative to the background. Ideally, for a 6:1 lesion/background count ratio, contrast = 0.987 and for the 3:1 ratio contrast = 0.944 in quad rings. **Conclusion:** The MAMMI-PET has excellent spatial resolution and high sensitivity for primary breast cancer lesions. The results show performance improvement, especially in the absolute sensitivity, because of the more rings introduced in the MAMMI PET. The performance of the scanner and the validation results are considered to be reasonable enough to support its use in breast cancer imaging. Optimization of the positioning device may increase visualization of the most dorsal lesions.

EP-1012

Evaluation of bone defect healing with different biomaterials in osteoporotic rats: functional assessment with dPET-CT using ¹⁸F-Fluoride

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The aim of this study was to measure and compare the effect of different biomaterials on the defect healing and osseointegration of osteoporotic bone defects in the rat femur using dPET-CT. Osteoporotic rats were operated to create a 4 mm defect in the distal metaphyseal femur with internal fixation. Four pairs of biomaterials based on calciumhydrogenphosphate (Group 2 & 3), hydroxyapatite-forming bone cement with and without strontium (Group 4 & 5), Xerogel (Group 6 & 7) and scaffold hydroxyapatite (Group 8 & 9) were inserted. Sixty-four rats were divided evenly into eight groups according to different biomaterials. A control group without any biomaterial (Group 1) was used for reference. After osteoporosis induction and followup femoral surgery, dPET-CT studies were performed with ¹⁸F-Sodium Fluoride. SUVs, a 2-tissue compartmental learning-machine model (K1-k4, VB, influx) and a non-compartmental model based on the fractal dimension (FD) were used for quantitative analysis. Volumes of Interest (VOIs) were placed in the defect and the bone-tissue interface. Visual analysis demonstrated an enhanced tracer uptake in the defect and the bone-tissue interface for all biomaterials used. The quantitative analysis of NaF demonstrated that FD, reflecting tracer heterogeneity, showed significant differences between the control group and other biomaterial groups except the Phosphate Prestructured Gelatin mineralized with Calcium + Strontium (PPGC+S with 3:7 of Ca/Sr, Group 3) and the Strontium-containing Hydroxyapatite bone cement (pS100, Group 4) in the defect. Moreover, FD showed significant differences between the control group and other material groups except PPGC+S with 5:5 of Ca/Sr (Group 2), Group 3 and Xerogel+calcium carbonate (B30K20, Group 7) in the bone-tissue interface. On the other side SUV showed significant differences between the control group and other biomaterial groups except Group 3 and scaffold hydroxyapatite

and collagen type I (MK-K, Group 8) in the bone-tissue interface. In the both VOIs, SUV showed significant differences between the pair of PPGC+S (Group 2 and 3). No other significant differences were observed for the remaining three biomaterial pairs (Group 4–9). Besides, k3, reflecting the formation of fluoroapatite revealed the best differentiation between the control group and the pair of PPGC+S (Group 2 and 3) in the defect ($p < 0.05$). For most biomaterials, SUV and FD were the most sensitive parameters to reveal the best differentiation between the control group and the biomaterials in the defect and the bone-tissue interface. The data give evidence that all biomaterials used in this study led to an enhanced osseointegration.

EP-1013

Reliability of 18F-FDG PET Radiomic Features: a Phantom Study to Explore Sensitivity to Image Reconstruction Settings, Noise, and Delineation Method

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Background: ¹⁸F-FDG PET radiomic features contain valuable information regarding diagnosis, prognosis, and treatment-follow-up in cancer patients. Before radiomic features can be applied in the clinic, their sensitivity to various confounding factors has to be determined. This study aims to investigate the influence of underlying data (object size and contrast), reconstruction method, noise, discretization, and delineation method on the reliability of radiomic features. **Methods:** The NEMA image quality phantom was scanned with various sphere-to-background ratios, including negative contrasts. The data was reconstructed using various reconstruction algorithms and scan durations (noise). For every specific reconstruction and noise level, ten statistically equal replicates were generated. The spheres were delineated using a CT and a PET-based (41% SUV-max) segmentation. 246 radiomic features were extracted from each dataset. Before textural features were calculated, images were discretized using a fixed number of 64 bins (FNB) and a fixed bin width of 0.25 (FBW). To assess the feature reliability, the intraclass correlation coefficient (ICC) was calculated over the ten replicates. ICCs higher than 0.8 were considered as good reliability. **Results:** In general, hot spots and larger spheres resulted in a larger number of reliable features compared to cold spots and smaller spheres. E.g. for an EARL-compliant reconstruction (OSEM, 4mm smoothing, 300s scan duration), larger and smaller spheres yielded good reliability for 35% and 27% of the features extracted from hot spots, while for the cold spots this was the case in 22% and 20%. Images reconstructed with point-spread-function (PSF) resulted in the highest reliability when compared with OSEM or time-of-flight (TOF), e.g. PSF: 53%, OSEM: 30%, TOF: 32% reliable features (unsmoothed data, 300s scan duration). With decreasing image noise (increasing scan duration and smoothing) the number of reliable features increased. Discretization with FBW resulted in more reliable features than discretization with FNB. For the EARL-compliant reconstruction and larger hot spots, discretization with FBW led to a good reliability

in 89%, compared with 35% for FNB. In the cold spheres, CT-based segmentation resulted in a larger number of reliable features. **Conclusions:** Various factors influenced the reliability of ¹⁸F-FDG PET radiomic features: Discretization with FBW outperformed FNB and is therefore preferable. Reduction of image noise improves reliability, as well as increasing object size and activity uptake. Therefore, features reliable for one tumor type might not be translated to other tumor types. Use of PET radiomic features requires standardization of image quality with good statistical quality rather than very high resolution.

EP-1014

NEMA NU2-2012 performance evaluation of the Philips Vereos PET/CT System

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Purpose: To evaluate the physical performance of the Philips Vereos PET/CT system according to the NEMA NU2-2012 standard. **Methods:** Spatial resolution, sensitivity, count-rate performance, count rate accuracy and image quality were measured according to the NEMA NU2-2012 standard. All measurements were performed according to the predefined and implemented NEMA NU2-2012 acquisition protocols at a clinical installation of a Philips Vereos PET/CT system. Evaluation was performed using the software provided by the vendor. **Results:** Average (radial and tangential) transverse spatial resolution was 4.2 mm, 4.5 mm and 5.5 mm FWHM for 1 cm, 10 cm and 20 cm radial offset of the center of the FOV, respectively. Axial spatial resolution was 4.2 mm, 4.4 mm and 4.6 mm FWHM, respectively. The average sensitivity was 5.2 kcps/MBq. A Peak NEC of 153.4 kcps was measured at an activity concentration of 54.9 kBq/mL. The scatter fraction at the NEC peak was 33.9% and the maximum count rate error at and below the NEC peak was 6.8%. Contrast recovery coefficients varied from 54.3% (10 mm sphere) to 83.9% (22 mm sphere) for the hot spheres, and between 81.4% (28 mm sphere) and 87% (37 mm sphere) for the cold spheres for a sphere to background ratio of 4:1. **Conclusion:** The overall performance characteristics of the Vereos PET/CT system are comparable to state of the art PET/CT systems. However, the peak NEC occurs at a comparably high activity concentration (in PET/CT systems not based on a 1-to-1 coupling of the detectors, the NEC peak is usually found <30kBq/ml). This indicates a good ability of the Vereos PET/CT system to measure high count rates.

EP-1015

A novel phantom technique to investigate how different PET scanners measure the same activity shapes and textures

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Aim: Our study aimed to compare PET/CT scanners of different vendors from the aspect of recovering irregular activity distributions. The crucial point to answer this methodological question is the availability of a phantom, which allows to produce irregular activity distribution with high reproducibility. **Materials and Methods:** A Na²² calibration point source was attached to a high performance positioning stage, controlled by a Matlab software. According to the trajectory of the point source in the field of view, arbitrary activity distributions can be imitated during a relative short (1h) static acquisition. Regular (cube, spherical shell) and irregular (texture type) 3D patterns were generated and measured in 5 human PET/CT scanners, namely: Philips Gemini TF 64, Mediso AnyScan PET/CT, GE Discovery MI digital, Siemens Biograph Truepoint 64, GE Discovery IQ. Image reconstructions were performed according to the routine protocol. The reconstructed images were analysed using InterView Fusion visualization software and quantitative comparison were performed based on local and global statistical parameters. **Results:** Due to the computer controlled precise positioning (range of μm) and time controlling (range of msec) accuracy, the reproducibility of the phantom exceeds the value of 99%, consequently superior to the conventional phantom measurements. The coefficient of variation of the voxels within a homogeneous pattern were less than 3%, which is similar or even better than in case of water filled phantoms. Inhomogeneous 3D textures with activity concentrations in the range of 0 to 20 kBq/ml were imitated. The calculated texture parameters differed by up to 10–15% between individual scanners, highlighting the possible lower reliability of texture parameters. **Conclusion:** Preparation of any irregular activity distribution is feasible with precise positioning of a point source in the PET scanner field of view. This phantom method eliminates the so-called cold wall effect, as a visible effect of cold plastic walls within the section of conventional phantoms.

EP-1016

Evaluation of Novel Data Driven Respiratory Gating Waveforms

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Aim: To evaluate the clinical robustness of a commercially developed data driven respiratory gating algorithm based on principal component analysis. **Methods:** 150 sets of adult FDG PET/CT examinations comprising a total of 1105 acquired bed positions were used for the assessment. These arbitrarily chosen data are representative of FDG scans currently performed at our institution on a D710 PET/CT scanner (GE). Data were acquired for 4 min/bed position (3 min/bed for legs). The prototype data driven gating algorithm was applied to each bed position, including those where minimal respiratory motion was expected. The algorithm provided a signal-to-noise measure of respiratory-like frequencies within the data, denoted as *R*, derived from

the power spectrum of the transformed dataset. Qualitative evaluation was performed by visual examination of the auto-scaled waveform, with each waveform scored on a three-point scale assessing its suitability for clinical use (Score *S* of 0= no respiratory signal, 1= some respiratory-like signal but indeterminate, 2= acceptable signal considered to be respiratory). Images were reconstructed using quiescent period gating (retaining 50% of coincidences) and compared with non-gated images reconstructed from the first 2 minutes of the acquisition. The SUV_{max} of a well-defined lesion in the thorax or abdomen was measured and compared between the two reconstructions. **Results:** From the 1105 bed positions, there was a strong ($r>0.7$) and statistically significant correlation between *R* and the waveform scores from visual assessment. 82% of waveforms with *R*>15 were scored as acceptable for respiratory gating (*S*=2). On average, there were 1.2 bed positions per patient examination with *R*>15. Waveforms with high *R* and *S* were found to originate from bed positions corresponding to the thorax and abdomen: 95% of waveforms with *R*>15 had bed centres in the range 31–66 cm inferior of eye level. For regions where respiratory motion was expected to be minimal such as the head and legs, *R* tended to be <6 (mean=4.4) and *S* tended to be 0 (mean=0.1). Initial analysis of images from the first 12 patients found 10 lesions for SUV comparison. The use of DDG increased the SUV in 7/10 of these, and in 2 cases the increase was considered large (>40%). The median increase in SUV_{max} was 5%. **Conclusions:** For this prototype DDG algorithm, the majority of waveforms with high *R* corresponded to part of the patient where respiratory motion was expected, and the waveforms were deemed suitable for respiratory gating when assessed visually.

EP-1017

Comparison of timing and energy resolutions between digital and analogic last-generation PET cameras

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Introduction: Fully-digital PET cameras have been introduced with a new technology involving SiPM solid state detectors with a 1:1 coupling with scintillator crystals. The number of photo-detectors is dramatically higher for digital than for analogic PET cameras, a property that is expected to reduce the piles-up effect at high count rates. The aim of this study was to evaluate this piles-up effect according to the evolutions of energy and timing resolutions for growing recorded activities and in a comparative way between digital (Vereos, Philips®) and analogic (Ingenuity TF, Philips®) last-generation PET cameras. **Methods:** The Wang's method previously described to evaluate the timing resolution from the Noise-Equivalent-Count Rate (NECR) measurement was applied for the time-of-flight (TOF) and adapted for the

energy resolution. List-mode data were obtained on both Ingenuity TF and Vereos according to the NECR measurement of the NEMA NU-2 2012 standard. Timing and energy resolutions were assessed over 15 million prompt events for each frame recorded with an activity concentration lower than the NECR peak. **Results:** At the low activity concentration of 1 kBq/ml, timing and energy resolutions were, respectively, 325 ps and 11.0% for the Vereos and 575 ps and 11.2% for Ingenuity. For higher activity concentrations and up to the NECR peak (55 kBq/ml for Vereos and 24 kBq/ml for Ingenuity), these parameters were stable for the Vereos, with < 2% relative variations, but markedly shifted for Ingenuity TF, up to 936 ps for timing resolution and 12.6% for energy resolution. **Conclusion:** The digital but not the analogic last-generation PET camera exhibit stable timing and energy resolutions over a large range of activity concentrations. This property should particularly benefit to dynamic studies such as those commonly planned with rubidium-82, oxygen-18, nitrogen-13 or carbon-11.

EP-1018

Monte Carlo studies of sensitivity and scatter fraction (SF) of a compact total body PET scanner design with monolithic scintillators

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Background and Aim: Total body PET (TB-PET) is an emerging concept that is gaining more interest in the field of medical imaging and consisting of an optimized geometrical design of the current state-of-the-art whole-body PET scanners. The design under study is characterized by an increase in the body coverage by the detectors with a typical axial field of view (FOV) of 104 cm, the standard sitting height of a human to ensure that the most important organs of the body are imaged simultaneously. The aim of this work is to simulate the potential TB-PET system using the Geant4 application for tomographic emission (GATE) simulation package and study the sensitivity and scatter fraction (SF) following the National Electrical Manufacturers Association (NEMA) NU 2-2012 protocol. **Materials and Methods:** The scanner design consists of 36 detector modules per ring, and each module is made up of 50mm x 50mm x 16mm monolithic LYSO crystals which energy resolution was set to 11% and with a low energy threshold of 440 keV. The sensitivity of a 70cm long line source was evaluated for the full length of the scanner using ¹⁸F radionuclide surrounded by known absorbers, then the results were extrapolated to find the sensitivity in an attenuation free environment. Additionally, a 511 keV back-to-back gamma line source of the same length and 5 MBq activity placed at the center, then at 10cm from the center of the FOV was simulated for different axial lengths of the scanner starting at 5 cm for one ring, up to 104 cm, for 20 rings repeated in the axial direction with a gap of 0.2 cm. For SF studies, a 5 MBq ¹⁸F line source inside a 70 cm long water phantom was used.

Results and Conclusion: For the simulated 104 cm-long scanner, the line source sensitivity varied slightly from 162 cps kBq⁻¹ for the ¹⁸F source to 168 cps kBq⁻¹ for the back-to-back gamma source which shows a huge gain when compared to the 14 cps kBq⁻¹ NEMA sensitivity of the 20cm axial FOV Discovery MI scanner. A significant increase in sensitivity is observed with increasing number of rings from 0.618 cps kBq⁻¹ for one ring to 168 cps kBq⁻¹ for 20 rings for a back-to-back gamma line source at the center of the FOV. Also the simulation shows a 34% SF for the 104 cm-long scanner, with small variations for different values of the axial FOV.

EP-1019

Optimization of a block-sequential regularized expectation maximization reconstruction algorithm on a novel Si-photomultiplier based PET-CT for ¹⁸F-flourocholine whole-body scans

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Purpose/Introduction: Positron emission tomography with computed tomography (PET-CT) using silicon (Si) photomultiplier (PM) based technology was recently introduced. One manufacturer provides a block-sequential regularized expectation maximization algorithm called Q.Clear (GE Healthcare). Q.Clear requires a noise-penalizing determining factor (β). The optimal β for best image quality is currently unknown for ¹⁸F-flourocholine PET-CT. The aim was to compare the image quality for different time per bed positions and reconstruction protocols for patients with prostate cancer being examined with ¹⁸F-flourocholine PET-CT. **Subjects & Method:** Thirteen clinical patients admitted for whole-body ¹⁸F-flourocholine PET-CT were included and scanned on a Discovery MI system (GE Healthcare). Patients were administered with 4 MBq/kg one hour before image acquisition. PET data was reconstructed using Q.Clear with β of 150, 200, 300, 400, 500 and 550, with 1.5 and 2 min/bed position. Reconstructions with standard ordered subset expectation maximization (OSEM) with 4 iterations, 16 subsets, 6 mm Gaussian post filter and point spread function at 2 min/bed position was used for comparison. Thus 13 different reconstructions were created for each patient. Region of interests were drawn in one image for one pathological pelvic lymph node, local background adjacent to the lymph node, muscle and blood pool (two different backgrounds, for noise estimation) per patient and were copied to all other image sets. Contrast-to-noise ratio (CNR) for each lesion were calculated as $(SUV_{max} \text{ in lesion} - SUV_{mean} \text{ in local background}) / SD_{background}$. CNR for all 13 reconstructions for each patient was ranked (1-13) and then the mean rank for all reconstruction sets were calculated. **Results:** The highest CNR was obtained for β 300 (2min/bed position) when using muscle as background, β 300 and 400 (2min/bed position) when using blood pool as background. The OSEM reconstruction had lowest CNR for both muscle and blood pool backgrounds. The noise within both muscle and blood pool decreased with increasing beta value, as did lesion SUV_{max} . Noise level in muscle and blood pool for OSEM were similar to that

of Q.Clear with β 400 and 500 for 2 and 1.5 min/bed position, respectively. **Discussion/Conclusion:** In order to receive a high CNR in ^{18}F -flourocholine PET-CT images, images should be acquired using 2 min/bed position and using a β of 300–400 in the Q.Clear algorithm if 4 MBq/kg is administered. If acquisition time or administered activity is reduced, a higher β results in better CNR. **Keywords:** Digital PET; image quality, oncology, ^{18}F -flourocholine; optimization of protocol

EP-1020

qPET: a system for assessing the arterial input function for PET quantification

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Introduction: PET scans allow using molecules labeled with radionuclides to target physiological functions. This capacity is only fully exploited if a dynamic protocol is used alongside a suitable algorithm to extract parameters of interest. This quantification often requires to collect arterial blood samples, which is highly invasive, cumbersome and logistically not always possible. Thus, non-invasive systems are of high importance in nuclear medicine. In a previous work, we developed a detector to be placed near superficial arteries, measuring in real-time the number of counts per second. The characterization of the detector was made resorting to an acquisition board where the device was wired. However, in a real clinical setting, connecting wires would hamper the procedure. In this work we present and assess a wireless solution. **Methods:** The acquisition board of the previous detector was replaced by a simple circuit combining a voltage comparator with an eight-bit counter connected to an XBee wireless module. The comparator defines a voltage window corresponding to the average signal originated by the detection of a 511 keV photon. If the signal of the detector falls within the comparator window, one valid event is produced. The output of the comparator is then used as a clock signal to drive the counter, which adds events at each detection of a new 511 keV photon. The Xbee module reads the eight bits of the counter and transmits them to another module connected to a computer. The data acquisition from all detectors is coordinated by the computer, which after reading the 8 bits from a specific Xbee activates the counter reset, initiating a new counting. This simple procedure is repeated for each detector at a predefined rate. A small battery supplies the power of the wireless detector module. **Results:** The wireless detector solution was compared against the board-based solution measuring a 60 μCi ^{22}Na source. The results obtained show agreement between the two solutions. **Conclusions:** The integration of the wireless module and the detector makes the set extremely portable and easy to use. Preliminary tests show that the system does not interfere with patient's movements nor with the PET acquisition protocol. This approach is non-invasive, simple and fast and may be used in the future to assess in real-time the concentration of the

radiopharmaceutical in the arterial blood. **Financial support:** This work is supported the Portuguese Foundation for Science and Technology grants: PTDC/BBB-BMD/5378/2014 (POCI-01-0145-FEDER-016813) and UID/NEU/04539/2013 (POCI-01-0145-FEDER-007440).

EP-1021

^{18}F -FDG oncologic PET/CT phantom-based image quality assessment and clinical protocol optimization in a recently installed SiPM PET/CT device

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Aim: The goal of this study was to investigate the image quality achievable in a recently installed Philips Vereos SiPM TOF PET/CT and to assess optimal acquisition and reconstruction parameters for ^{18}F -FDG oncologic PET/CT protocols. **Materials and Methods:** We performed NEMA/IEC NU2 phantom list-mode (300s long) TOF PET acquisitions. Three experimental setups were obtained by varying the activity concentration ratios (CR: 10:1, 5:1 and 2:1) between sphere inserts (10, 13, 17, 22, 28 and 37mm diameter) and the phantom background (5 kBq/mL). A standard 90s acquisition (no post-filtering, FOV: 70cm, cubic pixel size: $4\times 4\times 4\text{mm}^3$) was reconstructed varying the number of iterations (ITn) between 1 and 10 (15 subsets) to test signal recovery in spheres according to size. Fixing ITn=3, list-mode acquisitions were reconstructed with 10, 30, 60, 90, 180 and 300s time per bed position (T_{bp}) to mimic different acquisition statistics. Background activity cross-calibration with the local activimeter and background coefficient of variation (COV) were assessed. A COV $\leq 15\%$ was assumed acceptable for image noise. Recovery coefficients (RCmax and RCmean), hot constant (Q_{H}) in spheres and cold constant (Q_{C}) for the lung insert (cylinder of 5cm diameter and 16cm long, density: $0.3\text{g}/\text{cm}^3$) were assessed according to NEMA/IEC NU2 standards. The Rose criterion was used to determine lesion detectability (CNR>3). **Results:** The background cross-calibration was always within 5%. Fixing a local standard $T_{\text{bp}}=90\text{s}$, the signal recovery in spheres assessed by RCmean and Q_{H} converged for ITn ≥ 3 irrespective of the sphere size, a COV $\leq 15\%$ was obtained as ITn ≤ 6 . With ITn=3 a COV $\leq 15\%$ was obtained for $T_{\text{bp}}\geq 60\text{s}$ for all tested phantom reconstructions. Lesion detectability was obtained for all sphere except for the 10 and 13mm for CR=2:1. Signal recovery in the lung insert was always $\geq 80\%$. RCmean and RCmax do not varied significantly with T_{bp} except for RCmax, which tend to increase for $T_{\text{bp}}\leq 30\text{s}$ due to an important image noise level. RC values were well above the present EANM/EARL recommendation for multicentre studies. **Conclusion:** We presented a phantom-based optimization for the oncologic ^{18}F -FDG PET/CT protocol in a recently installed SiPM PET/CT device. Correct device cross calibration was observed. Signal recovery in spheres converged for ITn=3. With ITn=3, acceptable image noise was obtained for $T_{\text{bp}}\geq 60\text{s}$. Lesion detectability according to sphere size was always obtained except for the 10 and 13mm spheres

in the most challenging realisation CR=2:1. Valuable information was obtained to ensure the use of an optimized clinical protocol design.

EP-1022

Prognostic Value Of Metabolic Parameters On Baseline 18F FDG PET/CT In Small Cell Lung Cancer

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Purpose: Maximum standardized uptake value (SUVmax) is the primary quantitative parameter given in 18F-FDG PET/CT reports. Calculations derived from three dimensional metabolic volumetric images have been proposed to be more successful than SUVmax alone in prognostication with a lower interobserver variability in many cancers. We aimed to determine the prognostic value of metabolic parameters on baseline 18F-FDG PET/CT in small cell lung cancer (SCLC) patients. **Subjects and Methods:** In the study, 38 consecutive SCLC patients who were referred to 18F-FDG PET/CT for staging between October 2006-January 2011 were included. Metabolic tumor volume (MTV), SUVmax, SUVmean, SUVpeak and total lesion glycolysis (TLG) were calculated. Overall survival (OS) was calculated from the date of the initial PET/CT to death from any cause. Survival tables were obtained and Kaplan Meier curves were reconstructed. Mantel- Cox regression analysis was performed in order to investigate if any of these parameters have an effect on survival. **Results:** A total of 38 (34M, 4F, age:65.76 ±8.18) patients were enrolled. Mean MTV, SUVmax, SUVmean, SUVpeak and TLG values were calculated as 273.38cm³, 14.67g/dL, 6.41g/dL, 10.97g/dL and 4234.20 respectively. Median follow-up was 761.23±873.21 days. Since basal 18F-FDG PET/CT scans, all patients were lost in the follow up except for two patients. MTV was a significant prognostic factor in SCLC patients. Estimated mean survival times were 261.0±45.6 (95%CI:171.6-350.3) days in patients with MTV value above the calculated median 174, and 577.0±124.0 (95%CI 333.7-820.2) days in patients with MTV<174. The difference was statistically significant with a p=0.009. **Conclusion:** Baseline whole body MTV reflecting total tumor load is a prognostic index in SCLC. SUV may be insufficient to predict prognosis.

EP-1023

Comparison of conventional and Si-photomultiplier-based PET systems for image quality and diagnostic performance

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Background: A new generation of positron emission tomography with computed tomography (PET-CT) was recently introduced using silicon (Si) photomultiplier (PM)-based technology. Our aim was to compare the image quality and diagnostic performance of a SiPM-based PET-CT (Discovery MI; GE Health-

care, Milwaukee, WI, USA) with a time-of-flight PET-CT scanner with a conventional PM detector (Gemini TF; Philips Healthcare, Cleveland, OH, USA), including reconstruction algorithms per vendor's recommendations. **Methods:** Imaging of the National Electrical Manufacturers Association IEC body phantom and 16 patients was carried out using 1.5 min/bed for the SiPM PET-CT and 2 min/bed for the conventional PM PET-CT. Images were analysed for recovery coefficients for the phantom, signal-to-noise ratio in the liver, standardized uptake values (SUV) in lesions, number of lesions and metabolic TNM classifications in patients. **Results:** In phantom, the correct (>90%) activity level was measured for spheres ≥7 mm for Discovery MI, whereas the Gemini TF reached a correct measured activity level for the 37-mm sphere. In patient studies, metabolic TNM classification was worse using images obtained from the Discovery MI compared to those obtained from the Gemini TF in 4 of 15 patients. A trend toward more malignant, inflammatory and unclear lesions was found using images acquired with the Discovery MI compared with the Gemini TF, but this was not statistically significant. Lesion-to-blood-pool SUV ratios were significantly higher in images from the Discovery MI compared with the Gemini TF for lesions smaller than 1 cm (p < 0.001), but this was not the case for larger lesions (p = 0.053). The signal-to-noise ratio in the liver was similar between platforms (p = 0.52). Also, shorter acquisition times were possible using the Discovery MI, with preserved signal-to-noise ratio in the liver. **Conclusions:** Image quality was better with SiPM-based PET compared to conventional PM-based PET. Although no gold standard was available, the results indicate that the new SiPM-based PET-CT generation will provide potentially better diagnostic performance.

EP-1024

Quantitative evaluation of the Mediso high resolution PET/CT system LFER150 using non-human primate brain imaging

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Purpose/Introduction: The Mediso LFER150 is currently the only commercially available high resolution PET/CT system mainly dedicated for non-human primate (NHP) imaging. The gantry bore diameter of the system is 26 cm. The transaxial and axial fields of view are 15 cm and 20 cm respectively. Resolution at the center of field of view is 1 mm in images reconstructed with full detector modeling. These characteristics make the LFER150 particularly suitable for use in the brain or whole body imaging of NHPs. The main objective of this study was to compare the LFER imaging capabilities with that of the current gold standard system for high-resolution PET, the Siemens HRRT system, using optimized reconstruction parameters with the improved CT-based three component (air, tissue, bone) attenuation correction. **Subjects & Methods:** Two cynomolgus monkeys were used for this study. Each NHP underwent four PET measurements with [¹¹C]raclopride and [¹⁸F]FE-PE2I using the LFER and the HRRT. The NHPs were anesthetized intravenously using ket-

amine/xylazine combination. Data acquired with the LFER150 were reconstructed using the latest Tera-Tomo 3D algorithm (10 iterations, 9 subsets), with high regularization, median and spike filter turned on and with detector modeling corrections and three component material map (air, tissue, bone) attenuation correction. Data acquired with the HRRT were reconstructed using the 3D-OSEM algorithm (10 iterations, 16 subsets) with PSF correction applied. Binding potential (BP_{ND}) was calculated using the simplified reference tissue model with the cerebellum as reference region. D_2/D_3 receptor availability with [^{11}C]raclopride was estimated in the caudate and putamen, whereas dopamine transporter availability with [^{18}F]FE-PE2I was estimated in the caudate, putamen and substantia nigra. **Results:** The average BP_{ND} for [^{11}C]raclopride estimated from data obtained with the LFER150 and the HRRT were respectively 4.9 and 4.6 in the caudate and 5.7 and 4.3 in the putamen. The corresponding BP_{ND} values for [^{18}F]FE-PE2I obtained with the LFER150 and the HRRT were respectively 7.3 and 5.4 in the caudate, 7.2 and 5.6 in the putamen and 1.4 and 1.3 in the substantia nigra. **Discussion/Conclusion:** The BP_{ND} values obtained with the LFER150 were similar or slightly higher than those obtained with the HRRT. The present results indicate that the quantitative performance of the LFER150 for imaging the dopaminergic system in the brain of NHPs is comparable to the HRRT. This study suggests that the LFER150 is a suitable PET/CT system for high resolution imaging of the brain in NHPs.

EP-1025

Assessing the effect of CT Metal Artefact Reduction on PET quantification for lesions near a metal implant

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Background: CT artefacts produced by metal implants adversely affect the attenuation correction of PET images. A variety of Metal Artefact Reduction (MAR) techniques have become available for routine clinical use. The MAR software provided with the GE Discovery PET/CT systems is licensed for CT artefact reduction but has not been validated for PET attenuation correction. **Aim:** To evaluate the effect of CT Metal Artefact Reduction (MAR) on PET attenuation correction and SUV quantification near a metal implant. **Methods:** A phantom with uniform background of ^{18}F and a 25.4mm sphere filled at a 4:1 activity ratio was used to assess the effect of MAR on PET quantification. The phantom was imaged with and without a hip prosthesis (femoral stem and acetabular cup) placed 4 cm away from the surface of the sphere on a GE Discovery MI (DR) scanner. Images were reconstructed using CT attenuation correction maps produced with and without MAR. Additionally, FDG PET/CT scans from 6 patients with metal hip prosthesis were retrospectively reconstructed using MAR attenuation correction and reviewed side by side with the PET without MAR. **Results:** In the phantom reconstruction without MAR, the CT artefacts from the metal prosthesis resulted in overestimation of PET background activity inside the acetabular cup (SUV_{mean}

increase of 47%) and underestimation in areas with low intensity streak artefacts (SUV_{mean} decrease of 18%) when compared to the scan without metal prosthesis. The SUV_{mean} of the sphere did not demonstrate a measurable difference in the presence of the implant. When MAR was applied, the attenuation artefact on PET images reduced in intensity and extent but was still visible. Quantitatively, the PET background SUV_{mean} inside the acetabular cup was overestimated by 20%, while in areas of residual streak artefacts the SUV_{mean} was underestimated by 12%. Visual analysis of patient data also indicated that MAR reduces the extent of PET attenuation artefacts and improves visualisation near the implant, though no additional lesions were identified for this small cohort. **Conclusion:** The phantom study highlighted that use of MAR for PET attenuation correction reconstruction improves quantification of background areas in the vicinity of metal implants. Reduction of artefacts was also observed in the small dataset of patient scans reviewed, however MAR did not affect the number of lesions detected. Further research with a larger cohort of patients and a variety of metal implants is required to fully assess the clinical value of using MAR in PET attenuation correction.

EP-1026

Evaluation the Impact of Target-to-Background Ratio on Detectability Performance for Low-Dose ^{90}Y PET/CT Imaging- A Phantom Study

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Purpose: The aim of this study was to investigate the impact of target-to-background ratio (TBR) on lesion detectability performance and quantitative accuracy using PET/CT imaging of low-dose ^{90}Y for the purpose of dosimetry. **Methods:** In this study a Jaszczak phantom containing five hot syringes (internal diameters 30.5, 22, 17.5, 13.65, and 9.15mm), was imaged via a Siemens Biograph 6 True Point PET/CT scanner. To apply four target-to-background ratios (TBR1, 10:1; TBR2, 20:1; TBR3, 40:1; and TBR4, 80:1), the syringes were filled with various uniform concentrations of ^{90}Y (activity concentration range, 2.07 MBq/mL to 14.03 MBq/mL). The phantom was imaged for 45 minutes and the raw data were reconstructed for 128 various parameters/algorithms. For the optimized reconstruction parameters, the quantitative accuracy and detectability performance were evaluated using contrast-to-noise-ratio (CNR) and recovery-coefficient (RC), taking partial volume effects (PVEs) into account. **Results:** In this study the optimized reconstruction parameters regarding higher detectability and quantification performance are identified [1]. Thus, the higher TBR led to higher detectability performance, regardless of the lesion size and activity concentration. For TBR3 and TBR4, all the syringes were detectable using the optimized reconstruction parameters. Syringes with diameter greater than 13.65 mm were detectable for all the TBRs. The recovered activities were underestimated generally with

the highest underestimation for TBR1 decreasing to the lowest for TBR4. For TBR3 and TBR4 the amount of underestimation is less than 15%. The amount of underestimation for lesions with diameters greater than 17.5 mm and 13.65 mm were limited to –15% for TBR1 and TBR2 respectively. **Conclusions:** For depicting the distribution of ^{90}Y , PET/CT imaging even with a low TBR is feasible above a given threshold for the lesion size and activity concentration. PET/CT imaging of lower TBRs could be fruitful by increasing the scan duration or activity concentrations using the optimized reconstruction parameters. [1]. M. Khazaei, A. Kamali-Asl, P. Geramifar, A. Rahmim, "Low-dose ^{90}Y PET/CT imaging optimized for lesion detectability and quantitative accuracy: a phantom study to assess the feasibility of pretherapy imaging to plan the therapeutic dose", Nucl Med Commun, vol 38(11), pp. 985–997, Nov 2017

EP-1027

Influence of BMI on image quality and acquisition protocol for digital PET/CT

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Introduction: To determine whether a body mass index (BMI) adapted acquisition protocol is needed for the Vereos digital PET/CT system to obtain a constant image quality. **Subjects & Methods:** Sixty six patients with a BMI varying from 18 to 30 kg/m² were selected from routine clinical PET program on the digital Philips Vereos PET/CT with TOF+PSF reconstruction. Two protocols were studied: (1) injected activity 2.5 MBq/kg and acquisition time 150 sec/bed position (bp), (2) injected activity 3 MBq/kg and 120 sec/bp. BMI was studied as a continuous variable and further categorized as: BMI [18, 22[(a), [22, 26[(b), and [26, 30[(c) kg/m². VOIs were drawn in healthy tissue: lung parenchyma and liver. The SUV_{mean} and standard deviation were measured and the coefficient of variation (COV=SD/mean) calculated. Median [min-max] values of the COV were computed. The difference of COV between the 3 BMI groups in lung and liver were studied with the bilateral and non-parametric Kruskal-Wallis test. **Results:** Graphically, no correlation was found between the COV and the continuous BMI values for the different VOIs and protocols. For protocol 1, the median lung COVs for the different groups were (a): 23.3 [21.2–37.8], (b): 24.4 [21.8–33.7] and (c): 24.6 [21.5–37.2] and the median liver COVs were (a): 11.8 [10.3–13.9], (b): 13.3 [12.0–15.4] and (c): 13.2 [12.0–16.1]. For protocol 2 the median lung COVs for the different groups were (a): 25.9 [16.4–42.6], (b): 26.36 [23.1–31.5] and (c): 27.2 [20.8–31.5] and the median liver COVs were (a): 13.0 [10.3–15.4], (b): 13.1 [10.8–14.6] and (c): 14.3 [10.4–16.1]. For the lung COVs, no significant between group differences were found: protocol (1) $\chi^2=1.5$ with $p=0.47$ and protocol (2) $\chi^2=0.25$ with $p=0.88$. For the liver COVs, we found a significant difference for protocol (1) $\chi^2=9.47$ with $p=0.008$ but not for protocol (2) $\chi^2=2.81$ with $p=0.24$. Importance of the statistical significance of liver COV for protocol (1) seems minor, as the median difference of 1.4 was close to standard deviation values of 1.5. **Conclusion:** A weight adjusted acquisition protocol for the Vereos digital PET/CT system

was not necessary, as the image derived quality parameter COV were similar among BMIs categories.

EP-1028

Normalization of Digital Photon Counting PET/CT via EARL-Compliant Reconstruction: An Intra-Individual Comparison Study

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Aim: Next-generation digital photon counting PET/CT systems have improved system sensitivity and time of flight timing resolution which enable precise, high definition imaging. In order to fit harmonization protocols such as EARL, a secondary reconstruction approach must be employed. We analyzed and validated a vendor suggested EARL-compliant reconstruction protocol using clinically acquired data sets, via intra-individual comparison with images from a conventional imaging system.

Materials and Methods: 40 patients underwent PET/CT imaging on a conventional system (Philips Gemini TF 64, cPET) approximately 75 minutes post-injection of 480 MBq ^{18}F -FDG. Either 55 or 90 minutes post-injection, a second acquisition was performed on a pre-commercial release digital photon counting PET/CT system (Philips Vereos, DPC dPET). Listmode data were reconstructed with default settings: cPET - 4mm isotropic voxel, 3 iterations, 33 subsets; DPC dPET - 2mm isotropic voxel, 3 iterations, 11 subsets, point spread function correction and a 4.1 mm Gaussian filter applied. DPC dPET data were also reconstructed with an EARL-compliant protocol - 4mm isotropic voxel, 3 iterations 13 subsets, 5mm Gaussian filter which was previously validated via phantom data. Regions of interest (ROIs) were placed over target lesions and in a variety of background tissues for quantitative comparison. **Results:** The average SUV_{max} of target lesions for the default DPC dPET reconstructions was 9.7. The cPET average SUV_{max} was only 6.5, as anticipated due to partial volume effects in smaller lesions. The EARL dPET reconstruction results were comparable to cPET with an average SUV_{max} of 6.6. The decrease was due to an increase in partial volume effects introduced by the use of a smaller reconstruction matrix in addition to the smoothing of the Gaussian filter alone. In background tissues, the SUV_{mean} varied by less than 5% among all reconstruction settings. **Conclusion:** Application of an EARL-compliant reconstruction protocol results in quantitative values which match conventional EARL PET/CT values. In this intra-individual comparison study we validated and presented the ability of DPC HD dPET data to conform to ongoing normalization efforts as well as to provide quantitative results in line with what conventional imaging would have produced.

EP-1029

The Related Factors with Brown Fat Activation in ^{18}F -FDG PET/CT

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Aim: The aim of this study to explore the factors can be associated with brown fat uptake in 18F-FDG PET/CT imaging. **Material and Methods:** In this retrospective analysis, 18F-FDG PET/CT reports of patients who underwent whole body PET/CT between the dates of Jan 2014 and Feb 2018 was searched from database. Brown fat uptake was reported in totally 121 patients. Forty patients were excluded from analysis because their blood test results or PET/CT images were not available. Finally, PET/CT images of eighty-one patients (mean age: 34.8 ± 15.9 , 57F; 24M) were reevaluated and standardized uptake value (SUV), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) for brown fat tissue were calculated. Additionally hepatosteatosis index and abdominal fat tissue thickness were calculated from CT images. Also patients were divided into four groups according serum TSH levels (<0.46, 0.46–2.31, 2.31–4.00 and >4.00 mIU/L). Relationship between these parameters with age, gender, body mass index (BMI), mean outdoor temperature, levels of serum glucose, thyrotropin stimulating hormone (TSH), bilirubin, total cholesterol (T-chol), low-density lipoprotein (LDL) and triglyceride (TG) was analyzed. **Results:** Median (min-max) values for BMI, outdoor temperature, blood glucose, T-chol, LDL, TG, TSH levels were calculated as 22.3 kg/m² (14.3–33.6), 2°C (–10–24), 87 mg/dL (69–145), 175.5 mg/dL (118–331), 101.5 mg/dL (56–244), 104.5 mg/dL (32–598), 2.1 mIU/L (0.06–100). Based on thyroid hormone status 70 (86%), 9 (11%) and 2 (3%) patients were euthyroid, hypothyroid and hyperthyroid. According to TSH levels 4 (5%), 39 (48%), 25 (31%) and 13 (16%) patients were in groups <0.46, 0.46–2.31, 2.31–4.00 and >4.00 mIU/L, respectively. Median (min-max) values for SUV, MTV, TLG and abdominal fat tissue thickness were found as 7.0 (2.0–37.0), 23.2 (2.0–116) and 106488 (10–1710022), 15 mm (3–46), respectively. Hepatosteatosis index was 0–5%, 6–30% and >30% in 57 (70%), 21 (26%) and 3 (4%) patients, respectively. In the multivariate analysis, only significant relationship was between low BMI ($p=0.026$), young age ($p=0.046$) and SUV. Thyroid hormone status and TSH levels was not related with metabolic brown fat parameters. However TSH levels and hepatosteatosis index ($p=0.027$) and abdominal fat tissue thickness ($p=0.001$) were significantly related. **Conclusion:** Patients with low BMI and young age seem to have higher metabolic brown fat activity. Although it is associated with higher hepatosteatosis index and abdominal fat tissue thickness, TSH level was not directly related with metabolic activity of brown fat tissue.

EP-1030

Evaluation the Effect of AFOV on the Sensitivity of the SIEMENS Biograph Vision First Digital PET System: a Monte Carlo Study

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Aim: In this study, the impact of AFOV on the sensitivity of SIEMENS Biograph Vision digital PET-CT system using Monte Carlo method is quantitatively examined based on NEMA NU 2-2012 standards. **Materials and Methods:** Biograph vision is the first SIEMENS digital PET-CT. This system consists of 60,800 LSO detection elements with dimensions of 3.2×3.2×20 mm. These elements are arranged in a 5×5 array in a crystal block with dimensions of 16×16 mm coupled to a 4×4 array of SiPMs with dimensions of 16×16 mm. 8 crystal blocks in a 2×4 array form a sub-module and by putting 8 sub-modules in a linear array, a module is constructed. By repeating 38 modules in a cylindrical arrangement, the system gantry is made. The Axial Field of View (AFOV) is 263 mm, consisting of 8 sub-modules with linear layout and 80 detector element rings. In this study, we have reduced the AFOV to 230 and 200 mm by eliminating 1 and 2 sub-modules (70 and 60 detector element rings) and its impact on the sensitivity of the system is quantitatively investigated. Reducing the AFOV, reduces the system's final cost without affecting the spatial resolution. The NEMA NU 2-2012 standards were used for evaluating sensitivity. The system was well defined in the GATE Monte Carlo code in details. **Results:** The sensitivity of the system with 260 mm AFOV (80 detector rings) calculated 14.9 cps/kBq, which shows a 2.5% error compared to the reported 15.3 cps/kBq for the system. By removing a sub-module, the sensitivity of the system with 230 mm AFOV is calculated 11.7 cps/kBq and effective sensitivity is almost 67.5 cps/kBq. By eliminating 2 sub-modules and reducing the AFOV to 200 mm, the sensitivity of the system is 8.5 cps/kBq. **Conclusion:** Since the main cost of the PET system is its detector part, it can be said that by removing a sub-module from 8 sub-modules (reducing the number of detection element rings from 80 ring to 70 rings) and reducing the AFOV, will decrease approximately 12.5% of the cost of manufacturing the system, while without affecting the spatial resolution, the system's sensitivity is still good and the effective sensitivity of the system remains the highest effective sensitivity of any TOF PET systems. By removing 2 sub-modules the cost of building system is reduced by approximately 25% while the sensitivity of the system is still higher than the previous generation of PET systems.

EP-1031

Enhancing tracer research and development: Removing the single fluid bus constraint with point to point routing on ISAR

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Objective: Tracer development and the implementation on a synthesis module is a complex and time-intensive task. Furthermore, synthesis routines must be adapted to the synthesis platform in use. Commonly utilized single fluid bus architectures put multiple constraints on synthesis planning & execution. This work shows the advantages of custom-tailored fluid

paths leveraging up to 70 individually addressable valves on a chip-based consumable. **Methods:** The ISAR synthesis platform replaces traditional stopcock valve manifolds with a fluidic chip that integrates all fluid paths (tubing) and valves into one consumable. These fluid paths can be custom tailored to the application and utilize up to 70 membrane valves in total, without a dependency between channel routing and valve position. The basic radiochemistry techniques (e.g. azeotropic drying, hydrolysis) are developed by adapting the GE FASTlab [^{18}F]FDG citrate process without compromising the synthesis route. In a second step [^{68}Ga]PSMA-11 is developed on ISAR. The chip is designed for a dual run scenario with individual uncontaminated reaction structures for two runs, using only a single set of fluid containers. Based on the same principle, a 9-run scenario is applied for [^{13}N]NH $_3$ with a single production line for each run. **Results:** [^{18}F]FDG synthesis resulted in a yield of 65% n.d.c. in less than 25 min at 47% less precursor consumption. This was achieved in 6 months development time and successfully scaled from 200 MBq to 170 GBq input activity. Based on the experience with [^{18}F]FDG, [^{68}Ga]PSMA-11 was synthesized on ISAR and transferred towards a dual run within a few weeks resulting in 44% n.d.c. yield in less than 11.5 min synthesis time at 50% reduced peptide consumption. Multi-run synthesis of [^{13}N]NH $_3$ resulted in an average yield of 96% d.c. for all 9 runs on a single chip without opening the hot cell and was accomplished within 2 weeks. **Conclusion:** By replacing traditional stopcock valve manifolds and tubing by a chip-based consumable, fast implementation times for radio-tracer synthesis can be achieved, without major changes in the original process. Despite ISAR novelties in technical design & operation, it was demonstrated that synthesis outcomes can be improved while associated production processes can be accelerated. In addition, the elimination of the single fluid bus constraint enables quick process scalability to multi-run processing. **Acknowledgments:** The authors gratefully acknowledge the financial support from the German Federal Ministry of Education and Research (BMBF).

EP-1032

Detection of epileptogenic focus with two new methods of processing of SPECT and PET cerebral images: PET-ANALYSIS and PISCOM

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Aim: Functional neuroimaging studies such as PET with ^{18}F -FDG and perfusion SPECT provide valuable information for the pre-surgical localization of the epileptogenic focus (EF). Interictal FDG-PET shows the hypometabolism of dysfunctional brain areas related to the EF. PET-Analysis is a SPM-independent application that performs a parametric analysis of each FDG-PET voxel with a base of normal studies. This software in validation phase provides a more easy and intuitive graphical user interface for physicians not used to programming language that allows to detect hypometabolic zones of difficult visual identification. Furthermore, subtraction between ictal and interictal SPECT coregistered with MRI (SISCOM) can improve the sensi-

tivity and specificity of presurgical identification of EF, with higher rates of favorable postoperative results. We hypothesized that a reprocessed interictal FDG-PET to assimilate the features of the SPECT could be used as a valid baseline study for the ictal SPECT subtraction within the SISCOM procedure (PISCOM) for the pre-surgical EF localization. We are presenting a retrospective analysis of a case with two nuclear imaging processing methods: PET-Analysis and PISCOM. **Materials, Methods & Results:** An 18-year-old male patient has been suffering of epileptic seizures characterized by paresthesias and involuntary movements in the left extremities during 4 years. The seizures lasted a few seconds with a frequency of 2-3 times/24h. Treatment with multiple antiepileptic drugs has failed. The following diagnostic tests were performed: Critical and intercritical video-EEG: generalized non-localizing irregularities of non-specific nature. MRI: Right posterior insular cortex dysplasia. SISCOM: Focal uptake increase in left fronto-parietal cingulate. FDG-PET: Normal distribution of FDG. Multidisciplinary epilepsy committee considered the right insular dysplasia as the possible cause of seizures, thus posterior or right insular resection was performed. Anatomopathological result showed a grade I ganglioglioma and the patient has been showing a favourable outcome (Engel class I) for 5 years. The recent retrospective analysis of this case with two new methods of image processing showed: PET-Analysis: Right posterior insular hypometabolism. PISCOM: Increased focal uptake in right posterior insular cortex. **Conclusions:** PET-Analysis and PISCOM, successfully located the EF (concordant with the MRI), when the other of the nuclear medicine studies didn't achieve satisfactory results. Although further research studies are needed to define the possible role of these new techniques, PET-Analysis and PISCOM are two new nuclear imaging processing methods that could increase the diagnostic performance of nuclear medicine tests for the detection of EF.

EP-1033

Imaging and reconstruction Parameters using PET/CT for post therapeutic Imaging after Y90 SIRT - a feasibility study

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Aim: Post-therapeutic imaging after SIRT is obligatory to scan for proper distribution of Y-90-spheres as well as to rule out any extrahepatic accumulation. Quantification of activity distribution is needed to perform post-therapeutic dosimetry and can be achieved by PET/CT imaging instead of Bremsstrahlungs-SPECT. The aim of this study is to analyze reconstruction parameters in Y90-PET/CT after SIRT to evaluate the feasibility of an institutional standard for post-therapeutic imaging in a patient setting instead of a phantom study as already published. **Material and Methods:** A patient underwent both Bremsstrahlungs-SPECT/CT and Y90-PET/CT (Siemens Biograph mCT, time-of-flight, point-spread-function, 20 minutes list-mode per bed position) after SIRT. The PET images were reconstructed for the following parameters: acquisition time (5-20min), Gaussian filter with FWHM setting (8-12mm), matrix size (128x128, 256x256,

512x512) and number of iterations (1-5) with 21 subsets each. SUVmax, SUVmin, SUVmean and standard deviation (SD) were analyzed using 3 VOIs (homogenous lesion in liver segment I, inhomogenous partially necrotic lesion in segment VIII and non-tumorous parenchyma segment VIII). Additionally, the differently reconstructed images were assessed visually and compared to SPECT/CT images considering their diagnostic value.

Results: A reduction of acquisition time from 20 to 10 minutes did not impact SUVs markedly, whereas a further reduction to 5 minutes led to a significant decline in SUVmean, SUVmax and SUVmin. (SUVmean values homogenous lesion: 14.58, 22.02, 23.83 and 24.29 at 5, 10, 15 and 20 minutes respectively, SUVmean inhomogenous lesion: 20.01, 22.98, 24.03, 25.26; SUVmean healthy liver tissue: 2.90, 4.69, 4.43 and 4.98). There was a slight increase of SUVmean values using 2 iterations compared to only 1 in tumor lesions (23.09 to 23.83, 23.71 to 24.08), whereas SUVmean in healthy liver decreased from 5.35 to 4.43 (2 iterations). SUVmax, SUVmin and SD differed between a matrix size of 128 compared to 256 whereas there was no change compared to 512. Setting the Gaussian's filter FWHM from 8 to 12 mm decreased SUVmax and SD, while SUV min increased. **Conclusion:** PET/CT seems to excel Bremsstrahlungs-SPECT/CT. Considering visual image analysis as well as SUV mean, max, mean and SD a reduction of acquisition time per bed position to 15 minutes is feasible using TOF-PET and PSF combined with reconstruction using a 256x256 matrix, 2 iterations with 21 subsets and a Gaussian-filter set to 10.0 mm FWHM. Validation is needed in the setting of a clinical study.

EP-1034

The Additional Value of FDG PET/CT in Oncology Patients Compared With Contrast-enhanced CT

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Introduction: FDG PET/CT has become an essential clinical tool for follow up of oncology patients thanks to its high sensitivity and specificity for detection of malignant lesions and the whole body scanning mode. Aim: To determine whether and in which conditions FDG PET/CT demonstrates additional findings after contrast CT examination. **Material and Methods:** We reviewed the examinations of 30 patients that came in our clinic between November 2017 and April 2018. All of them had been evaluated with contrast CT and were reexamined in 2 months with FDG PET/CT in order to obtain better confidence about the the presence or lack of dissemination of the primary tumor. Five had ovarian cancer, 4 had non-small cell lung carcinoma (NSCLC), 2 had renal cell carcinoma, 5 had breast carcinoma, 7 had malignant melanoma, 3 had carcinoma of the uterine cervix and 4 - colorectal carcinoma. The examinations were performed on GE Discovery IQ, according to a standard protocol after i.v. injection of 2.5 MBq/kg FDG. The exclusion criteria were: blood glucose level > 8 mmol/l and short intervals after operation, radiotherapy or chemotherapy. **Results:** Three additional lytic bone lesions were found, 2 myocardial metastases and 1 non-enlarged adrenal involvement were proved (in NSCLC, breast and kidney carcinoma). The elevated tumor marker in ovarian carcinoma in

patients with negative CT findings were related to peritoneal lesions (n= 3) and to normal size involved lymph nodes (n=2). Multiple subcutaneous and muscular lesions were additionally proved in melanoma patients. In the follow-up of 2 NSCLC patients 1 non-expected synchronous carcinoma of the colon was proved. In addition to the standard ordered subset expectation maximization (OSEM) we also used Q.Clear, which is a bayesian penalized likelihood reconstruction algorithm that may increase the visibility of lesions, improving signal to noise and signal to background ratios. **Conclusion:** In many cases FDG PET/CT may add information about the dissemination of variety of tumors, regarding soft tissue or bone lesions as well as detection of second primary. Often it may change the management and the prognosis of the patient.

EP-1035

Dual-Time ⁶⁸Ga-RM2 Imaging for Staging Patients with Newly Diagnosed Intermediate or High Risk Prostate Cancer Using PMT and SiPM-Based Detectors PET/CT

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Purpose: ⁶⁸Ga-RM2 is a synthetic bombesin receptor antagonist that targets gastrin-releasing peptide receptors (GRPr). GRPr are highly overexpressed in several human tumors, including prostate cancer (PCa). In this study we aim to compare the diagnostic performance of a new PET/CT scanner (Discovery Molecular Insights - DMI) using silicon photomultipliers (SiPM) detectors vs standard LYSO detectors PET/CT (Discovery 690 - D690) in patients with newly diagnosed intermediate- or high-risk prostate cancer patients, following a single injection of radiopharmaceutical. **Methods:** Ten patients were prospectively recruited to undergo imaging on the D690 and DMI scanners, in randomized order. Images from the DMI PET/CT were reconstructed using ToF and a Bayesian penalized likelihood algorithm (Q.Clear) whereas images from the D690 PET/CT were reconstructed using time-of-flight (ToF) and an ordered subset expectation maximization (OSEM) protocol. Two experienced nuclear medicine physicians reviewed both scans for each patient in random order, recorded the number and location of each lesion, and acquired standardized uptake value (SUV) measurements. **Results:** Three patients underwent imaging on the D690 PET/CT first followed by the DMI scanner, and seven underwent scanning in the reverse order following i.v. administration of 4.1 ± 1 mCi (range: 3.4 - 6.7). The delay between scans was 32 ± 9.3 minutes (range: 23 - 49). The average PSA was 9.8 ng/mL. ⁶⁸Ga RM2 PET detected the prostate cancer in all patients. The mean lesion SUV_{max} measurements were higher on DMI than D690 regardless of the timely order of the scan (6.6 vs. 6.4 for D690 used first and 9.7 vs. 8.5 for DMI used first). **Conclusions:** These preliminary results suggest that ⁶⁸Ga RM2 PET can accurately detect intermediate- or high-risk prostate cancer. In addition, the SiPM-based DMI PET/CT system offers better performance and superior detector technology and image quality compared to conventional LYSO-based D690 PET/CT. These results need to be confirmed in larger studies.

EP-77

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Instrumentation -> PET/MR

EP-1036

Evaluation of PET and MR compatibility of dedicated radiotherapy positioning devices

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Introduction: The aim of this study was to evaluate the compatibility of dedicated positioning devices developed for PET/MR imaging integration into radiotherapy planning. **Subjects & Methods:** The X-Tend Flat Table Top and specifically radiofrequency coil holders designed for radiotherapy use were tested on an integrated Biograph mMR PET/MR scanner (Siemens Healthcare). The attenuation of the glass fiber plate and radiofrequency coil holder, as well as related quantification effect on PET signal, were evaluated by the use of a 68-Ge sealed cylindrical phantom. CT scan of the equipment was also performed to calculate the transmission factor at 511 KeV. Magnetic field homogeneity was assessed by means of a field sequence with 0.1 ppm/line. MR image quality (in terms of artifacts, geometrical distortion, image uniformity and signal-to-noise ratio (SNR)) was compared between the radiotherapy and diagnostic setup (i.e. with and without the radiotherapy positioning devices). Coil holders were tested for the “head&neck” and “body” configurations. A spherical N_2SO_4 doped water phantom (diameter 17 cm) and a LiterMarcol-Oil phantom (diameter 24 cm) were employed for “head&neck” and “body” acquisitions, respectively. All the image quality indices were evaluated and estimated for clinical T2-weighted and diffusion-weighted (DW) sequences. SNR was estimated through the multiple acquisitions (i.e. 30) method. **Results:** The radiotherapy table photon attenuation was estimated to be around 90% by PET scan, in agreement with CT result. The dedicated radiotherapy positioning devices did not affect appreciably magnetic field homogeneity, and did not yield evident artifacts or geometrical distortion both in T₂-weighted and DW images. When radiotherapy devices were used, image uniformity had a reduction of about 10% for “head&neck” configuration, while it was unchanged for “body” configuration. For “head&neck” and “body” scans, radiotherapy configuration, as compared to diagnostic set-up, showed a relevant SNR reduction for T₂-weighted (> 35%) and DW (> 40%) imaging. **Conclusion:** Based on our preliminary results, the dedicated radiotherapy positioning devices seem to be PET and MR compatible. However, further investigation is needed to assess the actual effect of radiotherapy table attenuation on PET contrast of lesions. Also, the SNR reduction effect in MR clinical images are under evaluation by means of volunteer scans.

EP-1037

Back to 511 keV Attenuation Correction - A Head Coil System with Orbiting Transmission Source for PET/MRI Validated in a Porcine Study

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Purpose: Without photonic transmission sources in PET/MRI, methods for attenuation correction (AC) rely on segmentation of MR images or other specialised MR-sequences and atlases to derive a μ -map of the tissue. Most methods neglect attenuation of bone to a significant extent, which leads to a bias in quantification of tracer uptake in PET. We have developed a head coil with an integrated transmission source system for PET/MRI to enable direct measurement of attenuation using 511 keV photons. **Materials and Methods:** Our head coil system is based on a setup called the “liquid drive” presented by Jones et al. It consists of both a hydraulic part for driving a point source on a helical path around a head-and-neck MR receiver coil. Both parts are fully integrated within one device. Using sinogram windowing, emission and transmission data of an acquisition can be separated. This allows for post-injection measurements and reduces scatter in the transmission channel. To obtain the μ -map the logarithm of the ratio of a blank and a transmission sinogram is calculated and reconstructed using an OSEM algorithm. The performance of the transmission source system is evaluated using the μ -map of four different AC methods for comparison. Following successful phantom measurements, a piglet with a weight of 15 kg was injected with 53 MBq of [18F]-labelled Sodium Fluoride ([18F]-NaF). The μ -map obtained with our head coil system on a Siemens Biograph mMR is compared with the standard MR based μ -map obtained with a Dixon sequence as well as an UTE sequence. Additionally, a CT using a Siemens Biograph 16 and a 511 keV transmission scan using a Siemens ECAT EXACT HR+ as the ground truth were acquired for comparison. The CT is converted to a μ -map using Carney's bilinear scaling. The median difference is given in absolute units of the linear attenuation coefficient (LAC) for three ROIs (whole head, pharynx and mandible) in the μ -map. **Results:** For all ROIs, the LAC values acquired with our head coil system differed the least compared to the data acquired on the ECAT (0.002cm⁻¹, 0.006cm⁻¹, 0.006cm⁻¹). The biggest difference for the whole head was found in comparison with the CT (0.013cm⁻¹); for the pharynx and the mandible in comparison with the UTE MR-AC sequence (-0.055cm⁻¹, 0.015cm⁻¹). **Conclusion:** We successfully demonstrated the feasibility of post-injection simultaneous to emission 511 keV transmission scans in PET/MRI. The results are in very good agreement with the gold standard method.

EP-1038

Comparison of Two Methods of Respiratory Motion Management for Peri-Diaphragmatic Lesion Assessment in PET/MRI

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Purpose: To evaluate two methods of respiratory motion management in PET/MRI by comparison with the ungated PET

reconstruction within the same patient. **Methods:** Between January and March 2018, 40 patients were referred for whole-body PET/MRI staging of peri-diaphragmatic tumours (^{18}F -FDG in 36 and ^{18}F -DOPA in 4 patients). All underwent a dedicated free-breathing gated acquisition of the upper abdomen using both an abdominal cushion and a self-navigation signal from a radial VIBE sequence to record the respiratory motion, on a Biograph mMR (Siemens, Erlangen, Germany). PET images were reconstructed ungated as well as using two methods of motion management. The first one (HD-Chest®, method A) collects the counts within a breathing amplitude from abdominal cushion which has the least motion (end-exhalation phase). The second (BodyCOMPASS®, method B) divides the respiratory cycle in 5 bins according to the self-gating signal and, using the entire PET record, applies deformation fields derived from the radial VIBE on the different bins to elastically match the end-exhalation bin. Influence of the two methods on tumour SUVmax, barycentre of the metabolic tumour volume and the kidneys (41% SUVmax isocontour), and normal liver heterogeneity index in a spherical VOI (SUVmax/SUVmean), was assessed. **Results:** SUVmax of the 52 peri-diaphragmatic tumours was slightly higher with method A than with method B, 6.78 ± 4.22 vs. 6.51 ± 4.67 , respectively ($P=0.04$), while they did not differ significantly from ungated MR attenuation-corrected (MRAC) values (6.56 ± 4.38). A significant difference in the barycentre Z-coordinate (cranial-caudal direction) was also found between the two methods compared with non-attenuation-corrected (NAC) tumour metabolic volume, NAC-A distance $0.20 \pm 0.40\text{cm}$ vs. NAC-B distance $0.36 \pm 0.44\text{cm}$, $P<0.0001$. Slightly higher distances were found when considering the kidney displacements ($n=80$), 0.29 ± 0.33 vs. 0.55 ± 0.41 , respectively ($P<0.0001$). Finally, normal liver uptake was more heterogeneous using method A vs. method B, with heterogeneity indexes of 1.37 ± 0.01 vs. 1.35 ± 0.02 , respectively ($P=0.02$). **Conclusion:** Method A leads to slight overestimation of SUVmax and more heterogeneous uptake than method B, due to lower count statistics. Motion compensation significantly corrects the Z-position of tumours, allowing an improved matching of PET with MRI in simultaneous free-breathing PET/MRI acquisitions.

EP-1039

ADC-corrected SUV derived from voxel-based SUV-ADC scatter plots for the evaluation of soft-tissue tumor malignancy and treatment response in FDG-PET/MR hybrid imaging: Preliminary results

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Objective: Incorporation of apparent diffusion coefficient (ADC) into SUV of FDG might overcome the limitation of a single voxel measurement by using maximum standardized uptake value (SUVmax). In this study, a new parameter, “cellular SUV” (cSUV) was developed using ADC-corrected-SUV. The purpose of the present study was to investigate the feasibility of cSUV

in the evaluation of malignancy grade and treatment effect of soft-tissue tumors. **Materials and Methods:** The consecutive 126 patients with tumor of soft tissue and bone were included in this study, and examined with FDG-PET/MR hybrid imaging. Diffusion-weighted-MR and 18FDG-PET images were simultaneously acquired along with 3D-T2-weighted images. ADC and SUV of the tumor were extracted on a voxel-by-voxel basis, and semilog-scatterplot of SUV/ADC vs. ADC was generated for each tumor. cSUV was assigned as a value on the regression line where ADC was $0.5 \times 10^{-6} \text{mm}^2/\text{sec}$. Cluster analysis using k-means clustering algorithm was also applied with cSUV-measurement when a tumor consists of multiple components such as liposarcoma and tumors with large necrotic portions. The cSUV was compared with SUVmax to assess diagnostic performance for differentiating high-grade tumor and determining tumor response to the treatment. The statistical analysis was also performed with receiver operating characteristic (ROC) analysis for differentiating malignant from intermediate/benign group. A subanalysis of 13 patients who underwent chemotherapy ($n=11$) and heavy-particle radiotherapy ($n=2$) was performed with the % change of SUVmax and c-SUV between pre- and post-treatment. **Results:** Malignancy grades of the 126 tumors were histologically classified into high-grade sarcomas ($n=79$), intermediate-grade ($n=12$) and benign tumor ($n=35$). cSUV showed higher value than SUVmax in the range of SUVmax greater than 8, while cSUV was found nearly equivalent to SUVmax in the range of SUVmax less than 8. The mean and standard error of cSUV and SUVmax were 9.5 ± 0.94 and 6.6 ± 0.5 for high-grade, 5.0 ± 1.6 and 4.4 ± 1.2 for intermediate, 4.0 ± 0.64 and 3.1 ± 0.3 for benign group. In differentiating high from low/intermediate grade tumors, the area under curve for cSUV (0.77) was equivalent to SUVmax (0.78). Tumor response according to PERCIST was classified into partial response ($n=5$), stable disease ($n=7$) and progressive disease ($n=1$). % change of cSUV demonstrated decrease of more than 30% in 2 patients with stable disease and no interval change in 2 with partial response, which agreed well with the findings of % total lesion glycolysis. **Conclusion:** cSUV could be a promising imaging biomarker for the assessment of malignancy grade and monitoring treatment response.

EP-1040

PET/CT-MR guided radiation therapy workflow

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Introduction: In radiotherapy, an emerging procedure is the combination of multimodal imaging, PET/CT and MRI, to contour target volumes and organs at risk. In practice, PET/CT and MRI are rigidly registered to the planning CT of radiotherapy to perform the volume delineation. Acquiring images using the same patient position is necessary to get acceptable contours definition. However, better precision could be obtained by performing PET/CT and MRI examinations successively by keeping patient in the same position. Materials used to his aim and preliminary results are presented. **Methods:** PET/CT were

performed on a Discovery 710 (GE®) and MRI on an Optima MR450w (GE®). Both imagers were equipped with lasers and rigid flat panels. Zephyr XL (Diacor®), which is a mobile table on air cushion system, was used to transfer immobilized patients from one modality to the other. PET/CT and MRI were registered to the planning CT of radiotherapy by using « Integrated Registration » software of the AW Server 3.2 (GE®). Rigid registration matrix of PET/CT and MRI were then used to calculate the pitch and roll values. These values obtained for immobilized patients moved with this mobile table were compared to those obtained by repositioning patients for each modality with lasers only. **Results:** Six patients were acquired by using the mobile table and 10 without. For PET/CT and MRI the pitch and roll median values by using Zephyr XL (Diacor®) were $0.06^\circ \pm 0.33$ and $0.11^\circ \pm 0.45$, respectively. By repositioning the patients, these values were $0.34^\circ \pm 1.75$ and $-0.23^\circ \pm 1$, respectively. **Conclusion:** In multimodal imaging combining PET/CT and MRI to guide radiotherapy, these preliminary results suggest that a mobile table on air cushion system, Zephyr XL (Diacor®), could reduce position uncertainties during the rigid registration process with the planning CT of radiotherapy. If confirmed, it could improve the PET/CT-MR guided radiation therapy workflow by increasing the accuracy of the delineation.

EP-1041

Insert mouse PET, for high-field MR, based on one single monolithic scintillator

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Introduction: Most commercially available PET are based on pixelated technology. As an alternative, monolithic scintillators have been employed and photon absorption location is calculated with high precision from the shape of the scintillation light distribution. 3D absorption localization for both pixelated and continuous crystals is inaccurate at the edges because the light pattern is truncated, leading to a degradation of the spatial resolution. Spatial resolution will improve if the edges of the scintillator are removed. Using a single crystal scintillator tube would effectively remove all edges. **Methods:** We acquired a coincidence data set using standard continuous scintillators and compared the resolution in the reconstructed image with that obtained using the same data but omitting coincidences with one or both photons near a crystal edge. Images were reconstructed using LORs that included the entire crystals and with LORs involving only the inner 60% of each crystal, simulating the proposed continuous-tube detector behavior. The data set was acquired using a mini Derenzo (0.75 mm) imaged with a prototype Bruker small animal PET insert. The insert is currently installed at University of Leuven. **Results:** We have reconstructed the data using MLEM algorithm with 35 iterations, voxel and virtual pixel sizes of 0.25 mm and 1.5 mm, respectively. This scanner employs continuous crystals (10 mm thickness), which are suitable to simulate an ideal detector without edge effects. Projections through the hot rods were obtained and fitted with

Gaussians. The fitted Gaussian width (which is proportional to FWHM) is 1.45 mm on average for the Original data set and 1.19 mm for the Filtered data set. This represents a roughly 23% increase in resolution. The measured spatial resolution for the Albira Si insert is 0.75 mm. Based on these results, the resolution of the proposed system is estimated to be 0.6 mm. **Conclusion:** A PET scanner built around an 'edgeless' scintillator tube design is expected to have a spatial resolution of 0.6 mm, which approaches the spatial resolution limits of PET. We will show a design based on a single tube with an inner circular face and 10 faceted outer faces. Simulations and reconstruction data is currently undergoing.

EP-1042

Tumour-benign classification of PET-MRI radiomic features in prostate cancer patients with machine learning approaches

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Introduction: Prostate cancer is the most common type of cancer in men representing a wide range of pathologies from benign alterations to aggressive tumor patterns. Our goal was to establish a tumour-benign predictive model built on large-scale analysis of radiomic PET/MRI, PSA as well as patient demographics features with supervised Machine-Learning (ML) approaches. **Materials and Methods:** Hounded and twenty-two prostate cases were collected having a dual-tracer multi-parametric PET/MRI including ¹⁸F-FMC, ¹⁸F-FMC+⁶⁸Ga-PSMA^{HBED-CC} (dual-tracer) PET, furthermore, T2, ADC, iAUC, KEP, Ktrans and Ve MRI images. In addition, each case had the respective PSA blood values and histopathological analysis which served as ground truth for the predictive analytics. Semi-automated delineation of IgPIN, hgPIN, BPH, Prostatitis, and Gleason regions in PET/MRI images was performed in the Hybrid 3D software (Hermes Nuclear Diagnostics, Stockholm, Sweden). Tumour-to-background ratio (TBR) of PET region voxel values were calculated (background: gluteal muscle). Overall 589 in vivo features including general, histogram, shape, gray-level co-occurrence matrix (GLCM), gray-level zone size matrix (GLZSM), neighborhood gray-tone difference matrix (NGTDM) and fusion features were extracted in addition to patient age and the PSA values per lesion. Establishment of the tumour-benign predictive model was performed by applying automated feature selection and feature weight estimation via machine learning (ML) approaches [1]. Predictive performance was estimated by Monte Carlo cross-validation. **Results:** The cross-validation revealed 83% sensitivity, 80% specificity, 81% accuracy, 87% positive-predictive value and 74% negative-predictive value of the machine learning established tumour-benign predictive model. Overall 20 features were selected by ML as predictive including GLCM features from VE, ADC, KEP, iAUC, Fusion features from the combination of PSMA+FMC, FMC+Ktrans, PSMA+VE, FMC+ADC and NGTDM features from iAUC, PSMA, ADC, KEP. Neither T2 MRI, nor PSA or patient features were selected by ML as relevant for tumour-benign classification. **Conclusions:** Differentiation of

tumour and benign lesions in multi-parametric PET/MRI based on radiomics in vivo features is feasible with a high accuracy.

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EP-78

e-Poster Area

Technical aspects -> Instrumentation and data analysis
-> Instrumentation -> SPECT and SPECT/CT

EP-1043

The Added Benefit of Hybrid SPECT/CT in Bone Scintigraphy in Breast Cancer

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Introduction: In breast cancer, bone is the first site of metastasis. Bone scintigraphy is frequently used for detecting malignant bone involvement. However, in planar mode, the lack of specificity of bone scintigraphy can cause false positives and false negatives. The aim of our work was to show the added benefit of SPECT/CT over planar bone scintigraphy in diagnosing malignant bone involvement in patients followed for breast cancer.

Subjects & Methods: It was a descriptive and retrospective study of 97 patients being followed for breast cancer. These patients with equivocal bone metastatic status on planar scintigraphy underwent a SPECT-CT of a selected volume. Clinical/imaging follow-up and/or histopathology were taken as the reference standard. **Results:** The analysis of the whole body planar scintigraphy revealed 164 equivocal foci of fixation. These foci sat preferentially on the axial skeleton, more precisely in the spine (52.4% of foci) and the chest (15.8%). The most frequent spinal involvement was in the dorsal spine. The indeterminate foci explored by SPECT/CT were classified into metastatic in 29% of the cases, benign in 54%. The other 17% of the foci remained equivocal. The seat of the lesions was rectified in 10 cases. The SPECT/CT also allowed visualizing 14 new lesions not seen on the planar bone scintigraphy. After SPECT/CT we were able to classify 75.2% of the patients and 24 patients remained with indeterminate status. SPECT/CT was used to classify two patients from metastatic to non-metastatic. The final diagnosis retained by the clinician was concordant with results of SPECT / CT in all positive cases. **Conclusion:** The SPECT/CT allowed an improvement in the sensitivity and specificity of the bone scintigraphy, by removing the indeterminacy on equivocal lesions seen on planar bone scintigraphy, by specifying the localization and the exact extent of the lesions and by bringing out new lesions not seen on planar bone scintigraphy, so it could have a significant improvement of patient's management.

EP-1044

Quantitative 4D-MSPECT Stress Radionuclide Myocardial Perfusion Imaging Predicts Significant Coronary Artery Stenosis

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Background: Stress radionuclide myocardial perfusion imaging is one of the initial evaluation methods of coronary artery disease. Nuclear medicine physicians usually use qualitative analysis method to interpret result. However, quantitative analysis has better reproducibility of measurements and equal diagnostic accuracy of visual observers. In this study, we used quantitative method of 4D-MSPECT software to evaluate ability to predict coronary artery stenosis. **Methods:** 122 patients who suspected coronary artery disease were done myocardial perfusion scan and followed by cardiac catheterization. Perfusion severity scores of 3 coronary arteries and left ventricular ejection fraction (LVEF) values from 4D-MPECT software were analyzed with to predict significant coronary artery stenosis and factor association. **Results:** Higher perfusion severity score of 3 coronary arteries had more significant coronary artery stenosis. Significant coronary artery stenosis had higher mean difference of severity scores of myocardial perfusion, wall motion, wall thickening and LVEF than controls in all 3 coronary arteries (p value <0.05) except in wall motion severity score of left circumflex artery (p value = 0.479). **Conclusion:** Severity scores of stress radionuclide myocardial perfusion imaging and LVEF from 4D-MSPECT software can predict significant coronary artery stenosis of all 3 main coronary arteries and higher perfusion severity score had higher change for significant coronary artery stenosis. **Keywords:** coronary artery disease, radionuclide myocardial perfusion imaging

EP-1045

Image contrast of ^{177}Lu -filled spheres as measured with a GE Discovery 670 CZT SPECT/CT system

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Aims: Fractionated therapy with ^{177}Lu -Octreotate is an effective treatment option for patients with generalized neuroendocrine tumors. The most frequently applied therapy protocol with ^{177}Lu -octreotate is based to providing patients of four treatment cycles of 7.4 GBq. However, an increased number centers also administer an individualized amount of activity, based on e.g. absorbed dose calculations. These absorbed dose calculations rely on quantitative images obtained with a scintillation camera. The aim of this study was therefore to evaluate a potential improved quantitative imaging capabilities ^{177}Lu when using the new GE Discovery 670 CZT SPECT system with solid-state detectors. We compare the results from this SPECT system to results obtained on a standard GE Discovery 670 PRO SPECT system equipped with NaI(Tl) crystal. **Materials and methods:** We used a phantom, originally designed for image quality controls of PET systems (NEMA NU 2-2001). Six spheres were filled with a concentration of 8:1 relative to the background activity. Acquisition was performed over 120 projection views around 360° using a 128x128 matrix and 30 sec per frame. For the CZT system, we have a custom-made medium energy collimator and

for the 670 PRO system, a standard MEGP collimator was used. The energy window settings were $208 \text{ keV} \pm 6\%$ and $208 \text{ keV} \pm 10\%$ for the CZT and the PRO, respectively. A low-dose CT was acquired for attenuation correction. Images were reconstructed using OS-EM (8 subsets and 4 iterations). No scatter correction or resolution recovery was performed since the aim was to study the difference in system performance. We evaluated the differences between the systems in terms of percentage image contrast of the spheres relative to the background. **Results:** The percent contrasts for the smallest to the largest sphere were for the PRO system 10, 14, 21, 33, 40 and 51 % while for the CZT system they were 10, 12, 35, 53, 60 and 63 %. These results indicate that that, because of the superior spatial- and energy-resolution for the CZT system, the image contrast is improved and because of this potentially make the ^{177}Lu images more accurate and quantitative. **Conclusions:** Quantitative imaging with a GE Discovery 670 CZT system on ^{177}Lu provides a better image contrast as compared to using a GE Discovery 670 PRO system.

EP-1046

Calibration of a SPECT/CT System for $^{99\text{mTc}}$ Activity Quantification

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Aim: To verify a methodology for quantitative SPECT calibration and to evaluate the activity quantification performance of our SPECT/CT scanner (SYMBIA T2 - SIEMENS). **Materials and Methods:** Quantitative SPECT/CT studies can be performed using the methodology proposed by Zeintl et al [1]. The instrumentation consists of an uniform cylindrical phantom (5680 mL) and an IEC NEMA torso-phantom containing hot sphere inserts with volumes in the range (0.5 - 25) mL. $^{99\text{mTc}}$ was used to prepare the radioactive solutions. Different sphere-to-background ratio (R_{SB}) were used (61:1, 44:1, 33:1, 10:1). Images were reconstructed using the proprietary OSEM 3D algorithm (FLASH 3D, Siemens Healthcare), CT-based attenuation correction, energy window-based scatter correction. The phantom results were extended to $^{99\text{mTc}}$ -MAA patient acquisitions for activity quantification in liver lesions. **Results:** A calibration factor of 17190 cps/mCi was obtained for $^{99\text{mTc}}$. Recovery coefficients vary from 90% (for volumes ≥ 25 mL) to 20% (for volumes up to 0.5 mL). Hot sphere contrast and activity quantification improve with higher updates (iteration number and subsets) while the sphere to background ratio and the background variability increase. For 128 updates (16 iterations/8subsets) and no post-smoothing filtering the activity recovery for a volume ≥ 25 mL is about 90% with a background variability $>10\%$. A balance between activity recovery and background variability ($<10\%$) is obtained with 8 iterations, 8subset and no filtering. Applying the phantom results to 8 MAA- $^{99\text{mTc}}$ patient acquisitions, activity accumulated in liver lesions can be determined with an accuracy $\leq 10\%$. **Conclusion:** With the proposed methodology spect activity quantification can be reached with an accuracy $\leq 10\%$ for $^{99\text{mTc}}$ acquisitions. In the future the method will be tested also with

other isotopes used in the clinical practice. It can be particularly useful in those SPECT systems where quantification methods are not yet commercially available. **References:** [1] J. Zeintl et al. "Quantitative accuracy of clinical $^{99\text{mTc}}$ SPECT/CT using ordered-subset expectation maximization with 3-dimensional resolution recovery, attenuation, and scatter correction," *Journal of Nuclear Medicine*, vol. 51, no. 6, pp. 921-928, 2010

EP-1047

Utility Of ^{123}I -MIBG Standardized Uptake Value In Patients With Refractory Pheochromocytoma And Paraganglioma

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Introduction: Single photon emission tomography (SPECT) with *metaiodobenzylguanidine* (MIBG) is an important diagnostic tool in refractory pheochromocytoma and paraganglioma. Tumor-to-background ratio (TBR), which has a limitation affected by the setting of background, has been used to assess disease activity because of a difficulty of SPECT quantification. Recent quantification technique of SPECT/CT would bring advantages in image interpretation. The aim of this study is to assess the relation of ^{123}I -MIBG maximum standardized uptake value (SUV_{max}) to the TBR and urine catecholamines in patients with refractory pheochromocytoma and paraganglioma. **Methods:** This study included 13 patients with malignant pheochromocytoma and paraganglioma who underwent ^{131}I -MIBG therapy. In total, 26 ^{123}I -MIBG SPECT/CT scans were acquired before and after the therapy. The observed lesions in whole-body images were analyzed and the maximum number of lesions per scan was 10. ^{123}I -MIBG SUV_{max} was calculated semi-automatically by Q.Metrix package (GE Healthcare). The TBR was manually calculated as following formula and averaged in serial 3 slices: (Max count in the lesion - max count of background) / max count of background. Background was set in contralateral area. When a background region of interest could not be set in the area, it was set in a thigh. Urine catecholamine was collected to examine disease activity. The TBR and urine catecholamines were compared with ^{123}I -MIBG SUV_{max} by linear regression analysis. A P value less than 0.05 was considered as statistically significant. **Results:** All patient had MIBG-avid lesions on ^{123}I -MIBG SPECT/CT. A good relation between ^{123}I -MIBG SUV_{max} and TBR were observed ($r^2=0.72$, $y=0.80x$). Additionally, ^{123}I -MIBG SUV_{max} was significantly correlated with urine catecholamine hormones: dopamine, $r^2=0.17$, vanillylmandelic acid, $r^2=0.28$, homovanillic acid, $r^2=0.17$, and normetanephrine, $r^2=0.30$, respectively. **Conclusions:** The ^{123}I -MIBG SUV_{max} demonstrated similar trends with the TBR and reflected urine catecholamines. The semi-automatic quantification method of SPECT/CT would be important tool to evaluate disease activity.

EP-1048

A Crosstalk Compensation for Simultaneous $^{99\text{mTc}}$ / ^{123}I / ^{111}In Triple-isotope SPECT Imaging by Filtering Technique and Artificial Neural Network

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Aim: To reduce scan time and avoid mis-registration artifact, triple isotope simultaneous acquisition (TISA) of SPECT can be used to visualize three radiotracer distributions at the same time. However, TISA is troubled by the crosstalk when the photopeaks are close, e.g. ^{99m}Tc (140 keV) and ¹²³I (159 keV) or ¹²³I (159 keV) and ¹¹¹In (171 keV). Artificial neural network (ANN) is mostly employed to tackle the crosstalk. Conventional ANN techniques require more than 20 energy windows which are not supported by current SPECT. In this study, we incorporated ANN with attenuation information by applying a filter on the collimator using only six energy windows to toggle the crosstalk. Preliminary study shows this technique is feasible for clinical applications. **Materials and methods:** A metal filter placed over the collimator can be used to attenuate photons of different energy by various degrees. Based on the attenuation difference of the gamma from each isotope, we successfully decontaminated the crosstalk in dual isotopes simultaneous acquisition (DISA) using only 4 energy windows in the past. In this study, we extend the filtering technique to TISA. ANN consisted of three layers: input (12 nodes), hidden (12 nodes), and output (3 nodes) was constructed. Photon counts in the six energy windows ([90 105], [105 120], [120 130], [130 150], [150 166], and [225 265] keV) from scans with and w/o filter are fed into ANN. The outputs are the projection data of the three isotopes with crosstalk and scatter corrected. A GATE Monte Carlo code is used for the TISA SPECT simulation. **Results:** A gold filter with 0.1 mm thickness is attached to one of the collimator of a dual-heads E.CAM (Siemens, German) for the TISA simulation study. Preliminary results show that the crosstalk is successfully resolved by the proposed method. The results show that quantitative recovery from mixed ^{99m}Tc, ¹²³I, and ¹¹¹In sources is comparable to that from matched single-isotope sources. **Conclusion:** In this study, a TISA SPECT technique to tackle the crosstalk using a filter is proposed. Projection data with and without filter are inputted to an ANN to separate the energy spectrum of the three isotopes. Due to the extra information provided by the filtering, only 6 energy windows are needed. This method is simple to perform and yet generates promising results.

EP-1049

Sentinel Lymph Node Fingerprinting

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When locating Sentinel Lymph Nodes (SLN), surgeons use the state-of-the-art imaging devices, such as a 1-dimensional gamma probe or less widely spread a 2-dimensional gamma camera. These devices project the 3D subspace onto a 1D respectively 2D space, hence losing accuracy and the depth of the SLN which is very critical, especially in the head and neck area with many critical structures in close vicinity. Recent methods which

use a multi-pinhole collimator and a single gamma detector image try to gain a depth estimation of the SLN. The low intensity of the sources together with the computational cost of the optimization process make the reconstruction in real-time very challenging. In this paper, we use the optimal design approach to improve the classical pinhole design, resulting in a non-symmetric distribution of the pinholes on the collimator. This new design shows a great improvement of the accuracy when reconstructing the position and depth of the radioactive tracer. Then, we formulate our Sentinel Lymph Node Fingerprinting (SLNF) algorithm, inspired by MR-fingerprinting, for fast and accurate reconstruction of the tracer distribution in 3D space. As a further advantage, the method requires no pre-processing, i.e. filtering of the detector image and is very stable in its performance even for low exposure times. In our ex-vivo experiments, we successfully located multiple Technetium 99m (Tc-99m) sources with an exposure time of only one second and a very low relative L²-error. These promising results under short exposure time are very encouraging for the biopsy for SLN. They can give the surgeon an accurate 3D position estimation of the sentinel lymph node and hence, can potentially reduce the trauma for the patient.

EP-1050

Manual fusion as an alternative for nuclear medicine departments with dedicated equipments: how to improve the sensitivity, specificity and accuracy of the diagnostic test in the detection of axial skeletal injuries. Our experience

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Purpose: to compare the sensitivity and specificity in SPECT of bone and in the manual fusion of SPECT-CT in axial lesions. We believe that this could be a good alternative for places with dedicated SPECT, to increase sensitivity and specificity. Determine the accuracy of the different diagnostic tests compared to the likelihood ratios. **Subjects and Methods:** Oncology patients with CT; performed at our institution the same day we did SPECT, with hypermetabolic lesions, between 2016 and 2018, 75 injuries in total. We use Horos Software for the fusion of the images of the modalities, the studies were valued by the nuclear physicians. Planar images, SEPECT, CT and SPECT-CT were evaluated. **Results:** For the calculation of Sensitivity (S) and Specificity (E) Fisher's Exact Test (p < 5%) was used and SPECT-CT Fusion was considered as Standard Gold. The diagnostic accuracy of the different tests used was measured through the likelihoods ratio (LR +, LR -). For the statistical analysis, the SPSS software and the Diagnostic Test Calculator were used respectively. The first findings of four groups of comparative diagnostic tests were: for planar scintigraphy, 29 positive lesions (S = 65.90%, E = 61.29%). In SPECT, 30 positive lesions were recorded (S = 68.20%, E = 77.41%). For CT we found 34 positive lesions (S = 77.27%, E = 93.54%). As a second finding, the diagnostic accuracy was statistically significant in SPECT (p = 0.0001) and CT (p = 0.0001) than in planar scintigraphy (p = 0.0333). As a third finding the values of likelihood ratios: Planar scintigraphy (LR + = 1.50 and LR - = 0.50), in SPECT (LR + = 3.0 and LR - = 0.41), in CT (LR + = 12 and

LR- = 0.24) in Fusion SPECT-CT (LR + = 99999 and LR- = 0.00). **Conclusion:** The added value of the fusion in the final diagnosis, which is the clinical utility over the initial diagnosis in planar scintigraphy, was 36.00%. The impact of positive LR values greater than 10 and negative LR less than 0.1 in the fusion manual SPECT-CT indicates that it is highly relevant, together with the $p = 0.0001$ value, which determines with high certainty a change in clinical behavior and the taking of subsequent exams. We can say that it is a method available to increase the sensitivity and specificity in the accuracy of the etiological diagnosis, for those centers that do not have hybrid equipment.

EP-79

e-Poster Area

Technical aspects -> Radioprotection and dosimetry
-> Dosimetry -> Preclinical and clinical dosimetry and radiobiology

EP-1051

Impact of tumour morphology on routine clinical dosimetry calculations in molecular radiotherapy

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Aim: Molecular radiotherapy delivers radiation to malignant cells whilst minimising the damage to healthy tissue via the interaction of radiopharmaceuticals with molecular sites and receptors. Accurate tumour dosimetry following molecular radiotherapy is essential to enable the investigation of absorbed dose-response correlations and treatment optimisation. This is often performed using so-called S-values calculated under the assumption of a unit density spherical representations of a tumour with uniform uptake. The aim of this study was to quantify the effect tumour shape on absorbed dose estimates. **Materials and Methods:** The general purpose EGSnrc/EGS++ Monte Carlo (MC) code [1] was used to generate the S-values needed to perform tumour dosimetry for a range of radionuclides: ³²P, ⁸⁹Sr, ⁹⁰Y, ¹³¹I, ¹⁵³Sm, ¹⁶⁶Ho, ¹⁷⁷Lu, ¹⁸⁶Re and ¹⁸⁸Re. The decay data from the RADTABS/MIRD software was used [2]. Sphere S-values commonly used for tumour dosimetry calculations were calculated for volumes ranging between 0.01 and 6000 ml. To study the impact of tumour shape on the self-irradiation absorbed dose S-values, a set of constant volume cylinders was used: 1, 5, 10, 20, 50 and 100 ml with radii ranging between 0.3 and 5 cm. Cylinder S-values were calculated and compared to the sphere values. **Results:** A dependency between the cylinders' surface area to volume ratio and the S-values was found for cylinders of the same volume. For a given volume, the cylinder S-value peaked at the smallest surface area and the differences between cylinder and sphere S-values increased as the surface area diverged from the smallest value. The smallest and largest differences were observed for low and high energy radionuclides,

respectively. As an example, for a 10 ml tumour, the differences ranged between 0.03% and 4.1% for ¹⁷⁷Lu, and between 1.9% and 36% for ⁹⁰Y, corresponding to cylinder radii of 1.25 and 3.5 cm. The differences between cylinder and sphere S-values decreased for larger tumour volumes. **Conclusion:** Sphere S-values routinely used in clinical dosimetry can significantly overestimate the absorbed dose delivered to tumours in patients undergoing molecular radiotherapy, in particular for high energy radionuclides such as ⁹⁰Y. For a given tumour volume, the error introduced in the tumour absorbed dose increased with the surface area. Further tumour shapes and a correction method will be investigated. [1] Kawrakow I et al. EGSnrc C++ class library Report PIRS-898 (2017). [2] Eckerman KF, Endo A. MIRD: radionuclide data and decay schemes. (2007).

EP-1052

An individual approach to Molecular radiotherapy dosimetry using 3D printed phantoms

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Bringing Molecular radiotherapy dosimetry up to the standard set by European Directive 2013/59/Euratom [1] requires consideration of a range of factors. Notable of these is the wide variation in anatomy from patient to patient, particularly when organ deformation by bulky disease is considered. These geometrical effects coupled with varying biokinetics, mean that the dose received from standard administered activity may vary by up to an order of magnitude [2]. An accurate determination of both self- and cross-dose from the MRT therapy may be achieved using Monte Carlo methods, enabling dosimetry on a voxel-by-voxel basis. Validation of these simulations may be achieved via imaging millimeter accurate 3D printed organ sets, derived from CT scans of real patient geometries, with patient representative doses. Accuracy of dose calculation using two SPECT cameras and dosimetry software packages may also be assessed. A series of patient organ phantoms has been manufactured and SPECT scans performed using both ^{99m}Tc and the β emitting ¹⁷⁷Lu; emerging clinically for PRRT. The ultimate aim is the creation of a database of patient specific S-factors, which give a measure of the dose per unit activity for defined regions of source and target. This would enable dose to be determined on an individual patient basis, improving with the granularity of the database. [1] European Society of Radiology (ESR, D Akata, E.J. Adam, J. Damilakis, H. Ducou lePointe, R. Loose, C. Owens, G. Frijia, F. Kainberger, Laura Oleaga, M. Prokop, Eliseo Vano, Ahmed Meghzifene, Graciano Paulo, David Koff, W. Stiller, and D. Sheppard. Summary of the European directive 2013/59/Euratom: essentials for health professionals in radiology. 6:411–417, 08 2015. [2] L. Bodei, M. Cremonesi, C. Grana, P. Rocca, M. Bartolomei, M. Chinol, and G. Paganelli. Receptor radionuclide therapy with ⁹⁰Y-[DOTA]0-Tyr3-octreotide (⁹⁰Y-DOTATOC) in neuroendocrine tumours. European Journal of Nuclear Medicine and Molecular Imaging, 45(8):1366–72, July 2004.

EP-1053**3D verification of radiation therapy plans with the cylindrical dosimeter as a prototype of the body form**

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Introduction: According to the AAPM TG-119 protocol, the criterion for passing the radiation therapy plan is gamma index $\gamma(3\%, 3\text{ mm}) \geq 95\%$. It was shown in [1] that the use of $\gamma(3\%, 3\text{ mm}) \geq 95\%$ criterium for several IMRTs and VMAT plans gives large systematic errors in the dose value comparing with $\gamma(2\%, 2\text{ mm}) \geq 95\%$. The AAPM TG-119 protocol [2] was changed by a new protocol AAPM TG-244 [3] for the commissioning of the treatment planning systems for IMRT and VMAT and QA procedures. VMAT plans also need volume dosimetric verification. The purpose of this work was to verify the Monaco plans for VMAT irradiation using a set of equipment of the dosimetric phantom ArcCHECK together with the SNC Patient and 3DVH programs at the Elekta Synergy accelerator according to AAPM TG-244, and to estimate the differences between the 2D and 3D estimates. **Material and Methods:** For the analysis, four radiotherapy VMAT plans for different localizations and fractional regimes were taken: head-neck (70 Gy/27 fraction), prostate (35Gy/5fraction), brain (60Gy/30fraction) and liver (30Gy/2 fraction). All plans were created using planning system Monaco v.5.10.02. Dose delivery was carried out using Elekta Synergy linac. VMAT plan verification was done using cylindrical phantom ArcCHECK (Sun Nuclear) together with the SNC Patient and 3DVH software package. **Results:** A technical malfunction of the accelerator diaphragm was detected with the help of the criterion $\gamma(2\% \text{ L}, 2\text{ mm}, \text{TH} = 5\%)$ using an example of a few irradiation plans, which could not be detected at milder values of the gamma index $\gamma(3\% \text{ L}, 3\text{ mm}, \text{TH} = 5\%)$. Thus, the use of more stringent gamma-index criteria $\gamma(2\% \text{ L}, 2\text{ mm},)$ allows evaluation of distribution and find out the nature of the systematic errors that can be missed by using “soft” criteria or 2D-verification of plans. **Conclusion:** The use of 3D dosimetric evaluation with the help of the 3DVH program allows to proceed to more complex analysis of the results of verification of treatment plans. In this case, the value of the gamma index is only the first step to analyze the data obtained. The 3DVH software allows you to obtain a dose distribution in each voxel and patient contours, which makes it possible to analyze the DVHs. In this case, the conclusions on treatment plan passage should be based on the measured dose distribution for the target and the organs at risk.

EP-1054**Image-based internal dosimetry of Ac-225 labeled NOTA-trastuzumab in mice**

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Objectives: Targeted alpha therapy (TAT) offers to inhibit or kill the selected metastasis cancer cell. Actinium-225 (Ac-225) which is emitted alpha is a candidate of the radioisotope for cancer treatment of TAT. The aim of this study was to evaluate internal dosimetry of ²²⁵Ac-NOTA-trastuzumab using ⁶⁴Cu-NOTA-trastuzumab mice PET/CT image. **Methods:** ⁶⁴Cu-NOTA-trastuzumab was injected into a mouse 7.4 MBq intravenously. The injected mouse was scanned in the dedicated small animal PET/CT scanner (Inveon, Siemens Healthcare, Malvern, PA). After ⁶⁴Cu-NOTA-trastuzumab was administrated, the data were acquired at 6 time points after ⁶⁴Cu-NOTA-trastuzumab administration (1, 2, 6, 24, 48, and 70 h). Residence times were computed via time activity curves of the acquired PET time series data. The heart, kidney, liver, spleen and stomach were segmented in CT images for their absorbed fractions of total absorption. In order to calculate S-value Ac-225 absorbed dose was simulated by Geant 4 Monte Carlo simulations. The organ absorbed dose for Ac-225 labeled NOTA-trastuzumab was approximated by extrapolating ⁶⁴Cu-NOTA-trastuzumab data. The relative biological efficacy (RBE) of the alpha particles emitted from Ac-225, was estimated to be 5 (RBE = 5). The absorbed dose in all decay steps (²²¹Fr, ²¹⁷At, ²¹³Bi, ²¹³Po, ²⁰⁹Tl and ²⁰⁹Pb) was summed up after applying weighting factors in the two possible pathways of the Ac-225 decay chain, 2% for ²⁰⁹Tl and 98% for ²¹³Po. **Results:** Ac-225 self irradiation S-value in heart, kidney, liver, spleen, and stomach were 0.05, 0.02, 0.03, 0.20, 0.26 Gy-g/MBq-hr, respectively. Residence times of the heart, kidney, liver, spleen, and stomach were 3.33, 3.68, 2.66, 2.19 and 1.31 MBq-hr/MBq, respectively. The estimated ⁶⁴Cu-NOTA-trastuzumab absorbed dose in heart, kidney, liver, spleen, and stomach were 0.35, 0.25, 0.06, 0.53, and 0.09 mSv/MBq, respectively. The estimated ²²⁵Ac-NOTA-trastuzumab absorbed doses in heart, kidney, liver, spleen, and stomach were 0.17, 0.04, 0.09, 0.26 and 0.57 Sv_{RBE5}/MBq, respectively. **Conclusions:** In this study, the Ac-225 labeled NOTA-trastuzumab dosimetry was performed image-based Monte Carlo simulation with Ac-225 decay chain. As the result shows that stomach and spleen was the higher absorbed dose than heart, kidney, liver. This result of study may help to determine appropriate dose for treatment of HER2-positive cancer cell in clinical area.

EP-80**e-Poster Area**

Technical aspects -> Radioprotection and dosimetry
-> Radioprotection -> Radiation exposure & protection

EP-1055

¹⁷⁷Lu-DOTATATE Retention and Radiation Protection Precautions for Patients Undergoing Inpatient and Outpatient Peptide Receptor Radionuclide Therapy of Neuroendocrine Tumours

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Purpose: To determine appropriate radiation protection precautions to be followed by patients undergoing peptide receptor radionuclide therapy in order to restrict the dose received by the patient's family members to less than 5 mSv in 5 years, and to measure the percentage retained activity at discharge for inpatient and outpatient therapies. **Methods:** The percentage activity retention at the time of discharge was measured using retrospective data from 32 inpatient ^{177}Lu -DOTATATE (Mallinckrodt Radiopharmacy Services) administrations. Planar whole-body scans were performed at 4 time points post-administration and the geometric mean of the total counts was plotted against time. A least squares regression analysis method was used to derive the activity retention curves. It was assumed that dose rate measurements taken directly post-administration follow the same decay curve, and the cumulative dose received through contact with the patient was calculated by combining this with published social contact times. Precaution durations for inpatient and outpatient therapies were defined using an iterative process, calculating the number of whole days after leaving hospital on which contact should be limited so that the relevant dose constraint was not exceeded. The activity retention at discharge for 20 outpatient and 24 inpatient therapies with Lutathera® (Advanced Accelerator Applications) was also determined for comparison. **Results:** For inpatients receiving ^{177}Lu -DOTATATE from Mallinckrodt a mean of 32.9 % of the administered activity was retained at 18.1 hours after initial imaging. For Lutathera® patients mean retentions of 24.4 % at 18.2 hours and 37.3 % at 5.2 hours were measured for inpatients and outpatients respectively. Immediately after ^{177}Lu -DOTATATE administration the mean dose rate was measured to be 397 $\mu\text{Sv/h}$ at 0.1 m and 20 $\mu\text{Sv/h}$ at 1.0 m from the lateral mid-abdomen. Outpatients should restrict day contact and sleep separately from their partner for 15 days. Contact with children should be restricted for 15 days, 12 days and 9 days for children below 2 years of age, 2–5 years and 5–11 years respectively. One additional day should be added to these restriction periods for patients treated following an outpatient protocol (except children aged 5–11 years whose restriction period remains at 9 days). **Conclusion:** Contact restrictions are necessary to limit the radiation dose to members of patients' households. Applying these precautions restricts the dose received by family members to less than that required under UK legislation and demonstrates that ^{177}Lu -DOTATATE can be administered safely using both inpatient and outpatient therapy protocols.

EP-1056

Eye lens dose in Positron Emission Tomography staff

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The 2013/59/EURATOM Directive states, following ICRP recommendations, a new eye lens dose limit for occupational exposure equal to 20 mSv/year, averaged over a period of 5 years,

with no year exceeding 50 mSv, instead of the current limit of 150 mSv/year. **Objective:** To investigate the eye lens dose received by staff working in a PET facility, in order to determine whether eye lens dose monitoring or/and additional radiation safety measures are required. **Methods:** Eye lens dose exposure was measured for 1-week workload from 5 laboratory technicians and 4 nurses, obtaining a total of 10 and 6 measurements respectively. Technicians were involved in PET radiopharmaceutical (RF) synthesis, RF quality assurance, and syringe preparation. Nurses were taking part in RF administration, patient management, and PET/CT acquisition. The personnel were provided with 2 thermoluminescent dosimeters (TLDs): one calibrated in terms of $H_p(3)$ located near to the middle position between the eyes, and a whole-body dosimeter calibrated in terms of $H_p(10)$ and $H_p(0.07)$ positioned on the thorax. A variety of RF were synthesized in the laboratory, and very few were obtained from other centers. The RF was automatically transferred from the synthesis-cell to the dispensing-cell, where the syringe was automatically (FDG) or manually (other RF) loaded. When the syringe was extracted manually from the hot cell, it was placed in a 2.5 cm lead jug and moved to the lock-type-transfer. The nurse got the syringe and introduced it into a 5 cm lead protector. Then it was moved into an individual administration room and the RF was administered to the patient. **Results:** About 55 syringes/week were prepared and administered. The maximum technician eye lens dose measured was 25 μSv , and 6 measurements were below the detection limit of 15 μSv . Nurses eye lens dose ranged between 45 and 70 μSv , and their mean $H_p(3)/H_p(10)$ was 0.56 ± 0.09 (mean $\pm$ s.d.) and lower than 0.70. The estimated annual eye lens dose for technicians was below 1.2 mSv considering 48 working weeks/year, while for nurses the estimated annual dose ranged between 2.4 and 5.6 mSv, considering the measurements normalized to the number of administered RF and a work load of 1000 administrations/year/nurse. **Conclusions:** This study shows that, with the radiation safety procedures implemented in a busy PET facility, the new dose limit for the eye lens is unlikely to be surpassed by the PET laboratory technicians, and by the nurses attending the patient and acquiring the PET/CT.

EP-1057

Measurement of cumulative radiation exposure to children and adolescents in contact with outpatients treated with low dose radioactive iodine (I-131)

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Introduction: Patients treated with radioactive iodine (^{131}I) therapy represent radiation hazards to the public, medical staff, family members, caregivers and to the environment. Children and adolescents sharing the same home with outpatients treated with ^{131}I in the post therapy period require special concern as they represent a more vulnerable group to radiation effects.

Purpose: Measurement of cumulative radiation exposure (CRE) to children and adolescents household contacts of outpatients

treated with low dose ^{131}I . Other aim is to look for patients or contacts demographic and educational factors that can significantly affect radiation exposure to this vulnerable group of contacts. **Subjects and Methods:** Radiation safety instructions (RSI), especially those related to children and young adults, were properly explained by radiation safety officer (RSO) to 39 patients prior to outpatient therapy with ^{131}I doses ranging from 370–1110 MBq. Patients were accompanied by 63 family members in these educational sessions about RSI, out of them 13 were adolescents aged from 14–18 years and 17 were mothers of 23 household contacts less than 12 years of age. The whole number of children and adolescents sharing home with the patient in the post therapy period was 99 family members aged 18 years or younger, including 49 contacts less than 12 years. **Results:** CRE figures to children and adolescents ranged from 0.079 to 0.934 mSv, with a mean, median and seventy fifth percentile figures of 0.284 ± 0.168 mSv, 0.215 mSv and 0.333 mSv respectively. Children and adolescents had 100% compliance to radiation exposure constraint of 1 mSv with all CRE below this figure and 75% of them had CRE below 35% of this constraint. Out of all studied demographic and educational factors, the only factor that had statistically significant correlation with CRE was attending the RSI education sessions with significantly lower mean CRE figure of 0.184 ± 0.54 to adolescents and children of mothers who attended the RSI education sessions versus 0.298 ± 185 to those who did not attend those sessions with significant p value of 0.038. **Conclusion:** Outpatient low dose ^{131}I therapy, ranging from 370–1110 MBq, is a safe therapeutic modality for children and adolescents contacts sharing the same home with patients in the post therapy period with 100% compliance to radiation exposure constraint of 1 mSv, with an advice for all adolescents and mothers of children contacts to attend the direct RSI education session from qualified professionals, as it is the single factor associated with significantly lower CRE figures.

EP-1058

An User-Friendly Approach to the Evaluation of Skin and Eye Lens Doses to the Operators in Nuclear Medicine through Dedicated Monte Carlo Simulations in GAMOS

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Introduction: The manipulation of relevant activities of radionuclides during preparation and administration of radiopharmaceuticals in nuclear medicine procedures can expose operators to high levels of doses to the extremities, skin, eye lens and to the whole body. Of these, the superficial doses to the skin and eye lens are crucially dependent on the actual irradiation geometry, especially in presence of beta emitters. **Methods:** A dedicated Monte Carlo simulation in GAMOS (GEANT4-based Architecture for Medicine-Oriented Simulations) was set up in order to reproduce ^{13}N , ^{18}F , ^{44}Sc , ^{52}Mn , ^{64}Cu , ^{90}Y , ^{131}I , ^{153}Sm , ^{177}Lu and ^{188}Re nuclides in water solutions enclosed either in glass vials or in plastic syringes, of different sizes and filling volumes. Dose equivalents to the skin of the extremities and to the eye lens were estimated at different distances. A comparison was made with the results from the VARSKIN analytical code, assum-

ing the standard geometric lay-out of a volume source available in the code. **Results:** Dose equivalents, to the skin and eye lens, are reported for all the considered configurations, highlighting the importance of adopting a realistic geometrical configuration. Concerning skin doses, the comparison between VARSKIN results evaluated below the source bottom and the maximum exposition on the lateral surface at the source middle plane, evaluated by Monte Carlo simulations, reveals a qualitative agreement for a limited number of configurations only, since the different geometries affect the dose deposited in the scoring volumes. A further source of disagreement is related to the deterministic approach in which electron energy deposition is treated in VARSKIN and its influence in proximity of electron maximum range, and to the absence of bremsstrahlung emission. **Conclusions:** since GAMOS allows to set up a Monte Carlo simulation without need to modify directly the GEANT4 C++ code, case-specific realistic geometries defined for any nuclide of medical interest and results can be obtained in very reasonable computation times.

EP-1059

Evaluation of individualized dosage planning when performing Cadmium-Zinc-Telluride SPECT camera gated tomographic radionuclide angiography

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Aim: We have established an algorithm allowing individualized dosage planning (IDP) for $^{99\text{m}}\text{Tc}$ -labeled human serum albumin (HSA) when performing CZT SPECT camera gated tomographic radionuclide angiography. Our aim is to assess the ability to achieve a specific target count rate and to evaluate the feasibility of IDP. **Method:** Individualized tracer dosage in MBq with a specific target count rate (STCR) of 2.7 kcps was calculated prior to each examination based on age (A), gender (G (male = 1, female = 0)), weight (W) and height (H) of each patient using the following algorithm: $550 - (EXP(1.8 + G*0.06 - A*0.0021 + W*0.00005 - W*0.028 + H*0.0087) - STCR)/0.00756$. The algorithm was derived from and based on a multivariable linear regression analysis of registered count rates and patient data from 1065 acquisitions using a standard dose of 550 MBq HSA. A total of 222 eligible patients referred for routine assessment of left ventricular ejection fraction (LVEF) were registered from March 1st to April 16th 2018. Data were recorded on administered tracer dose, age, gender, height, weight, and count rate. All radionuclide angiographies were performed on a dedicated cardiac CZT SPECT camera, GE Discovery 530c. When no patient data were available the patient received a standard dose of 550 MBq HSA. **Results:** A total of 222 acquisitions were performed of which 3 were excluded from the analysis because of partially paravenous administration of HSA. In 29 cases (13%) there were not enough sufficient data for IDP. For the remaining 190 patients (65 men) the IDP was achieved, and in which the mean count rate ± 1 SD was 2.61 ± 0.76 kcps (range 0.99 to 6.08). Count rate was higher but varied less for men (2.83 ± 0.72 kcps, range 1.36 to 4.68) than women (2.50 ± 0.76 kcps, range 0.99 to 6.08). The current STCR

mean dose was 369 ± 145 MBq, (range 147 to 722) in contrast to the group who received standard dose of mean 534 ± 20 MBq (range 498 to 572). **Conclusion:** It is possible to reach a target count rate with individualized planning of tracer dosage using an algorithm including data on height, weight, gender and age for CZT SPECT camera gated tomographic radionuclide angiography. An overall reduction in dose was also obtained. Target count rate varies more for women, probably because of larger variations in chest circumference.

EP-1060

Size specific dose estimate (SSDE) for estimating patient dose from CT in myocardial perfusion SPECT/CT

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Purpose: Volumetric CT dose index (CTDIvol) is used for estimating patient dose from CT and does not take patient size into consideration. Size specific dose estimate (SSDE) is a new parameter that includes patient size factor in its calculation. Recent studies have produced mixed results on the utility of SSDE, especially when automatic exposure control (AEC) was used. The objective of the study was to find out if there is a relationship between patient size and each of the parameters, SSDE and CTDIvol, when AEC is used. **Materials and Methods:** CT data of consecutively selected 111 patients who had undergone myocardial perfusion imaging (MPI) SPECT/CT in department of Nuclear medicine, JIPMER were included for analysis. The scans were performed on Siemens Symbia T6 system with 6 slice CT scanner. AEC was used during acquisition (CARE 4D). The selected values for kVp, slice thickness and pitch were 130, 5 mm and 0.4 respectively. CTDIvol values of the CT scans were extracted for each patient. Effective diameter of each patient was calculated as geometric mean of anteroposterior and lateral diameters measured on axial CT images. Corresponding conversion factors for effective diameters were obtained from American Association of Physicists in Medicine (AAPM) report 204. SSDE was obtained as the product of CTDIvol and conversion factor values. Linear regression model was used to evaluate the relationship between patient size and the parameters SSDE and CTDIvol. **Results:** There were 79 males and 32 females. Their mean weight was 62 (11.5) and range was 34 - 103 kg. Median CTDIvol (mGy) on AEC mode was 7.27 (IQ range 7.27, 7.65) and mean effective diameter was 26.2 cm (2.4). Mean SSDE (mGy) was 10.6 (0.84). Good positive correlation was obtained between CTDIvol and effective diameter ($r=0.536$; $p<0.0005$). Strong inverse correlation was noted between SSDE and effective diameter ($r=-0.777$; $p<0.0005$). Linear regression model for establishing relationship between CTDIvol and effective diameter showed slope of 0.314mGy/cm ($R=0.561$; $R^2=0.314$; $P<0.0005$) whereas between effective diameter and SSDE slope was -0.23mGy/cm ($R=0.676$; $R^2=0.457$; $P<0.0005$). **Conclusion:** The study shows that CTDIvol and SSDE vary but divergently, with patient size. SSDE is a better estimate of patient radiation dose from CT of MPI SPECT/CT than CTDIvol in systems that use automated exposure control.

EP-1061

A Generic Calculator for Patient Restriction Calculations

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Introduction: Patient restrictions after receiving radionuclide therapy can be difficult to assess. Since it can involve patients taking time off work, possibly losing income, it is important that restriction periods take account of a patient's circumstances. A program has been developed which allows radiation doses to others to be estimated for any radionuclide situation and restriction periods calculated. **Method:** The program is written in Excel (Visual Basic). The program flows through separate worksheets, helping guide the user. The radiopharmaceutical model is chosen from a drop-down list. Users can also enter their own radiopharmaceutical model, with up to three exponential components. Dose rates at 5 distances can be entered (0.1m, 0.3m, 0.5m, 1m and 2m). This combined radiopharmaceutical and dose rate model can be stored for future use. Various pre-set models are available for I131 thyrotoxicosis, I131 ablation, and Lu177. However any radionuclide model or circumstance is easy to enter and can be stored if needed. The contact model is then entered e.g. for the patient's workplace. Various pre-set examples given (for contact with children at home, some examples of work etc). The user can also create contact models which can be stored. The calendar days that the model applies are then selected (up to 7 weeks) normally with pre-selected buttons (e.g. for Monday - Friday only). **Results:** Once the model is selected or set up, the program calculates the restrictions (days) for dose constraints of 0.3mSv, 1mSv, 3mSv and 5mSv. Daily dose figures can be also viewed if required. A feature is that once a contact model is entered the program immediately displays the relative contribution of dose at each distance. E.g. for I131 and a possible work-based contact model of 0.3hr@0.3m, 0.5hr at 1m, 4.5hr at 1m and 2hr@2m. The calculator immediately displays that the dose contribution is split as 41% for 0.3m, 22% for 0.5m, 33% for 1m and 4% for 2m. This illustrates that even short contact times at short distances can contribute significant dose. The patient can be shown that by restricting close contact times then doses are lower and restriction times are reduced. **Conclusion:** A flexible calculator is available which can be used in a wide range of circumstances to calculate patient restrictions. Radiopharmaceutical models and contacts can be entered either for a one-off calculation or can be stored for future use. The calculator is freely available from the author.

EP-1062

Evidence-based safety management for short-lived alpha emitters by grant of Nuclear Regulatory Agency of Japan

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Purpose: Diagnosis and treatment using radiopharmaceuticals currently continue to develop in nuclear medicine across the globe, and it is expected that alpha emitters will enhance substantially the efficacy of radionuclide therapy over the next decades as we have seen emerging application of radium-223 dichloride to castration-resistant prostate cancer with bone metastases. In this context, the Nuclear Regulatory Agency of Japan organized and supported projects for application of alpha emitters in radionuclide therapy since 2017. The purpose of this study, granted by the Agency, was to propose novel principles of radiation safety in laws and guidelines so that research and development of radionuclide therapy technologies using nuclides including short-lived alpha emitters are carried out under rational safety control based on scientifically accumulated data. **Methods:** We examined major issues on optimization of protection from the viewpoint of the personnel engaged in production and use of radiopharmaceuticals and from that of the general public in consideration of novel application of therapeutic radiopharmaceuticals by conducting surveys at facilities in Japan and overseas. **Results:** We surveyed circumstances on safety control of alpha emitters at facilities including National Institute of Radiological Sciences (Chiba, Japan) and Fukushima Medical University (Fukushima, Japan) which own accelerators for producing alpha emitters in Japan. We also visited University of Göteborg (Göteborg, Sweden), ARRONAX (Nantes-Saint Herblain, France), and IRSN (Institut de Radioprotection et Sûreté Nucléaire, Saclay, France), and investigated use, disposal, technical standards, GMP production, and regulations regarding of short-lived alpha emitters including astatine-211 and actinium-225. We summarized the results **Discussion and Conclusion:** We figured out the present and future needs of research and development for alpha radiopharmaceuticals in relation to clinical demands, safety management, and regulatory issues. As a result, we recognized that scientific evidence should be accumulated in order to establish safety management in facilities and to revise current regulations in accordance with the international basic safety standards for conventional and novel radiopharmaceuticals.

EP-1063

Dose estimation in caregivers of patients receiving high dose radioiodine therapy.

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Introduction: The aim of this study was to determine safety of the caregivers of patients of differentiated thyroid cancer who receive high-dose radioactive iodine (I-131) treatment **Methods:** The administered activity ranged from 50 mCi to 200 mCi. One or two designated caregivers received specific radiation safety training prior to treatment. One caregiver was allowed to stay adjacent to the room of patient to provide general patient support. Following the discharge as per International Atomic Energy Agency (IAEA) limit (5mR/hr), the caregivers were provided with a Thermo Luminescence Dosimeter (TLD) crystal in the form of a locket to be worn in the neck. The common activities

done by the care-givers in the first week after discharge included travelling together in a common vehicle, eating, sleeping in the next room or providing food and medications. Cumulative radiation dose to the care givers over a period of seven days post administration of I-131 was measured. The TLD crystal was analyzed in TLD reader. **Result:** Twenty two patients (8 male and 14 female) of differentiated thyroid carcinoma treated with high dose radioiodine I-131 were enrolled in this study. None of the patients had karnofsky performance score < 60. The radiation doses to caregivers of hospitalized patients treated with I-131 for thyroid cancer increased with increasing administered dose to the patient. The median dose received by the caregivers was 14.2mSv [9.73-24.2 mSv]. This was well above the constraints of the annual dose-limit to the general public as per the International Commission on Radiological Protection (ICRP) guidelines of 1mSv/yr **Conclusions:** Our study shows that caregivers of patients being treated by high-dose I-131 therapy end up receiving doses of radiation much higher than the recommendations. Measures should be introduced to strictly monitor radiation exposure of caregivers and educate them on radiation protection, both during and after I-131 therapy.

EP-1064

The effect of reduced administered activity and effective dose in younger patients underwent ¹⁸F-FDG PET/CT examinations

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The aim of the present study was to evaluate the effect of the reduction in administered activity and the total effective dose in younger patients underwent ¹⁸F-FDG PET/CT examinations. A sample of 185 younger patients (pts) (AGE<30aa) was collected from PACS in a 2010-2018 period. The patients were divided in two groups: group A (AGE≤18aa) 13 pts (16±2); group B (18aa<AGE<30aa) 172 pts (24±4). The groups were divided in two subgroups (group C 2010-2014; group D 2015-2018). Philips Gemini TOF PET/CT 16 slices system was used. Low-dose CT acquisitions were performed with 120 kV, 100mA, z-axis mA modulation, 5 mm slice thickness, 0.5 sec rotation. The ¹⁸F-FDG PET effective dose (E_{PET}) was calculated according ICRP 106 publication. The CT effective dose (E_{CT}) was evaluated by the use of CT-Expo software. Median and 25° and 75° percentile of the distributions were calculated. Mann-Whitney independent sample test was performed to evaluate the significant statistically differences between groups C and D for E_{PET} , E_{CT} and total Effective dose (E_{tot}) respectively for group A and B. 35 pts underwent repeated ¹⁸F-FDG PET/CT examinations. Group A: E_{PET} was 4.3 mSv (range 3.5-5.4) for group C and 2.8 mSv (range 2.7-3.4) for group D; E_{CT} was 6.0 mSv (range 5.8-10.1) for group C and 7.7 mSv (range 7.0-9.2). No statistically significant differences were found for PET ($p=0.0321$) and CT ($p=0.721$) for group A. Group B: E_{PET} was 4.4 mSv (range 4.1-5.0) for group C and 3.8 mSv (range 3.4-4.3) for group D; E_{CT} was 5.9 mSv (range 5.7-6.6) for group C and 6.1 mSv (range 5.9-6.4). Statistically significant difference ($p<0.0001$) was found for PET and no statistically significant difference ($p=0.0534$) for CT.

Group A: E_{tot} was 11.4 mSv (range 7.7–16.0) and 10.4 mSv (range 9.4–14.0); group B: E_{tot} was 10.6 mSv (range 6.3–27.8) and 10.1 mSv (range 5.3–15.3) for group C and D respectively. No Statistically significant differences were found for group A ($p=0.0212$) and B ($p=0.39$). A minimum of two times/year repeated examinations was found. The analysis showed an effect of the administered activity reduction on PET effective dose in 18–30 years old patients. The sample of 18 years old patients was statistically reduced to appreciate the effect. The total effective dose was strongly influenced by CT effective dose. This result could be caused by the use of CT z-axis mA modulation. Dose optimization in repeated examinations is essential for younger patients performing follow-up.

EP-1065

^{18}F -PSMA vs. ^{68}Ga -PSMA11; S-value Estimation in XCAT BMIs Using GATE Monte Carlo Code

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Purpose: recently introduced radiopharmaceutical ^{18}F -PSMA has attracted growing interests for prostate cancer imaging compared to other PSMA-targeted tracers such as ^{68}Ga -PSMA-11. The reason may be due to its longer half-life which makes it suitable for delayed phase imaging as well as lower irradiation from the patient to the other people after injection. Different aspects of ^{18}F -PSMA for prostate imaging have been the subject of much research. Pre-estimation of absorbed dose in critical target organs can be performed by atlas-based simulations thanks to advanced anthropomorphic phantoms and Monte Carlo codes. In this study we aim to calculate S-values of ^{18}F -PSMA and ^{68}Ga -PSMA-11 in different BMIs of XCAT male phantoms for pre-estimation of absorbed dose in critical target organs using Monte Carlo simulation. **Subjects & Methods:** Five BMIs of XCAT male phantoms were generated. The matrix size of each phantom was 128128300 and the dimension was 3.125 m³ to cover the desired region of the body. We chose spine, prostate, kidney, and salivary gland as the source organs and we calculated the S-value (mGy/MBq.s) in kidney, spleen, liver, salivary, prostate, spine, small intestine, and lung as the target organs. We employed GATE Monte Carlo code (version 7.2) to perform dosimetry calculations for 20 MBq activity of ^{18}F -PSMA and ^{68}Ga -PSMA-11. **Results:** The S-values of both in self-absorption and target organs were significantly lower for ^{18}F -PSMA compared to ^{68}Ga -PSMA-11. The highest difference between the absorption in kidneys, as one the most critical targets, is for BMI of 28.3. The highest S-value in prostate from prostate is 0.0175 mGy/MBq.s in BMI of 24.9 for ^{68}Ga -PSMA-11, whereas it is 0.0047 mGy/MBq.s in BMIs of 28.3 and 24.9 for ^{18}F -PSMA.

Moreover, when spine is considered as the source organ, the absorption in kidneys and prostate is approximately 100 times lower in ^{18}F -PSMA. **Conclusion:** We employed different XCAT BMIs to more specifically investigate the difference between the S-values of organs from the ^{18}F -PSMA and ^{68}Ga -PSMA-11 radiopharmaceuticals. Our results show that the absorbed dose falls down dramatically when ^{18}F -PSMA is employed instead of ^{68}Ga -PSMA-11. Despite to the fact that ^{18}F -PSMA production is more difficult than ^{68}Ga -PSMA-11, the lower absorbed dose in patient body may be another reason to put ^{18}F -PSMA in superiority for prostate cancer imaging.

EP-1066

Dosimetric measurements of the personnel working at a children's nuclear medicine unit

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Purpose: Our study involves the dosimetric measurements of the personnel working at Children's hospital nuclear medicine unit. Lack of previous data regarding dosimetric measurements of the personnel involved exclusively in pediatric examinations illustrated the necessity for such data. **Subjects - Methods:** The daily work of the unit involves SPECT/CT as well as PET/CT examinations. The personnel of the unit consist of three medical doctors, six technologists, one nurse and two medical physicists. All staff was carrying chest as well as finger's (TLD) dosimeters during daily practices. Dosimeters' reading were analyzed by the National Committee of Atomic Energy and the values of personal depth dose equivalent $H_p(10)$ for chest dosimeters and $H_p(0.07)$ for finger dosimeters were reported in a monthly basis. The handling of children during the injection of the dose and the imaging process can be long time processes that can affect the involved personnel regarding dosimetry levels. **Results - Discussion:** In SPECT/CT examinations the administrated doses range between 0.1 - 20 mCi and in PET/CT 0.9–12 mCi. The exposure of personnel to radiation is increased due to the handling of examined children during: the administration of the dose, where children proved to be 'difficult' to handle patients and during the actual imaging process, where children react due to claustrophobia, pain, clinical condition, psychological status, etc. risking to jeopardize imaging data. During the procedure, each staff member is involved in different - specific stages: physicists and some technologists measuring and preparing doses, medical doctors as well as nurse to locate vein and administer the prescribed dose and finally, technologists, nurse and medical doctors handling children during the imaging stage. Therefore, personal depth dose equivalent H_p was varied. Although, all measured annual doses are well within national limits, recorded relatively high doses of personnel involved in a specific step of the chain procedure would flag the need for consideration of further radioprotection measures. **Conclusions:** Nuclear med-

icine examinations in children population require longer exposure time periods to radiation either during the dose injection or during the imaging process. Relatively high doses that correspond to specific procedures indicate that further radioprotection measures need to be considered and applied.

EP-1067

Compartmental models for biokinetics and dosimetry of ^{68}Ga -labelled somatostatin derivatives

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Aim: The aim of this study was to develop compartmental biokinetic models for ^{68}Ga -DOTATOC and ^{68}Ga -DOTANOC - two ^{68}Ga -labelled somatostatin derivatives used for cancer imaging of tumors showing overexpression of somatostatin receptors.

Materials and Methods: Compartmental biokinetic models were established based on the data reported by Hartmann *et al.* [1] and Pettinato *et al.* [2] for ^{68}Ga -DOTATOC and ^{68}Ga -DOTANOC, respectively. Since both agents were administered via an intravenous bolus injection, we included blood as a central compartment in both models. Notable uptake of ^{68}Ga -DOTATOC was also observed in adrenals, kidneys, liver, red marrow, spleen, thyroid and urinary bladder contents. All these regions were included in the biokinetic model for ^{68}Ga -DOTATOC. The set of body organs and tissues considered in the biokinetic model for ^{68}Ga -DOTANOC comprised blood, lungs, kidneys, liver, pituitary gland, spleen, heart contents and urinary bladder contents. In both models, liver was represented by two sub-compartments defining a short- and a long-term retention of the considered agents. Two compartments were also used for kidneys, analogously to the commonly used representation of urinary tract in biokinetic models summarized by ICRP [3]. To account for activity accumulated in body tissues that were not explicitly modelled, rest-of-body compartment exchanging with blood was added to both models. Reference value of the total blood volume was assumed (5300 ml for adult male). First-order kinetics was considered. The parameters of the biokinetic models were estimated using the commercial software package SAAM II® (The Epsilon Group, version 2.3.1.1). **Results:** Compartmental model parameters were estimated from the experimental data with SAAM II software package. Based on the developed biokinetic models, time-integrated activity coefficients were computed. The latter showed an acceptable agreement with the corresponding values reported by Hartmann *et al.* [1] (2–18%) and Pettinato *et al.* [2] (3–33%) with the maximum difference for heart content in case of ^{68}Ga -DOTANOC. The predictions of the developed models will be further compared to the available published data. **Conclusion:** Compartmental models for biokinetics and dosimetry of two agents - ^{68}Ga -DOTATOC and ^{68}Ga -DOTANOC - were established. Both models satisfactorily describe the biodistribution of ^{68}Ga -DOTATOC and ^{68}Ga -DOTANOC in human body. 1. H. Hartmann *et al.*, Radiation exposure of patients during ^{68}Ga -DOTATOC PET/CT examinations. *Nuklearmedizin*, 2009. **48**(5):p.201-7. 2. C. Pettinato *et al.*, ^{68}Ga -DOTANOC: biodistribution and dosimetry in patients affected by neuroendocrine tumors. *Eur J Nucl Med Mol Imaging*, 2008. **35**(1):p.72-9. 3. ICRP, 2015. Occupational

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EP-1068

Optimization of CT protocols for thyroid and parathyroid SPECT/CT imaging

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Introduction: A national survey of patient exposures from hybrid imaging in Nuclear Medicine, performed in Bulgaria in 2014, revealed that single photon emission computed tomography/computed tomography (SPECT/CT) imaging of either thyroid or parathyroid glands was performed by applying a CT scan of the whole anatomical region, neck and chest, subject to SPECT. In most cases it was not necessary to perform a CT scan matching the whole SPECT region. The aim of this study is to propose an optimized CT protocol for patients sent for thyroid or parathyroid examinations by reducing the CT scan length. **Materials and Methods:** The standard CT protocols for both types of examinations on a GE Discovery NM/CT 670 Pro SPECT/CT system included neck and chest scan with the same exposure data, applying tube current modulation. After the optimization the CT scan was restricted to the region of radiopharmaceutical uptake. Comparison of scan length, dose-length product (DLP) and effective dose from the old and the new protocols was performed for patients with weights in the range 50–90 kg. Software was used to estimate effective dose from the CT scan separately for males and females. For that purpose, model of the CT scanner, exposure data, mean scan length and mean values of volume Computed Tomography Dose Index (CTDI_{vol}) and DLP of the patient's cohorts were introduced in the software. **Results:** A total of 17 patients (12 females and 5 males) undergoing either thyroid or parathyroid examination received CT of the neck and chest before the optimization. After the introduction of the optimized protocol, data were collected for a total of 70 patients (57 females and 13 males). After the optimization, the mean scan length for males was reduced from 39 to 22 cm (42 % reduction) and for females the reduction was from 44 to 22 cm (50 %). The mean DLP was decreased by about 34 % (from 138 to 91 mGy.cm mean value) for males and 48 % (from 147 to 77 mGy.cm mean value) for females respectively. The effective dose was reduced by 67 % (from 1.8 to 0.6 mSv) for males and 79 % (from 2.8 to 0.6 mSv) for females. **Conclusions:** A simple method for optimization of the CT part of hybrid SPECT/CT imaging of the thyroid or parathyroid glands was introduced. It led to significant decrease of the CT contribution to the total effective dose from the examinations.

EP-1069

Estimation of hand exposure due to potential radiopharmaceutical contamination

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When handling radiopharmaceuticals, there are cases of increased skin exposure of the hands among workers engaged in similar operations and procedures. An important goal of radiation protection is the introduction of reliable provisions aimed at ensuring adequate protection of workers against harmful effects of ionizing radiation. The proposed approach consist in identifying the requirements for radiation protection based on the evaluation of the distribution of the skin exposure in terms of HP(0.07) on hands during the preparation or administration of radiopharmaceuticals to patients. The currently introduced assessment of the dose distribution relies on the comparison of results obtained from the monitoring of several workers engaged in similar operations, multiple measurements of a selected worker or using the Monte Carlo method simulating individual operations which are considered important with respect to exposure of the worker. This method of assessing various techniques of handling radiopharmaceuticals permit not only to detect potential contamination but also to determine the exposure of the skin at locations where dose mapping has not been performed. The proposed method of assessing the manipulation with radiopharmaceuticals taking into account objectives of radiation protection has been examined for three workers who have shown a significant change in the dose distribution on hands comparing with the remaining two measurement cycles. The first worker prepared and administered ¹³¹I-labeled radiopharmaceuticals, the other prepared ¹⁸F-FDG while the third one injected the ¹⁸F-FDG to the patient. These workers were not aware of the causes of excessive exposure and therefore a computer simulation of the exposure was performed using the Monte Carlo method modeling basic operations of individual manipulations with the sources and specifying the location of the maximum local skin exposure on the hands and additionally also is able to determine the overall exposure of the hands as an entire organ. Using this method, it has been found that the first worker was probably contaminated, the second worker has possibly received excessive exposure to the part of his finger through the gap in the shield, and the third person during the administration of radiopharmaceuticals carried out several non-standard procedures caused by the patient's health conditions. The proposed method of assessment of radiation exposure is advantageous in specifying requirements for improving the quality of radiation protection of individual workers as well as entire working teams. **Acknowledgment:** The study has been supported by the project SGS18/100/OHK4/1T/17.

EP-1070

The Comparison of the External Dose Measurement of Children and Adolescent Patients With Adult Patients Treated with Radioiodine Therapy

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Objectives: For the adult patients, the rules that should be followed at home after the patient is discharged from the hospital are explained briefly in guidelines. However, it is difficult to apply these rules in case the patient is a child or adolescent. Childhood and adolescent patients have different characteristics compared to adults at diagnosis and during the treatment. Thus, radioactive iodine excretion is affected. In addition, since childhood and adolescent is a period that requires more attention and care, it requires different approaches after discharge. Parents or caregivers may have higher doses due to longer periods of time and longer periods of time with children. The aim of this study is to evaluate the radiation safety of children and adolescents patients with thyroid cancer who received radioactive iodine-¹³¹I(RIT) treatment by comparison with external dose measurements of adult patients according to their treatment doses and days of hospitalization, during discharge from the hospital. **Material and Methods:** In our clinic, we retrospectively evaluated external measurement doses of 158 children and adolescent patients and 158 adult patients who underwent RIT for well-differentiated thyroid cancer between 1984 and 2018. The maximum age limit for adolescent patients was accepted as 21, and patients above the age 21 is the adult patient group. During the RIT, the hospitalization time were grouped as 2, 3 and 4 days, and the radioactive iodine treatment doses as <3700 MBq, 3700 MBq and >3700 MBq. The external measurements were taken from the abdominal level at 1 m. Geiger Mueller Hand Monitor: NEB-211, Turkey) was used for external measurement. IBM SPSS Statistics 22 program was used for statistical analysis. **Results:** In <3700MBq, 3700MBq treatment doses; The values of external dose measurements of children and adolescents were statistically significantly higher than the adult group(p<0.05). Similarly, when the hospitalization time was 4 days; the values of external dose measurements of children and adolescents were statistically significantly higher than the adult group(p<0.05). **Conclusion:** Indicating the need for special precautions for children and adolescents, due to the facts that the disease is metastatic in children, need for repetitive treatment doses due to higher recurrence rate than adults, and inability to apply the radiation protection rules as strict as adults, different approaches in radiation safety rules are required for children and adolescents. In terms of radiation safety in childhood and adolescence, we suggest that more specific regulations for family members and caregivers should be established and informed.

EP-1071

Comparison of External Radiation Dose Rates Measured from ¹⁷⁷Lu-Octreotate/Octreotide, ¹⁷⁷Lu-PSMA and ¹³¹I Treated Patients

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Aim: New radionuclide treatments are developed and used to treat different cancers. The patients emit radiation for some time after the treatment, and the dose rate depends on the radiopharmaceutical that is used, patient's metabolism and tumor

burden. Considering radiation exposure to the medical staff, patient's family members and public, it is necessary to investigate external radiation dose rates from the patients treated with radionuclide therapy. We measured and compared external radiation dose rates measured from ^{177}Lu -octreotate, ^{177}Lu -octreotide, ^{177}Lu -PSMA, and ^{131}I treated patients after their treatment at the time of imaging. **Materials and Methods:** We performed dose rate measurements using RDS-31 Multi-purpose Survey Meter (Mirion) at one meter (1 m) distance from 10 ^{177}Lu -octreotate or ^{177}Lu -octreotide (mean administered activity $A=6.9\pm0.3$ GBq, range 6.5–7.5 GBq), and 10 ^{177}Lu -PSMA treated patients (mean $A=6.4\pm0.2$ GBq, range 5.9–6.6 GBq) at approximately 24 hours and one week after treatment. We also measured the dose rate from 12 ^{131}I treated patients (mean $A=3.8\pm0.1$ GBq, range 3.7–4.0 GBq) at one week after treatment. Each time, background reading was measured and subtracted. All the patients had their first cycle of treatment. **Results:** The mean dose rate at 1 m for ^{177}Lu -octreotate/octreotide treated patients was 4.2 ± 1.4 $\mu\text{Sv/h}$ (range 2.0–7.0 $\mu\text{Sv/h}$) and 0.6 ± 0.6 $\mu\text{Sv/h}$ (range 0.14–1.6 $\mu\text{Sv/h}$) at 24 h and one week after treatment, respectively. The mean effective half-life estimated by monoexponential fitting was 50.2 ± 21.0 h (range 28.1–77.0 h). For ^{177}Lu -PSMA treated patients, the mean dose rate was 10.8 ± 3.7 $\mu\text{Sv/h}$ (range 6.8–15.8 $\mu\text{Sv/h}$) and 2.0 ± 1.8 $\mu\text{Sv/h}$ (range 0.2–5.5 $\mu\text{Sv/h}$) at 24 h and one week after treatment, respectively. The mean effective half-life was 55.0 ± 26.5 h (range 24.5–97.6 h). For ^{131}I treated patients the mean dose rate at 1 m one week after the treatment was 0.4 ± 0.5 $\mu\text{Sv/h}$ (range 0.1–1.6 $\mu\text{Sv/h}$). **Conclusion:** The dose rate measured at 1 m from the patient was significantly higher for ^{177}Lu -PSMA treated patients compared to ^{177}Lu -octreotate/octreotide treated patients at 24 hours ($p=0.0002$) and one week ($p=0.03$). On the other hand, the effective half-life was only slightly higher in ^{177}Lu -PSMA treated patients than in ^{177}Lu -octreotate/octreotide treated patients. At one week after treatment the dose rate from ^{131}I treated patients was lower compared to ^{177}Lu -PSMA and ^{177}Lu -octreotate/octreotide treated patients.

EP-1072

Estimate of possible radioactive contamination of workers' hands at nuclear medicine departments

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Aim: The preparation and application of radiopharmaceuticals are procedures during which the worker may be exposed to ion-

izing radiation and at the same time such operations could also result in radioactive contamination of his gloves or his hands. The aim of the paper is to find out the likely contamination of hands during the mapping of dose distribution on hands. This additional assumed contamination of the gloves will be assessed in relation to the frequency and the extent of radiation exposure.

Material and Methods: In this study, the workers from PET departments using radiopharmaceuticals labeled with ^{18}F , ^{11}C and ^{68}Ga and department engaged in the ^{131}I therapy in Czech Republic and Slovakia have participated. During the measurement the workers wore gloves with TLDs in 12 positions (in the case of the ^{131}I an additional TLD was fixed in the centre of the palm). In total, 126 measurements were accomplished. The possible contamination was estimated based on the TLD readings in 12 positions of each hand. The unexpected increase (more than 5 times) in the exposure detected by a TLD in a specific location was most probably due to the possible contamination. **Results:** Based on the results obtained up to now, the suspected possible contamination was most frequently observed on the right hand. The preliminary results suggest that in about 5 % of cases the suspected possible contamination may come from positron radiopharmaceuticals while in around 10 % cases possible contamination may result from handling with ^{131}I solution. In some cases, the contamination was estimated at several locations of one hand, or even on both hands. The subsequently observed contamination may account for a significant portion of the annual limit when considering the incidence of such cases and the number of patients (or activity handling). In one case, the possible local contamination was estimated to reach up to 200 mSv/GBq, which may pose a risk of exceeding the relevant annual dose limit. **Conclusion:** The preliminary results have shown that there may exist situations of possible contamination, which the workers are probably not aware of. From the measurements completed so far, where the possible contamination has been additionally estimated, it is possible to outline the importance of regular examinations aimed not as to the potential contamination of the gloves but also in any suspected situations which may lead to the contamination. **Acknowledgment:** This study has been supported under the project SGS18/100/OHK4/1T/17.

EP-1073

Eye lens doses of staff members in two Finnish nuclear medicine units

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Purpose: The aim was to study the level of the eye lens doses of technicians in nuclear medicine units of busy university hospitals, as the new radiation safety legislation reduced the eye lens annual dose limit to 20 mSv averaged over 5 years. **Subjects and Methods:** The measurements of eye lens dose equivalent ($H_p(3)$) were performed at nuclear medicine units of Helsinki and Oulu University Hospitals, where altogether 21 and 8 measurement periods were conducted based on the participation of 7

and 8 technicians, respectively. The length of one measurement period varied between 8 to 20 days, and was always synchronized with the periods of the official staff dosimeters for measuring the whole body dose ($H_p(10)$). $H_p(3)$ values were measured using EYE-D dosimeters with inserted thermoluminescence detectors (MCP-N) attached to technicians' glasses or to a head band. The detectors were calibrated and read in the Radiation Metrology Laboratory at STUK for gamma radiation, as it had the major impact on $H_p(3)$ with the radionuclides used. Time spent in different work tasks were monitored by specific forms filled in daily by each technician. The work tasks included PET-CT, gamma camera / SPECT-CT and radiopharmacy related tasks including patient preparation and care. For F-18-FDG studies, the radiotracer was provided by a commercial company and an automatic injector was utilized in both nuclear medicine units. After background correction, the collected $H_p(3)$ data were correlated to the $H_p(10)$ data. Also, the maximum and mean annual eye lens doses were estimated from the measurement data assuming similar working conditions and tasks for the technicians during the whole year. **Results:** A correlation was found between the measured $H_p(3)$ and $H_p(10)$ values (Pearson's coefficient $r = 0.90$). The mean (min-max) values of $H_p(3)$ and the corresponding values of $H_p(10)$ measured per period were 77 (0–250) μ Sv and 108 (0–300) μ Sv, respectively, including all technicians and measuring periods. The maximum estimated annual dose to the lens of the eye was below 4 mSv and the mean 1.2 mSv. The highest doses were obtained by technicians working with PET-CT related tasks. **Conclusion:** In this study, the eye lens doses correlated with the whole body doses. Also, the estimated annual eye lens doses for nuclear medicine technicians in these study settings seemed to stay well below the new eye lens dose limit.

EP-1074

Significant reduction of radiation dose with minimizing disruption of image quality in F-18 FDG PET/CT

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Aim: The aim of this prospective study was to optimize FDG PET/CT protocol to reduce radiation dose to patient as low as possible while minimizing image quality. **Materials and Methods:** All data was acquired from Discovery 690 PET/CT (LYSO crystal, 64-sliced CT, GE Healthcare). Torso PET/CT was performed with 2 minutes per bed and time-of-flight acquisition with other advanced techniques following F-18 FDG (3.7 MBq/kg) administration. After 5-time modification to decrease radiation dose progressively and to minimize disruption of image quality, standard CT protocol (standard protocol; 120 kVp, 80–200 mA, noise index 23, pitch 0.984 : 1, rotation time 0.5 sec, thickness 3.75 mm) was amended to modified low-dose CT protocol (modified protocol; Smart mA with 30–160/180 mA and modifying noise index by BMI, advanced reconstruction algorithm and arm-raising position). The total effective dose received by each patient was taken as the sum of the PET and CT components of the study. Effective dose of CT was estimated using dose-length product values from reports generated by the scanner and anatomy-specific conver-

sion factors. Effective dose of PET was calculated the whole body effective dose based on ICRP recommendations. Effective dose from modified protocol ($n=160$, 4th modification) was compared to standard protocol ($n=132$). **Results:** Compared to standard protocol, the total effective dose received by patient in modified protocol was 7.3 ± 1.6 vs. 12.1 ± 2.4 mSv, 6.5 ± 1.5 vs. 11.5 ± 2.3 mSv and 6.8 ± 1.7 vs. 11.5 ± 2.5 mSv in men, women and all patients consecutively (all $p < 0.001$). Modified protocol resulted in 63% reduction of CT effective dose and 41% reduction of the total effective dose of PET/CT. Effective dose from CT was $39 \pm 4\%$ in PET/CT and only 7 (4.5%) patients who had extremely high body weight and BMI exceeded 10 mSv using modified protocol. There was no significant difference in male (47% vs. 41%), age (61 ± 13 vs. 62 ± 15), body weight (59 ± 11 , $35 \sim 95$ vs. 59 ± 11 , $37 \sim 103$ kg), height (1.59 ± 0.08 vs. 1.59 ± 0.08 m) and BMI (23.2 ± 3.6 , $15.4 \sim 35.8$ vs. 23.4 ± 3.6 , $15.8 \sim 37.9$) between two groups (all $p > 0.05$). **Conclusion:** Modified protocol showed markedly decreased the total effective dose received by patient from PET/CT study and resulted in an effective dose of less than 10 mSv with minimizing disruption of image quality in most patients.

EP-1075

Neural networks prediction of ambient dose equivalent rate in low-dose I-131 outpatient treatments

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Introduction: The treatment for low-risk well-differentiated thyroid cancer consists in the administration of an activity of 1.1 GBq of I-131 after surgery. Such a low administered activity allows outpatient treatments in a Nuclear Medicine department without shielded rooms, provided that the radiation protection requirements are met. In our institution, one of these requirements is that, at the moment of discharge, the rate of ambient dose equivalent ($H^*(10)$) at 1 m must be below 40 μ Sv/h. Based in our experience, this value is reached on average six hours after intake. The aim of this work is to study if neural networks can be useful to predict if the $H^*(10)$ rate at 1 m will be below 40 μ Sv/h six hours after intake. **Material and Methods:** We designed a 2-layer feed-forward neural network model with one hidden layer of sigmoid neurons, followed by an output layer of linear neurons. The training algorithm was Bayesian regularization backpropagation. We used measurements of $H^*(10)$ rate at 1 m and at 10 cm taken approximately every 30 minutes after intake, over 172 patients treated between 2013 and 2017. For each patient, the first seven measurements (approximately until 4 h after intake) of $H^*(10)$ rate at 1 m, $H^*(10)$ rate at 10 cm, and time after intake, were used as input data for the neural networks. The measured $H^*(10)$ rate at 1 m (6 h after intake) was the target data. Patients were randomly divided into three disjoint sets: training (70%), validation (15%), and evaluation (15%). This procedure was carried out over 1000 networks, to obtain an uncertainty estimate of the predictions. Once trained, the networks were fed with the evaluation set, and the mean predicted values of $H^*(10)$ rate at 1 m (6 h after intake) was compared with the experimental values. **Results:** The mean difference over the 1000 neural networks between predicted and experimental val-

ues of $H^*(10)$ rates at 1 m (6 h after intake) was $(0.5 \pm 3.2) \%$ ($k=2$). The mean correlation coefficient was $r^2=0.84 \pm 0.13$. **Conclusion:** The values of $H^*(10)$ rate at 1 m (six h after intake) predicted by a neural network model are correlated with measured ones. This result allows to predict with two hours of anticipation if patient could be discharged, thus improving patient management.

EP-1076

Increase of the staff hand radiation exposure due to a new regulation of the radiation protection published by the State Office for Nuclear Safety

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Introduction: Radiation exposure of the population is increasing with participation of the medical irradiation. The state authorities' effort is to change this undesirable trend. Radioactivity of the radiopharmaceutical in the syringe must be measured before injecting it to the patient according to a new state regulation. National radiological standard (NRS) permits injection of radioactivity within the range of 25 % of the prescribed one. The goal of our study was to assess the difference between the calculated and the measured radioactivity and the difference of irradiation of the hands of the staff. **Methods:** All measurements were done with ^{99m}Tc HDP. We drew a volume calculated according to a specific radioactivity in the vial into the syringe (calculated activity) and we subsequently measured this syringe in a dose calibrator (measured activity). We used another finger dosimeter during this measurement. We calculated correlation coefficient (r) and compared measured and calculated activities using a paired t-test (level of significance 5 %), the dosimeter was evaluated separately as usual. We evaluated 169 syringes from 22 kits (specific activity 841.50–1195.57 MBq/ml), prescribed activity was 500–1000 MBq. **Results:** Values of measured and calculated activities correlated well ($r=0.981$, $p < 0.001$) but differed significantly ($t = -6.623$, $p < 0.001$). Median of the differences between the measured and the calculated activities was 16.44 MBq (–95.70 to 74.54 MBq), i.e. 2.01 % (–9.97 to 12.22 %). Radiation exposure to the hands of the staff increased during measurement from 1.92 mSv to 2.52 mSv (31.25 %). **Conclusion:** The tolerance of the injected radioactivity is abundantly met if the dose in the syringe is only calculated according to the specific radioactivity in the vial without measurement of the every single syringe. On the other hand, this measurement increases significantly radiation exposure of the staff hand (>30%).

EP-1077

Occupational exposure for eye, thyroid and gonads to medical workers operating in a PET/CT facility

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Purpose: Personnel monitoring results provide information on routine radiation exposure, assist in work planning and allow control of the workplace. The aim of this study was to mea-

sure the gamma dose received by dedicated medical workers operating in our PET/CT department to eye, thyroid and gonads. PET/CT studies are restricted to the use of F-18 FDG, FLT and FCH are used in our center. **Method:** To estimate the effective dose from external exposure, all 6 members of the staff (2 nurses, 2 medical physicists, 2 technologists) had TLD badges worn at plastic glasses, on the region of gonads and in front of the thyroid area. High sensitivity thermoluminescent dosimeters were used. The measurements that were made at all stages of the PET/CT procedure: dose segmentation, injection of the radiopharmaceutical, handling the patient and positioning the patient. **Results:** Results show that the mean daily effective dose ($\mu\text{Sv} \pm \text{SD}$) received by each member of the staff for eye were: Nurse1 13.4 ± 5.2 , Nurse2 12.19 ± 3.2 , technologist1 11.52 ± 4 , technologist2 12.10 ± 2.3 , Medical Physicist1 9.95 ± 2.1 , Medical Physicist2 8.72 ± 3.2 . The mean daily effective dose ($\mu\text{Sv} \pm \text{SD}$) received by each member of the staff for thyroid were: Nurse1 12.46 ± 4.4 , Nurse2 12.32 ± 3.7 , technologist1 11.63 ± 2.5 , technologist2 12.44 ± 2.4 , Medical Physicist1 8.98 ± 3.91 , Medical Physicist2 8.23 ± 2.85 . Finally the mean daily effective dose ($\mu\text{Sv} \pm \text{SD}$) received by each member of the staff for gonads were: Nurse1 11.98 ± 3.9 , Nurse2 10.26 ± 2.3 , technologist1 8.26 ± 1.6 , technologist2 11.49 ± 3 , Medical Physicist1 7.65 ± 3.6 , Medical Physicist2 7.12 ± 2.92 . **Conclusions:** From our results we can observe that the numbers are significantly lower than the recommended annual dose limit Cumulative dose to staff members.

EP-81

e-Poster Area

Bone & Joint: Dual-Energy X-Ray Absorptiometry

EP-0084

The utilization of proper knee position improves the precision of spinal DXA examination

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Introduction: Dual-energy X-ray absorptiometry (DXA) is the reference methodology for the diagnosis of osteoporosis and the assessment of the fracture risk. However, there are some groups of patients that cannot be positioned correctly, due to several medical conditions. In this study, we evaluated and compared the precision and the accuracy of the spinal bone mineral density (BMD) measurements obtained using two geometrical configurations of the patient's body relative to the scanning bed. **Subjects and Methods:** A Hologic Discovery-W fan beam bone densitometer has been utilized in 52 randomly chosen women (average age: 53.4 years, [32–65]). The influence of their positioning on the scanning bed was evaluated by four sequential lumbar spine scans with repositioning between them, i.e., all women were scanned twice using the standard lumbar spine scanning protocol ($\sim 90^\circ$ trunk to hip and $\sim 90^\circ$ hip to tibia angles for spine flattening and reduction of the spine to bed distance) and twice with no bending (i.e. the

entire leg laying on the upper surface of the scanning bed). **Results:** The short term *in vivo* measurement precision in the standard configuration, 1.11%, was superior to that with the modified one, 1.55%. Paired t-test revealed a statistically significant difference in the BMD values obtained using the two configurations, i.e. (0.921 ± 0.0144) g/cm² in the standard one and (0.941 ± 0.0148) g/cm² in the modified one. The corresponding difference, 0.020 g/cm² on the average, was not found to be dependent on the BMD value ($p=0.3$). **Conclusion:** In some patients, e.g. some trauma patients, it is hard to carry out spinal measurements using the recommended body posture. Scanning in the modified one introduces a bias and deteriorates the measurement precision. In such cases, femoral hip rather than spinal measurement could be carried for the initial evaluation. However in case that a spinal measurement has to be carried out, such in case of an on-going follow-up study, the BMD values obtained in the non-standard configuration have to be corrected due to 0.020 g/cm² bias, before reaching a medical decision.

EP-0085

The Relationship Between Serum Vitamin D Levels and Bone Mineral Density in Geriatric Patients

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Purpose: The aim of this study is to evaluate the relationship between serum vitamin D levels and bone mineral density (BMD) in geriatric patients. **Subjects and Methods:** Older than 65 years patients who were referred for BMD measurement evaluated retrospectively. Totally 103 patients (74 Female, 29 Male), (65-90 years old (mean: 71.2 ± 5.4)) included the study. Patients who treated with drugs affecting bone metabolism and a history of metabolic bone disease except osteoporosis were excluded. Serum 25(OH)D3, parathyroid hormone (PTH), calcium (Ca) levels and BMD measurement were recorded. 25(OH)D3 levels <15 ng/ml was accepted as vitamin D insufficiency. **Results:** The prevalence of vitamin D insufficiency was found 34% in all patients. The prevalence of vitamin D insufficiency in women (52%) was significantly higher compared to men (27%) ($p=0.032$). The prevalence of osteoporosis was found in 54% of all patients. The prevalence of osteoporosis was found significantly higher in women (62%) compared to men (35%) ($p=0.021$). There was no statistically significant difference between patients with normal vitamin D levels and patients with low vitamin D levels for both hip and vertebral BMD. There was no statistically significant correlation between BMD and vitamin D, PTH, Ca levels. **Conclusion:** In this study, there was no relationship between BMD and vitamin D levels in geriatric patients. There is need further studies with larger patient population in which repeated measures of vitamin D levels and many other factors affecting bone density are also evaluated.

EP-0086

Dual-Energy X-Ray Absorptiometry in the Evaluation of 1 Year Cross-Sex Hormonal Treatment

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Introduction: Gender dysphoria (GD) is defined as the suffering related to an incongruence between one's experienced and one's assigned gender of a duration of at least 6 months. Persons who experience gender-related distress might desire gender affirming treatment with sex steroids. Sex steroids are also important determinants of bone acquisition and bone homeostasis. Osteoporosis is defined as a skeletal disease, characterized by low bone mass and micro architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Dual-energy X-ray absorptiometry (DXA) which provides fast scanning, improved spatial resolution, applied to central and peripheral skeletal sites is currently used for detecting osteoporosis. Cross-sex hormonal treatment (CHT) in transgender persons can affect bone mineral density (BMD). The aim of this study was to investigate the first-year effects of CHT on BMD in transgender persons. **Material and Methods:** A total of 34 patients aged from 19 to 66 years (mean 35 years), 12 transwomen and 22 transmen, were included. All patients completed the first year of CHT. Twenty-one of 34 patients (9 transwomen and 12 transmen) underwent sex reassignment surgery (SRS). Transwomen (male-to-female transgenders) received estrogen and anti-androgens, whereas transmen (female-to-male transgenders) were treated with testosterone. A dual-energy X-ray absorptiometry (DXA) (Unigamma Plus, L'ACN, Milano, Italy) was performed at baseline and after one year CHT to measure lumbar spine (LS) and femoral neck (FN). BMD, T-score and Z-Score before and after 1 year of CHT were measured. **Results:** An increase of LS BMD was observed in 29 patients (85.2 %) and an increase of FN BMD was observed in 16 patients (47%). In transwomen, the difference of LS BMD mean was 0.11 (std 0.25), the difference of FN BMD mean was 0.08 (std 0.32). In transmen, the difference of LS BMD mean was 0.08 (std 0.21), the difference of FN BMD mean was 0.20 (std 0.36). There was no statistical significance of the LS BMD and FN BMD differences between the two groups. **Conclusion:** DXA is a valid method to evaluate the effects of cross-sex hormonal treatment in transgender persons. BMD increased overall in both groups after 1 year of CHT. LS BMD increased more in transwomen, but FN BMD increased more in transmen.

EP-82

e-Poster Area

Clinical -> Diagnostic study -> Adult study -> Oncology study -> Organ-based oncology -> Brain, malignant

EP-0399

Clinical impact of 18F-FAZA PET/CT in high grade glioma: correlation with hypoxia immunohistochemical markers and implications for radiotherapy boost

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Introduction: To investigate the correlation between hypoxia imaging data, by using 18F-FAZA PET/CT, and hypoxia immunohistochemical markers in patients with high-grade glioma (HGG) to explore the potential impact on radiotherapy treatment. **Subjects and Methods:** Prospective enrolment of 17 pts with brain MRI suggestive for HGG undergoing pre-treatment 18F-FAZA PET/CT. The following PET-derived parameters have been considered: SUVmax, SUVmean and metabolic tumour volume (MTV) at different thresholds of 40%, 50%, 60% (40-50-60), hypoxic volume (HV) estimated by applying different positivity thresholds to tumour to blood ratio (1.2, 1.3, 1.4) obtaining HV1.2, HV1.3, HV1.4. Seven/17 patients underwent surgical excision of the lesion (group 1) while 10/17 pts underwent stereotactic biopsy (group 2). Immunohistochemical analysis on the most representative tumor section were performed considering the following markers: hypoxia inducible factor 1 α [HIF-1 α], Carboxic Anhydrase IX [CA-IX] and Glucose Transporter-1 [GLUT-1] and a semiquantitative scoring system with five categories (0:0%, 1:<or=10%, 2:11-25%, 3:26-50% and 4:51-75%) was applied to define their expression. Tumor vascularity and proliferation (Ki-67) have been evaluated. Spearman's correlation was used for comparing PET-derived parameters and anatomopathological features. Seven patients were treated with radiotherapy and an additional radiation treatment plan has been simulated accounting for hypoxic subregions and integrated to standard planning target volume (PTV) to compare the possible complementary information provided by 18F-FAZA PET/CT. **Results:** 18F-FAZA PET/CT showed one lesion in 15/17 pts and multiple lesions in 2/17. According to WHO classification, 12/17 pts had grade IV glioma, 5/17 had grade III glioma. For HIF-1 α the following score/number of pts have been observed: 0/1, 1/15, 2/1. For CA-IX: 0/3, 1/8, 2/2, 3/3 and 4/1. Finally, for GLUT-1, 0/1, 1/2, 2/6, 3/6 and 4/2 have been observed. Mean Ki-67 value was 19% (range: 3-40%). For hypoxia, vascularization and proliferation assessment, surgical and biopsical samples have been considered separately for the analysis. In group1 (n=7) CA-IX correlated to all PET-derived parameters as follow: SUVmax (p=0.0002), SUVmean40 (p=0.0058); SUVmean50 (p=0.009), SUVmean60 (p=0.0153), MTV40-50-60 (p=0.0424), HV 1.2-1.3-1.4 (p=0.0058). In group 2 (n=10) SUVmax (p=0.0094), SUVmean40 (p=0.0107), SUVmean50 (p=0.0094), SUVmean60 (p=0.0154) correlated with tumour vascularization. In all 7 patients undergoing RT, the simulated treatment based on 18F-FAZA PET/CT showed hypoxia within the original PTV. **Conclusions:** The correlation between imaging parameters and hypoxia biomarkers supports the role of 18F-FAZA PET/CT as a reliable method for assessing tumour hypoxia in HGG, with potential relevant impact on personalized radiotherapy treatment by means of delivering radiation boosts on the more hypoxic areas.

EP-0400

Added value of ¹⁸F-Fluorocholine PET/CT combined to multimodal brain MRI in the early detection of progression in high grade gliomas

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Purpose: To analyze the usefulness of ¹⁸F-Fluorocholine PET/CT added to routine follow-up with brain multimodal magnetic resonance imaging (MRI) in the early diagnosis of tumor progression of high grade glioma (HGG). **Subjects & Methods:** Patients with cerebral HGG treated with surgery and adjuvant chemo-radiotherapy, monitored in the participating centers, were included prospectively in the GLIReDe (Glioma Imaging Recurrence Detection) study. Patients underwent ¹⁸F-Fluorocholine PET/CT at the moment of the first report suspicious or doubtful for progression in MRI following the Response Assessment in Neuro-Oncology (RANO) criteria. For ¹⁸F-Fluorocholine PET/CT, any uptake higher than background and outside physiological locations was considered as positive. For MRI, only a suspicious result was considered as positive. In addition, a combined evaluation was performed, considering progression when at least one imaging technique was positive. The final diagnosis (progression or not) was obtained by histological confirmation or clinical and imaging follow-up in the 6 months after the PET/CT. The concordance of both techniques (Kappa Cohen), their diagnostic performance and the association of their results with the final diagnosis were analyzed. **Results:** Nineteen patients (63% male) were included in this preliminary analysis (10 glioblastoma multiforme, 5 anaplastic oligodendroglioma and 4 anaplastic astrocytoma). Thirteen patients were confirmed of progression (8 of them histologically and 5 by clinical and imaging follow-up). PET/CT results were significantly related to the final diagnosis ($\chi^2=7.367$; p=0.044), while MRI results didn't show significant relation with the final diagnosis ($\chi^2=3.662$; p=0.103). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were respectively 54%, 100%, 100%, 40% and 65% for MRI; and 100%, 50%, 87%, 100% and 88% for PET/CT. The combined evaluation didn't show any difference with respect to the evaluation of PET/CT results alone. The concordance between both imaging techniques was low (Kappa=0.191; p=0.156). **Conclusion:** In patients diagnosed of HGG that received standard treatment, ¹⁸F-Fluorocholine PET/CT was superior to MRI in the diagnosis of progression attending to our protocol. Although combined evaluation did not offer any additional information, ¹⁸F-Fluorocholine PET/CT was very helpful in the cases of MRI findings doubtful for progression in order to avoid a delay in the diagnosis.

e-Poster Walks Technologists

804-1 Monday, October 15, 2018, 11:30 - 13:00, Meeting Room 31

Technologists: Technologist e-Poster Walk 1

E-TPW01

Necessity of extrinsic versus intrinsic calibration in gamma camera systems

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Introduction: Precise calibration of gamma camera is one of the major factors that affect the image quality and optimize the patient dose in nuclear medicine departments. The performance of a gamma camera system crucially depends on its calibration results. The intrinsic uniformity is the most basic and routine procedure of gamma camera system calibration, however the effects of collimator and any probable obstacle between patient position and detector (such as table) are connived. In this work, we showed the importance of extrinsic versus intrinsic uniformity calibration on the gamma camera systems performance.

Methods: Intrinsic and extrinsic calibration was performed sequentially on three independent dual head gamma camera systems. After each calibration the uniformity map was updated with the new coefficients. Before and after each calibration step, the intrinsic and extrinsic uniformity quality control (QC) was performed with the proper uniformity map. **Results:** The extrinsic QC results was not changed significantly after intrinsic calibration (in average from 6.17% to 6.07%), however the intrinsic QC results change was meaningful (in average from 4.13% to 1.22%). After we updated the uniformity map with extrinsic calibration, the extrinsic QC results dramatically improved (in average from 5.86% to 1.15%). **Conclusion:** We show that, since the actual gamma camera images acquired with collimators it is needed to perform the extrinsic calibration instead of intrinsic calibration to get the highest system performance.

E-TPW02

Repeatability of Semiquantitative Parameters of Extent and Severity of Perfusion Defects on Myocardial Perfusion Imaging

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Introduction: Although, myocardial perfusion imaging (MPI) scans are generally evaluated qualitatively, commercially available automatic analysis softwares were also available to evaluate these scans semiquantitatively. One of them which is widely used commercial software is quantitative perfusion SPECT (QPS,

Emory University, Atlanta/USA). The stress and rest images of gMPI are automatically analyzed by this software, and the extent and severity of the perfusion defects can be calculated semiquantitatively. The aim of this study was to investigate the impact of non-cardiac activities on repeatability of semiquantitative results of this software. **Material and Methods:** Cardiac Torso Phantom (Anthropomorphic SPECT Phantom, BIODEx, USA) was used for this study. The cardiac part of the phantom was filled with 116 cc water including 18.5 MBq (0.5 mCi) Tc-99m pertechnetate and the liver part of the phantom was filled with 1160 cc water. The phantom was imaged consecutively ten times by the solid state cardiac gamma camera (NM 530c, GE, Israel). After that, 92,5-185-277,5 MBq (2.5-5-7.5 mCi) Tc-99m pertechnetate were added respectively into the liver part of the phantom in separate days and consecutive 10 acquisitions were performed for each activity added. The extent (%) and severity (SRS: summed rest score) of perfusion defects were semiquantitatively calculated for each study by using QPS. Then, the coefficient of variation was calculated. **Results:** While the heart activity was 0,5 mCi during the all studies, the results of the study summarized in the following:a)While there was no liver activity, SRS, coefficient variation of SRS, extent of perfusion defects and coefficient variation of extent were 5,1±1,37, 26,87, 6,9±1,45 and 21, respectively. b)While liver activity was 2.5 mCi, SRS, coefficient variation of SRS, extent of perfusion defects and coefficient variation of extent were 10±0.94, 9.4, 13.7±0.82 and 5.98, respectively.c)While liver activity was 5 mCi,SRS,coefficient variation of SRS, extent of perfusion defects and coefficient variation of extent were 6.1±0.74, 12.13, 11.1±1.37 and 12.34, respectively.d)While liver activity was 7.5 mCi, SRS, coefficient variation of SRS, extent of perfusion defects and coefficient variation of extent were 5±2, 40, 8.9±2.42, and 27.19, respectively. **Conclusion:**The coefficient of variation is generally used in biological sciences to test the accuracy of the measurement of a laboratory process. In general, the acceptable maximum coefficient of variation in laboratory methods is 10%. It seems to be more accurate approach to correlate these semiquantitative parameters with qualitative evaluation of MPI scans than to rely alone on the numerical parameters calculated by automated analysis programs.

E-TPW03

The Effect of Regional Activity Accumulation on the Evaluation of Myocardial Perfusion Imaging: A Preliminary Phantom Study

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Introduction: Hypertrophic cardiomyopathy is defined as an increased left ventricular wall thickness that can't be attributed to the abnormal loading of the left ventricle alone. The most common form is asymmetric thickness in the anterior interventricular septum, followed by concentric hypertrophy and apical hypertrophy. In most cases, the diagnosis of false positive ischemia is reported because the radiopharmaceutical biodistribution is heterogeneously decrease in other segments on gated myocardial perfusion imaging (gMPI) scans of these cases. The aim of

this study is to investigate the effect of local increased activity on interpretation of gMPI scans by simulating the hypertrophic cardiomyopathy using a cardiac phantom. **Material and methods:** In the first part of the study, cardiac part of the cardiac torso phantom (Anthropomorphic SPECT Phantom, BIODEx, USA) was filled with 116 cc water including Tc-99m pertechnetate in a concentration of 0.015 mCi/cc, and then, the phantom was imaged at the solid state cardiac gamma camera (NM 530c, GE, Israel) for 5 min. In the second part of the study, a balloon filled with 40 cc water including Tc 99m pertechnetate in concentration of 0.025 mCi/cc, to simulate asymmetric activity distribution in hypertrophic cardiomyopathy, was placed in the cardiac phantom containing 76 cc water with Tc-99m pertechnetate in a concentration of 0.015 mCi/cc, and then, the phantom was imaged at the solid state cardiac gamma camera for another 5 min. The raw data acquired from both session was analyzed by using commercially available software of Quantitative Perfusion SPECT (QPS, Cedars-Sinai, Atlanta) and summed rest score and defect extent (%) were evaluated. **Results:** Although there was slight heterogeneity in the lateral section of the phantom (SRS: 8, Extent: %13) due to irregularities in mixing of the radioactivity in the water of the phantom, actually, activity distribution in the phantom was homogenous on the scans of the first section of the study. Whereas, there was a prominent activity in where the balloon was and activity globally decreased in other parts of the phantom (SRS: 43 and extent: %61) on the scans derived from the second part of the study. **Conclusion:** In our preliminary study, regional activity accumulation as it happens in the hypertrophic cardiomyopathy seems to negatively affect the image analysis and false positive ischemia may be reported. Therefore, it seems to be necessary that cardiac morphological information should be taken into consideration when evaluating the myocardial perfusion imaging scans of patients with suspected hypertrophic cardiomyopathy.

E-TPW04

Comparison of different attenuated mediums on the measurement of Effective Renal Plasma Flow using Camera-based clearance method

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Introduction: Camera-based clearance is one of methods to evaluate Effective Renal Plasma Flow (ERPF). Counts of full syringe, empty syringe and injection site are acquired to calculate the ERPF. To keep the syringe 30 cm distance from the detector while detecting the counts, technologists have to adjust the imaging bed or place a syringe support on the detector.

Aim: The purpose of the study was to evaluate whether different mediums between the detector and radiopharmaceuticals would affect the EFPFs when the counts of full syringe, empty syringe and injection site are applied. **Materials and Methods:** Thirty-one patients (18 males, age 55 ± 13 y/o) underwent renal scintigraphy with 8 mCi Tc99m-MAG3 intravenous injection and images were acquired by GE Infinia Gamma Camera. Under the Camera-based clearance method, three sets of counts of full sy-

ringe, empty syringe and injection site were measured with 30 cm distance from the detector by attenuation of imaging bed (carbon fiber), hollow corrugated box and air respectively. Data were analyzed by GE Xeleris software applying modified Gates method to calculate the total EFPFs. **Results:** There was a difference between hollow corrugated box and imaging bed used to evaluate the EFPFs (338.77 ± 82.82 ml/min vs. 357.64 ± 87.36 ml/min, $p < 0.001$). Comparing the EFPFs calculated by the counts of full syringe, empty syringe and injection site with attenuation of air and imaging bed, there was a difference significantly (321.87 ± 78.25 ml/min vs. 357.64 ± 87.36 ml/min, $p < 0.001$). The values of ERPF assessed by the method of Camera-based clearance would be underestimated when the material with low attenuation was used as a medium between the detector and radiopharmaceuticals. **Conclusion:** Different materials such as carbon fiber, hollow corrugated box and air used as mediums between the detector and radiopharmaceuticals would significantly affect the EFPFs. Imaging bed and syringe support with similar attenuation are recommended when measuring counts of full syringe, empty syringe and injection site.

E-TPW05

The Evaluation of Quantitative Accuracy According to Detection Distance in SPECT/CT Applied to Collimator Detector Response(CDR) Recovery

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Aim: Recently, with the spread of SPECT/CT, various image correction methods can be applied quickly and accurately, which enabled us to expect quantitative accuracy as well as image quality improvement. The purpose of this study is to find out quantitative change depending on the change in detection distance in SPECT/CT images with CDR(Collimator Detector Response) Recovery correction method applied. **Material and Methods:** To find out the error of acquisition count depending on the change of detection distance, we set the detection distance according to the orbit type as Circular type(X, Y axis radius 30cm, 30cm), Non-Circular type(X, Y axis radius 21cm, 10cm) and Non-Circular Auto type with Auto Body Contouring system (limit radius 1cm) and applied reconstruction methods by dividing them into Astonish(OSEM with CDR Recovery) and OSEM(without CDR Recovery) to find out the difference in activity recovery depending on the use of CDR Recovery. At this time, attenuation correction, scatter correction, and decay correction were applied to all images. For the quantitative evaluation, calibration scan (cylindrical phantom, ^{99m}Tc 123.3 MBq, water 9293 ml) was obtained for the purpose of calculating the calibration factor(CF). For the phantom scan, a 50 cc syringe was filled with 31 ml of water and a phantom image was obtained by setting ^{99m}Tc 123.3 MBq. We set the VOI(volume of interest) in the entire volume of the syringe in the phantom image to measure total count for each condition and obtained the error of the measured value against true value set by setting CF to check the quantitative accuracy according to the correction. **Results:** The calculated CF was 154.28 (Bq/ml/cps/ml) and the measured val-

ues against true values in each conditional image were analyzed to be Circular 87.5%, Non-Circular 90.1%, Non-Circular Auto 91.3% in OSEM and Circular 93.6%, Non-Circular 93.6%, Non-Circular Auto 93.9% in Astonish respectively. The closer the detection distance, the higher the accuracy of OSEM, and Astonish showed almost similar values regardless of distance. The error was the largest in the OSEM Circular(-13.5%) and the smallest in the Astonish Non-Circular Auto(-6.1%). **Conclusion:** SPECT/CT images showed that when the distance compensation is made through the application of CDR Recovery, the detection distance shows almost the same quantitative accuracy as the proximity detection even under the distant condition, and accurate correction is possible without being affected by the change in detection distance.

E-TPW06

Impact of the Myocardial Perfusion Gated-SPECT reconstruction method on the Left Ventricular Ejection Fraction

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Aim: Left-Ventricular-Ejection-Fraction(LVEF) can be calculated by myocardial-perfusion gated-SPECT (MPG-SPECT). Preceding quantification, data reconstruction can be done by applying distinct algorithms. When applying FBP or iterative reconstructions, the noise obtained in the short axis image can increase and bias in ventricular wall contour detection algorithm can be introduced, compromising the correct quantification. We aimed to study the impact of the MPG-SPECT reconstruction method on the LVEF and to evaluate if the type of study, stress or rest, have any influence on the results. **Materials and Methods:** Thirty consecutive **One-Day-MPG-SPECT Stress-Rest** studies were retrospectively selected based on the following exclusion criteria: time gap between **Stress** and **Rest** >4 hours; obese patients that are out of the gamma-camera **Field-of-View**; high-activity structures overlapped to the heart (liver/bowel) and extravasate/contamination. **MPG-SPECT** were reconstructed using four different algorithms: FBP, MLEM, OSEM and Astonish®. All data were evaluated with Autoquant®. The LVEF obtained with each one of the 4 algorithms was compared using ANOVA (statistical analysis was performed using SPSS 25). **Results:** The 30 selected MPG-SPECT were performed in 15 men and in 15 women. For both stress and rest datasets, the most significant difference was observed between FBP and Astonish® (4.67 points for Stress, 4.20 for Rest), and the lowest one was between MLEM and OSEM(1.40 for Stress, 1.13 for Rest). It has observed that the higher differences occurred when comparing FBP, MLEM and OSEM to Astonish® respectively, and that difference was higher for FBP (4.67 for Stress, 4.20 for Rest). The score differences between each pair of methods (FBP-Astonish®, MLEM-OSEM, MLEM-Astonish® and

OSEM-Astonish®) is not significant($p>0.05$) for stress and rest. A p -value<0.05 was obtained comparing FBP-MLEM and FBP-OSEM in stress and rest, a significant difference between stress and rest for this pair of algorithms was verified. There are significant differences for both stress and rest($p<0.05$) between FBP-Astonish® and FBP-MLEM, MLEM-OSEM and MLEM-Astonish®. There are significant differences for both stress and rest($p<0.05$) between MLEM-OSEM and OSEM-Astonish®. There are significant differences only for stress studies between FBP-OSEM and MLEM-OSEM($p<0.05$) and only for rest studies($p<0.05$) between FBP-MLEM and OSEM-Astonish®, FBP-OSEM and FBP-Astonish® and OSEM-Astonish® and between MLEM-OSEM vs MLEM-Astonish®. Significant differences between stress and rest($p<0.05$) were only found between FBP-MLEM($t=-2.594, p=0.015$) and FBP-OSEM($t=3.149, p=0.004$). **Conclusions:** LVEF obtained with MPG-SPECT depends on the reconstruction method applied. For a correct follow-up of the LVEF, stress and rest data of the same patient should be processed applying always the same algorithm.

E-TPW07

Feasibility of preclinical ¹²⁵I-EISB SPECT imaging on a small animal SPECT /CT

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Aim: We developed ¹²⁵I-EISB (1- (2-¹²⁵I-ethoxy) -2, 5 bis styryl benzene) which is a systemic amyloidosis imaging probe. Pre-clinical studies using ^{99m}Tc and ⁶⁷Ga have been performed on a small animal SPECT/CT (FX3300, Trifoil, USA). However, sufficient studies for ¹²⁵I SPECT imaging with small-animal SPECT/CT device have not been performed. The purpose of this study was to evaluate the feasibility of ¹²⁵I imaging for preclinical ¹²⁵I-EISB study on small animal SPECT/CT. **Material and Methods:** ¹²⁵I and ^{99m}Tc SPECT image quality was evaluated for uniformity, spatial resolution (FWHM) and count linearity by fundamental phantom studies. A small animal SPECT/CT having two CZT detectors and multi-pinhole collimator for mouse was used. Uniformity was evaluated with an acrylic cylindrical phantom. In the spatial resolution, three-point radiation sources were created in a self-made phantom used a teflon tube with an inner diameter of 0.6 mm. Spatial resolution was visually evaluated also using hot rod phantom and cold rod phantom. In concentration linearity, 12 kinds of ¹²⁵I point sources with different radioactivity levels were prepared and used. **Result:** With ¹²⁵I and ^{99m}Tc, integral uniformity was 23.49% and 20.11%, respectively. Coefficient of variation (CV) was 0.094 for ¹²⁵I and 0.068 for ^{99m}Tc. In the spatial resolution, the FWHM of the periphery part than the center part of both ¹²⁵I and ^{99m}Tc was longer and the FWHM of the center part with ¹²⁵I was almost the same value as ^{99m}Tc. In the hot rod phantom images, the size of hot rod was visually separated up to 1.2 mm for ¹²⁵I and 1.0 mm for ^{99m}Tc. In the cold rod phantom images, both ¹²⁵I and ^{99m}Tc were visually separated up to 1.6 mm. In count linearity, there was a correlation between the SPECT count on the image and the actual radioactivity up to 1.5 MBq. **Conclusion:** Image quality of ¹²⁵I is inferior to that of

^{99m}Tc on small animal SPECT/CT. Further improvement in ^{125}I imaging quality may be necessary for the preclinical ^{125}I -EISB study.

E-TPW08

Reproducibility of SPECT imaging with a conjugated gradient minimization reconstruction algorithm: a multicenter study of ^{99m}Tc quantification

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Background: Quantitative assessment using the standardized uptake value (SUV) for single-photon emission computed tomography / computed tomography (SPECT/CT) has been explored in clinical applications. This multicenter study aimed to investigate the reproducibility of quantitative SPECT imaging generated by the commercially available ordered-subset conjugated gradient minimization (OSCGM) reconstruction engine. In order to assess the quantitative accuracy of SPECT imaging by OSCGM reconstruction, factors affecting quantification in the multicenter setting such as radioactivity source, dose calibrators accuracy and reconstruction parameters were carefully controlled. **Methods:** Six institutions having installed SPECT/CT system Symbia Intevo participated in this multicenter study. The dose calibrator accuracy was first investigated by measuring the same lot of commercially available ^{99m}Tc vials five times at each institute over three days. A common cylinder phantom containing 0.100 MBq/ml ^{99m}Tc aqueous solution of was scanned at each institution. As an investigation for intra-institution variation, the phantom experiments were repeated 3 times. The intra- and inter-institution variations were evaluated with the coefficient of variation (CV) in the quantitative SPECT images. **Results:** The result of inter-institution variability was high compared to that of intra-institution (4.20% and 0.98%, respectively). Most institutions had the quantitative variability in the SPECT images less than 5%, however, one institution showed 8% quantitative variability. The accuracy of dose calibrator had direct influence on the quantitative accuracy on the phantom-based SPECT quantification. **Conclusion:** A commercially available quantitative SPECT application using OSCGM reconstruction engine had excellent reproducibility. The importance of quality control for the dose calibrators is also suggested based on the finding that its measurement accuracy directly affected the inter-institution reproducibility.

E-TPW09

Crosstalk correction for ^{201}Tl / ^{123}I dual-radionuclide imaging using a CZT SPECT camera

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Aim: A cadmium zinc telluride (CZT) detector single photon emission computed tomography (SPECT) device (CZT camera) has better energy resolution than a conventional NaI detector SPECT device, so it is reported its usefulness on dual-radionuclide imaging. Many studies in relation to the crosstalk on ^{99m}Tc and ^{123}I dual-radionuclide imaging were reported, but on ^{201}Tl and ^{123}I ones were little. The aim of this study was to evaluate the crosstalk ratio and its optimal correction method on ^{201}Tl and ^{123}I dual-radionuclide imaging using a CZT camera. **Materials and Methods:** ^{201}Tl , ^{123}I and $^{201}\text{Tl} + ^{123}\text{I}$ water solutions were injected into the myocardial part of a chest myocardial phantom, respectively. SPECT data were acquired with list mode using a CZT camera (Discovery NM 530c, GE). The crosstalk ratio was obtained from left ventricular count (LVC) in each energy window on single-radionuclide SPECT imaging. Dual-energy window (DEW) and triple-energy window (TEW) methods performed for the crosstalk correction on ^{201}Tl -energy window and ^{123}I -energy window on dual-radionuclide SPECT image. Finally, estimated LV radioactivity was calculated by multiplying LVC by cross calibration factor and compared that with actual LV radioactivity measured by a well-type scintillation counter. The recovery was defined as the value divided estimated LV radioactivity by actual LV radioactivity. **Results:** The crosstalk ratio from ^{201}Tl to ^{123}I -energy window and from ^{123}I to ^{201}Tl -energy window was 9.8% and 22.1%, respectively. The estimated LV radioactivity without crosstalk correction was overestimated in both energy windows (recovery of ^{201}Tl = 1.10 and recovery of ^{123}I = 1.27). TEW method was superior to DEW method for correcting crosstalk in ^{201}Tl -energy window (recovery = 1.02). However, correction of crosstalk in ^{123}I -energy window is underestimated by both of DEW and TEW methods (recovery of DEW = 1.25 and recovery of TEW = 1.22). **Conclusions:** TEW crosstalk correction for ^{201}Tl -energy window is useful on ^{201}Tl and ^{123}I dual-radionuclide imaging using a CZT camera. Further study for correcting the crosstalk in ^{123}I -energy window is necessary.

E-TPW10

The Usefulness of Flash 3D Applications to Shorten Scan Time for Bone SPECT

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Aim: In accurate image reconstruction impacts image quality and can result in both false positives and false negatives. Most of the reconstructed images are created using algorithms that do not account for the physical characteristics of the image acquisition system. Flash 3D Technology is a sophisticated new SPECT tomographic reconstruction algorithm. Flash 3D adds a post filter after reconstruction for noise reduction. The objectives of this study were to assess diagnostic reliability and accuracy in comparison with half time Flash 3D and full time Filtered Back Projection (FBP) in bone SPECT applications. **Material and Methods:** Twenty patients (11 female, 9 male) were imaged with Siemens Evo Excel gamma camera (Knoxville, USA) with low energy high

resolution parallel hole collimators. Patient preparation, acquisition parameters and reconstruction protocols for all patients were standardized. SPECT data were acquired between 2 and 4 h after intravenous injection of approximately 10MBq/kg of $^{99m}\text{TcMDP}$. Every patient was imaged twice with half time and full time SPECT protocols. Half-time SPECT acquisition protocol was as follows: 60 frames per detector head, each with duration of 15 s. Full time SPECT acquisition protocol was as follows: 60 frames per detector head, each with duration of 30 s. Full-time data were reconstructed using Standard filtered backprojection reconstruction, whereas half time data were reconstructed using Flash 3D software. The data were evaluated by two Nuclear Medicine specialist blinded to each other without knowing which protocol was used in the images. **Results:** No significant difference was found in the images of the patients. All images were evaluated as reportable. **Conclusion:** Our study showed that Flash 3D reconstruction algorithm was a reliable tool and can be used in painful of bone diseases to shorten the imaging time; providing high inter-observer agreement and similar diagnostic confidence compared with FBP.

E-TPW11

Development of a no-radiation-exposure, nonuniform attenuation correction method for brain perfusion single-photon emission computed tomography with an anatomically standardized brain attenuation map

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Aim: An attenuation correction (AC) method for brain perfusion single-photon emission computed tomography (SPECT) is necessary to quantify cerebral blood flow. Chang's method (uniform AC), and a nonuniform AC method that uses an attenuation map (μ -map) based on x-ray computed tomography (CT), have both been used for brain perfusion SPECT. The nonuniform AC method is superior to the uniform AC method because of the difference between the measurement and simulation data. However, the nonuniform AC method requires an expensive SPECT/CT unit. Further, the patient is exposed to radiation during CT scanning. If an anatomically standardized brain μ -map is applied for the AC correction, this method can be used by SPECT facilities without radiation exposure. The purpose of this study was to develop a no-radiation-exposure, nonuniform AC method for brain perfusion SPECT with an anatomically standardized brain μ -map. **Materials and Methods:** An anatomically standardized brain μ -map was obtained by analyzing sixty CT images of patients, 40–75 years of age) with statistical parametric mapping (SPM8). Thirteen brain perfusion SPECT images with ^{99m}Tc -ethyl cysteinate dimer were obtained by using the SPECT/CT unit. Scatter correction was performed using the triple energy windows method. After conversion by using the SPM8, all SPECT images were analyzed with a three-dimensional stereotactic region-of-interest template on anatomically standardized SPECT images, enabling objective estimation of the SPECT counts. SPECT counts obtained by conventional CT-AC

method (conventional SPECT) were compared with images obtained by SPECT that underwent AC by using the anatomically standardized brain μ -map. **Results:** Differences in the anatomically standardized brain μ -map regarding age and sex were not found. The mean error between conventional and standardized SPECT counts was $\pm 2.5\%$. Generally, the evaluation of cerebral blood flow has been performed using the mean value in each region of interest. Therefore, the mean error can be minimized. **Conclusion:** The no-radiation-exposure, nonuniform attenuation correction method for brain perfusion SPECT with an anatomically standardized brain μ -map can be useful for clinical analysis.

E-TPW12

Evaluation of optimized imaging quality of Tc-99m TRODAT-1 SPECT

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Purpose: Tc-99m TRODAT-1 has been clinically used to evaluate function of dopamine transporter. Low target total counts might be responsible for the differences in imaging acquisition and analysis resulting in different imaging quality among hospitals. The study observed the minimal target count needed for a better image quality. **Materials & Methods:** Striatal phantom filled with different target counts of Tc-99m in bilateral caudate and putamen nuclei (4:1, 3:1, 2:1 & 1:1 of the background counts, respectively, ranged 1285K~312K counts) and with total phantom counts of 1,500K, 4,000K, 9,000K (n=4 each) were prepared in this study. The SPECT parameters were set the same as routine protocol (360° rotation, projections at intervals of 3°, 20 sec/frame) and reconstructed using back-projection with Butterworth or Metz filter. Target ROIs were drawn by both manual and automatic semi-quantitative methods. Specific uptake ratios (SURs) were calculated accordingly and correlated with the corresponding real counts from a γ -counter using Pearson correlation coefficient. **Results:** Our data revealed that 1. The correlation coefficient of 3 different total counts (1,500K, 4,000K, 9,000K counts) were 0.752, 0.943, 0.975; 2. Images reconstructed using Metz filter, the SURs of 4:1 and 3:1 ratios were 1.696 and 1.223, respectively while those with Butterworth filter were 1.103 and 0.863. Some images reconstructed by Metz filter showed discordant results as total counts less than 4,000K which appeared not found by Butterworth filter. In addition, data using Butterworth filter showed better correlations of visual and automatic semi-quantitative analyses with the raw data. **Conclusion:** Using Metz filter reconstruction with imaging total counts over 4,000K could achieve promising target/noise contrast and enabled us to visually interpret imaging. In contrast, those below 4,000K, Butterworth filter reconstruction provided better correlation with real data. **Key Words:** Tc-99m TRODAT-1, SPECT, optimized imaging quality.

E-TPW13

Preliminary evaluation of attenuation correction influence for coronary flow reserve using a CZT-based gamma camera, in comparison with [¹³N]ammonia-PET/CT

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Purpose: The aim of this study was to assess whether the measured myocardial blood flow (MBF) and coronary flow reserve (CFR), estimated using cadmium zinc telluride (CZT)-based single-photon emission computed tomography (SPECT), were influenced by attenuation correction. **Materials and Methods:** 10 patients were prospectively evaluated. The patients underwent both CZT-based-SPECT and [¹³N]ammonia-PET/CT within one week; the PET scans were performed for patients with inconclusive CZT-based-SPECT examination. Studies were conducted at rest and during Regadenoson induced hyperemia for both SPECT and PET/CT scans. The single-day CZT-based-SPECT fixed activities of 99mTc-tetrofosmin were 185 MBq for the stress and 370 MBq for the rest acquisition. The delay between stress and rest scan was 2 hours. For stress imaging, an initial dose of 37 MBq was used to localize the patient's heart. Residual resting activity was subtracted from stress data and images reconstructed with CT-based attenuation correction (AC-CZT-based-SPECT), obtained from the [¹³N]ammonia-PET/CT, and without AC (NC-CZT-based-SPECT). MBF and CFR were assessed by Corridor4DM Reserve software for both AC-CZT and NC-CZT. The single day [¹³N]ammonia-PET/CT activities were 370 MBq for both stress and rest. MBF and CFR were assessed by Corridor4DM. **Results:** The [¹³N]ammonia-PET/CT MBFs (mean ± standard deviation) were 1.81±0.49 ml/mg/min for stress and 0.78±0.16 ml/mg/min for rest; the CFR was 2.34±0.49 ml/mg/min. The AC-CZT-Based-SPECT MBFs were 2.26±1.13 ml/mg/min and 0.80±0.24 ml/mg/min for stress and rest respectively; the CFR was 2.75±0.86 ml/mg/min. The NC-CZT-based-SPECT MBFs were 2.77±1.22 ml/mg/min for stress and 1.01±1.22 ml/mg/min for rest; the CFR was 2.78±0.93 ml/mg/min. These preliminary results showed a correlation between [¹³N]ammonia-PET/CT and NC-CZT-based-SPECT: R = 0.836, 0.255 and 0.701 for Stress-MBF, Rest-MBF and CFR respectively. The correlation between [¹³N]ammonia-PET/CT and AC-CZT-Based-SPECT was: R = 0.745, 0.532 and 0.870 for Stress-MBF, Rest-MBF and CFR respectively. **Conclusion:** This preliminary study seems to confirm that CZT-SPECT can be used for the MBF and the CFR evaluation and that CT based attenuation corrected SPECT acquisition have a better correlation with the same parameters calculated using [¹³N]ammonia-PET/CT scans.

E-TPW14

Effects of acquisition time and sphere size on PET image quality (SNR) and quantification (SUV)

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Objectives: Assessment of SNR (signal to noise ratio) parameter and SUV (standardized uptake values) parameter measured in PET images reconstructed at different time durations, using phantom data, to decrease acquisition time duration. **Methods:** NEMA IEC PET body phantom with 4 small cylinders (10 mm, 13 mm, 17 mm and 22 mm) was filled with a radioactive solution with cylinder-to-background activity concentrations of 4: 1. The scan was performed on Biograph mCT PET/CT scanner, manufactured by Siemens. Scanner combines a 40-slice CT and (LSO) PET system for whole body imaging with TOF capability. We performed a list mode scan that has enabled us image reconstruction at different time points. Image series with varying time durations were reconstructed and corrections applied. A center slice, where the image contrast was assumed to be high, was selected from the image slices. Two other slices, with respect to the selected center slice, were also selected. Making the total number of slices to be analyzed, three (-3 mm, 0, +3mm). Regions of interest (ROI) were drawn on each hot sphere and 12 circular ROIs were used with a diameter equal to the inner diameter of each hot sphere for background measurement. The evaluation of SNR, SUV max and SUV mean was made. **Results:** SNR parameter evidently increasing by extending the data acquisition time as well as by increasing the diameter of hot spheres. The reduction of data acquisition time has no direct effect on SUV parameter. Results of varying sphere sizes show SUV values decreasing when sphere size decreases. **Conclusions:** Changing the time of data acquisition protocols from the current 150 seconds to 120 seconds reduced SNR parameter by an average of 9.7%. SUV parameter remains the same.

E-TPW15

Optimization of β values of new penalized likelihood reconstruction algorithm Q.Clear in brain PET

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Aim: The penalized likelihood reconstruction algorithm (PL), Q.Clear (GE Healthcare), uses relative difference penalty as a regularization function to control image noise and the degree of edge-preservation in PET images. Optimization of PL reconstruction conditions (β value) according to the characteristics of PET images and traces is required. The present study aimed to optimize the β value of the PL method for brain PET using ¹⁸F-FDG and ¹¹C-PiB. **Material and Methods:** We used a Discovery PET/CT 710 with the PL method. Images acquired from a Hoffman 3D brain phantom, two patients with Alzheimer disease (AD) and two healthy controls using ¹⁸F-FDG and ¹¹C-PiB were retrospectively analyzed. The image reconstruction method was OSEM+ TOF and PL+TOF. We investigated β -values of 50 - 300 for PL+TOF in a phantom study. Contrast, noise and uniformity on PET images were calculated in physical evaluations. The targeted β value was restricted by the findings of the physical evaluation, and the optimal β value was subsequently deter-

mined by visual evaluation. The β values applied in the clinical study ranged from 150 to 350 and visually analyzed by three scorers and scored up to 5 points against the parameters of overall image quality, contrast, and noise. **Results:** Contrast and noise decreased as the β value of the PL+TOF method increased in the physical evaluation. The total value of all parameters was the highest when the β value was 200 for ^{18}F -FDG and 350 for ^{11}C -PiB in the visual evaluation. The PL+TOF was superior to OS-EM+TOF in terms of image quality according to both physical and visual evaluations. **Conclusion:** Our results suggest that the optimal β values of ^{18}F -FDG and ^{11}C -PiB for brain PET/CT images using Q.Clear are 200 and 350, respectively.

E-TPW16

Validation of non-blood sampling ARG method for cerebral blood flow quantification with I-123 IMP SPECT : comparison with O-15 gas PET steady state method

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Purpose: The aim of this study was to validate the non-blood sampling ARG method by comparing regional CBF calculated by the non-blood sampling ARG method and O-15 gas PET steady state method. **Methods:** Twelve patients (mean age = 64 ± 18 years old, male: female = 6: 4), who underwent both O-15 gas PET and I-123 IMP SPECT, were studied. All patients had given consent to participate in this study understanding the purpose and related risks. I-123 IMP SPECT was performed following ordinal ARG method with arterial blood sampling. Quantification of regional CBF was done on the QSPECT software using both sampled arterial blood data (ordinal ARG method) and analytically estimated arterial blood data (non-blood sampling ARG method). Quantification of regional CBF was also done on O-15 gas PET using steady state method. Processed CBF images from PET and SPECT were coregistered to the standard brain MRI image using 3D-SSP software. Using regions of interest drawn on standard brain templates, Correlation of regional CBF between SPECT and PET was investigated. **Results:** The correlations of regional CBF between blood sampling ARG method and O-15 gas PET and between non-blood sampling ARG method and O-15 gas PET were significant ($R=0.670, 0.648, P<0.01$). Although Both blood sampling and non-blood sampling ARG method showed significantly correlated regional CBF with O-15 gas PET, correlation in the higher regional CBF regions was somewhat lower in the blood sampling method. **Conclusion:** Non-blood sampling ARG method was validated by comparison with O-15 gas PET steady state method, showing feasibility and usefulness in routine clinical evaluation of CBF.

E-TPW18

How to decrease the radiation exposure with the help of a colleague

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The aim of this project is to measure the difference in radiation exposure to the personnel, when placing the patient in the PET-scanner from a close distance compared to a longer distance from the patient, with the help of a colleague. How much radiation exposure can be reduced? Background of this project is the new Ionising Radiations Regulations that was implemented by law in February 2018. One change was the limit of radiation exposure to the lens of the eye. The equivalent dose was decreased from 150 to 20 mSv/Year to medical radiation employers¹. At our department the technologists get approximately an effective dose of 4 mSv/year, estimating that 3 mSv/year is received just from placing the patient in the scanner. Even though we are exposed to a low dose, we wanted to see if we can improve our routines even further. **Materials and Methods:** Siemens Biograph 40/64 DMC 3000 Personal Radiation Dosimeter. The method of this study is using an electronic dosimeter to measure the real time dose rate in mSv/hour. The results were divided in two groups. One group where the dose rate was measured from the lens of the eye and one group measured from the chest. These groups were then divided in two - One group was measured while the staff was standing next to the patient pressing the buttons, and one group with staff positioning the patient bed from the control room. In this case the measured personnel could take a few steps back. We gathered 32 Measurements - eight in each group. All patients were injected with ^{18}F -FDG. The measurements was then applied statistics, to decide if the method can lower the radiation exposure significantly. The results showed a consistent reduction in radiation received, when positioning the patient bed from the control room. The average dose rate to the lens of the eye was 0,033 mSv/h standing next to the patient when positioning and 0,015 mSv/hour when positioning from the control room. The average dose to the chest was 0,045 mSv/hour when standing next to the patient positioning and 0,015 mSv/hour when positioning from the control room. Our conclusion is that with the help of a colleague from the control room, to position the patient bed, we can decrease the radiation exposure to the personnel. ¹<https://www.retsinformation.dk/Forms/R0710.aspx?id=197135>

E-TPW19

Whole Body and Hand Doses Exposed By Nuclear Medicine Personel During Gallium-68 DOTATATE and PSMA PET-CT Studies

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Objective: The purpose of this study is to determine all body and hand doses exposed by personnel during Ga-68 DOTATATE and Ga-68 PSMA studies, which are used to visualize neuroendocrine tumors and prostate cancers and asses them in terms of radiation safety. **Materials & Method:** Dosimetric data of two personnel (one engineer and one technician) working between July 2017 and April 2018 on the Ga-68 DOTATATE and PSMA studies at the PET-CT center of the University of Health Science, Okmeydani Training and Research Hospital Nuclear

Medicine Clinic were evaluated. The engineer was engaged in the synthesis of Ga-68 studies, and the technician was responsible for the injection and imaging procedure. Hand doses and whole body were measured with EPD (electronic portable dosimeter) and OSL (optically stimulated luminescence). The doses they received during the 10-month period were assessed. Working time, number of patients, number of injected doses and dosimetry data were noted. In each patient, the time between injection and time of discharge was also evaluated. During this time, the dose received was measured and recorded with EPD. Calibration of the EPD was done in the standard dosimeter and electronic laboratory of Turkey Atomic Energy Institution Cekmece Nuclear Research and Education Center. OSL the readings of whole body and hand dosimeters were made in 2-month periods. **Results:** The number of Ga-68-DOTATATE and Ga-68PSMA patients was 250 in 10 months' time. The total dose exposed at the synthesis stage <0.1 mSv. The average time from the injection time till the end of the imaging for a patient was 102 ± 31.21 minutes. The mean injected dose was 4.06 ± 1.07 mCi, the dose exposed by the technician responsible for imaging and injection from a single patient was 1.32 ± 0.55 μ Sv. At 10 months, the mean total body dose was 0.18 ± 0.08 mSv, the mean hand dose was 0.27 ± 0.07 mSv. **Conclusion:** Ga-68 DOTATATE and Ga-68 PSMA are new radiopharmaceuticals used in the imaging of patients with neuroendocrine and prostate cancer. Due to their characteristics of high-energy positron emitters, the dose received can be higher than other nuclear medicine procedures. In current study, the doses received from the Ga-68 synthesis and imaging procedures were found to be very low and well below the permissible limits due to the use of a fully automated synthesis unit and compliance with safety regulations.

E-TPW20

Finger dose reduction by using ArcoNuk a semi-automatic prototype injector system

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Aim: Goal of this study is to determine if the use of a prototype semi-automatic injector system (ArcoNuk) for the dose preparation and injection of a diagnostic radiopharmaceutical tracer, like Tc-99m, results in a significant finger dose reduction to the radiographer as well as in sparing time. **Method:** 40 patients for a myocardial scintigraphy exam were divided into 2 groups of 20 patients. The prescribed activity of the first group was prepared and injected manually while for the second group the activity was prepared and injected using the ArcoNuk injector system. The finger dose was measured by a TLD finger ring dosimeter which was worn on the index finger of the non-dominant hand of the handling radiographer. The measurements were done among 4 radiographers using 2 different TLD finger rings for each of them, one for the manual procedure and the other for the ArcoNuk system. A comparison of the preparation and injection time for both methods was also calculated using measurements with a stop-watch. **Results:** It was observed that the finger dose can be reduced by at least 50% using the Ar-

coNuk system. There is not a significant time difference for the preparation and the administration of the radiopharmaceutical tracer between the manual procedure and the use of the injector (7min 30 sec with ± 30 sec incertitude). **Conclusion:** The use of the ArcoNuk injector system allows a significant finger dose reduction for the radiographer without increasing the time duration for the preparation and the application of the needed dose per patient. **Keywords:** Injector system, manual preparation, finger dose, radiopharmaceutical tracer.

E-TPW21

Radiation Exposure of Extremities for Surgical Staff Performing Sentinel Lymph-Node Removal Procedure

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Background: Sentinel lymph-node scintigraphy is a useful method for accurate staging of different tumors and a helpful tool in personalized therapy for oncological patients. The radiation exposure for surgical staff has been a concern since the sentinel lymph-node detection method was developed.

Objective: The objective of the study was to determine and quantify the exposure to radiation of the non-dominant index for the surgeon performing sentinel lymph-node removal and to determine, if there is an irradiation risk imposed during the surgical procedure. **Method:** We performed a study over a period of one year, where we evaluated the exposure of surgeon's non-dominant index during 208 sentinel lymph-node removal procedures. The pharmaceutical was administrated via intradermal injection in four peritumoral or perilesional injection sites. The equipment we used consisted of EuroProbe3 for sentinel lymph-node detection and ring TLD dosimeter placed on the surgeon's non-dominant index. **Results:** The clinical distribution was: 111 melanomas, 88 breast carcinomas, 7 vulvar carcinomas and 2 penial carcinomas. The administered activity showed an average of 39.55 MBq ($SD \pm 1.96$) Tc-99m nanoalbumin compound. The non-dominant index exposure ranged between 0.10 mSv and 0.13 mSv/month with a cumulative dose of 1.31 mSv/year (0.262% from the extremity dose annual limit), thus 6.29 μ Sv per procedure. **Conclusion:** The surgeon received a minimal dose for the non-dominant index. The values we recorded did not pose any additional concerns or restrictions, the exposure being under the limits and constraints established by regulations, close to the detectability limit of the dosimeter. The procedure is safe in terms of radiation protection, respecting the limitation and optimization principles.

E-TPW22

Practical considerations in a prospective complex dosimetry research study

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Although radiation dosimetry in molecular imaging has advanced significantly in the past decade, the calculation techniques developed can be complex and are not easily applica-

ble to routine diagnostic studies. This study will adapt specific techniques to a limited patient cohort undergoing a range of diagnostic procedures to determine the accuracy with which a practical method of dosimetry may be performed. The aim of this work is to discuss the research technologists' role in the development and putting in practice a complex dosimetry research study involving a multidisciplinary team. As part of the recruitment process, patients will be sent information regarding the study prior to their appointments at the Nuclear Medicine department. A detailed Patient Information Sheet and consent form will be designed and sent with the appointment letter. Patients may also be contacted by a member of the Patient and Public Involvement to further explain the study and assess patient willingness to participate. In this prospective non-interventional pilot study, patients will be imaged with each of the following radioisotopes: ^{99m}Tc -MDP, ^{99m}Tc -MAG3, ^{99m}Tc -DMSA, ^{99m}Tc -pertechnetate, ^{18}F -FDG, ^{68}Ga -PSMA and ^{68}Ga -DOTATATE, with the goal of recruiting 5 patients for each nuclear medicine procedure. Over a period of approximately 24 hours post injection, patients will be scanned and up to 10 external radiation retention measurements using a standardised procedure will be acquired. A patient forum was held and patients had no major concerns about the burden of extra dosimetry scans. Factors to be investigated will include the image acquisition parameters, the number and timing of images and of external retention measurements and image processing methods. Patient feedback on experience of dosimetry scanning will also be assessed in the form of a questionnaire. The research is implemented in a multidisciplinary environment (physicians, physicists, trial coordinator, patient representative, technologists/radiographers) highlighting the importance of a thorough research process design, such as protocols, data acquisition, processing, analysis and delivery of results. A successful outcome from this study would lead to a deeper understanding of the issues encountered (for example, optimum imaging time, radiotracer retention times etc). In the longer term, the effect of low doses and low dose rates would be comprehensively addressed. Successful completion and implementation of this complex research study requires close collaboration between different teams in different departments. Encouraging staff to become familiar with important aspects of complex research studies and helps with the understanding of its key components.

804-2 Monday, October 15, 2018, 11:30 - 13:00, Meeting Room 32

Technologists: Technologist e-Poster Walk 2

E-TPW23

Fishing for Molybdenum in the Conditions of Waste Liquids

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Introduction: In the production of sorption generators technetium-99m based on the use of highly enriched molybde-

num-98, the cost of high. The average market price of 1mg of molybdenum-98, enriched to 98.6%, was more than \$4. Activation of molybdenum-98 occurs in nuclear reactors in accordance with the radiation capture reaction (n,γ). Radionuclide molybdenum-99, used to produce diagnostic technetium-99m, is formed during neutron irradiation of targets from enriched molybdenum-98. For the production of molybdenum-99, it consumes less than $2 \cdot 10^{-3}\%$ of the total mass of molybdenum-98 in the irradiated target. Most of the expensive molybdenum-98 goes to liquid waste. To produce a technetium-99m generator with a specific energy activity of 19GBq, 120-130mg of activated molybdenum-98 is used. **Aim:** To reduce the cost of technetium-99m generators obtained by sorption concentration technology, it is necessary to develop a technology for recovering molybdenum-98 from liquid waste. **Methods:** For the extraction of molybdenum-98, various procedures for the concentration of molybdenum-98 and attempts to precipitate it in the form of salt were studied. The sulphide deposition of molybdenum-98 was more successful. The extraction procedure comprises the steps of forming a regenerating solution, the preparation of MoS_3 by thiosal intermediates and further heat treatment prior to the formation of molybdenum-trioxide 98. **Results:** The conducted set of studies made it possible to find the sequence of stages of waste processing. We found the optimal concentration of an alkaline solution of molybdenum-98, which makes it possible to obtain a molybdenum-98 thiosalt with a maximum oxygen substitution by sulfur atoms. In addition, saturation of thiosalate with an excess of hydrogen sulfide and subsequent acidification of the solution with hydrochloric acid makes it possible to achieve recovery of molybdenum 98 from 98%. Purification of the solution from precipitated impurities other metals occurs during the intermediate stage. Molybdenum trisulphide, formed during the treatment of the solution, is extracted from the solution by filtration using filters with a pore diameter of not more than $5\mu\text{m}$. At the final stage of extraction of molybdenum-98, stepwise heating of molybdenum trisulphide to 600°C was carried out, which made it possible to obtain the final product in the form of molybdenum-trisulphide-98. **Conclusions:** The developed procedure for extraction of molybdenum from liquid radioactive waste can be used to increase the profitability of production and reduce the cost of the technetium-99m generators. The molybdenum-98 extraction method can be used to extract other molybdenum isotopes, for example ^{100}Mo , used to produce ^{99m}Tc on a cyclotron.

E-TPW24

Quality Control of 99m-Technetium-Based Reconstituted Radiopharmaceutical over time

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Aim: Technetium-99 is the decay daughter of 99m-Technetium which is present in all 99m-Technetium generator eluates along with the desired radionuclide 99m-Technetium. Radionuclidic impurities such as large amounts of Technetium-99, free 99m-Technetium or hydrolyzed reduced 99mTc can degrade image quality and affects the patient's overall radiation

dose. The study aims to assess the purity level of compounded ^{99m}Tc -Technetium radiopharmaceuticals over time and beyond the manufacturer's recommended expiration time. **Methods:** Radiochemical purity of sixty ^{99m}Tc -Technetium-based Mag 3, MDP, Sestamibi, MAA, DTPA, and DMSA, were assessed by thin-layer chromatography (TLC) at 0 and every hour subsequently up to 10 hours to assess the ratio of radionuclide activity to the total radioactivity of reconstituted ^{99m}Tc -Technetium radiopharmaceuticals. The radiochemical impurities are separated due to differing affinities to the various TLC strips. Single or two-solvents chromatographic system were used to separate the bound from the free pertechnetate, depending on the radiopharmaceutical. The chromatographic strips were then counted with a multi-channel analyzer to determine the percent bound. **Results:** The results show a regressive linear curve for all pharmaceuticals over time. There were no significant inter-variances results found. The mean radiopharmaceutical purity was 95.78% (SD 2.34%). The lowest purity level at 10 hours was 92.02% (Range 92.02– 98.63%; Median 96.6%). **Discussion & Conclusion:** The study found that radiochemical purity remained above the recommended level of 90%, at a mean of 4.78% for MDP; 4.98% for Sestamibi; 2.13% for Mag 3; 3.22% for DTPA; 5.5% for MAA; and 5.98% for DMSA, and past the recommended expiry time in the package inserts by an average of 1.2 hours in the study time of 10 hours, falling within the practical usage time in a nuclear medicine facility. The most observed impurities were hydrolyzed reduced technetium.

E-TPW25

Validation of an alternative method for Quality Control of Lymphoseek® (^{99m}Tc -Tilmanocept)

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^{99m}Tc -Tilmanocept is an engineered radiopharmaceutical specifically designed for sentinel lymph node (SLN) identification. Its multiple diethylene-triamine-pentaacetic acid (DTPA) moieties chelate and bind tightly to Tc-^{99m} , while its multiple mannose moieties serve as ligands for multivalent binding to mannose receptors (CD206) expressed on the surfaces of reticuloendothelial cells resident in lymph nodes. To improve the Quality Control method of ^{99m}Tc -Tilmanocept in comparison with that described in the data sheet maintaining the same results (RCP%>90%). To label Tilmanocept, the kit vial was reconstituted with 0.5 ml $^{99}\text{Mo}/^{99m}\text{Tc}$ generator eluate (85–96 MBq), followed by 15 min incubation at room temperature. After adding physiological solution to a final volume of 1.25 ml, the RCP% was measured by instant thin-layer chromatography (TLC) using Whatman grade 1 stripes as stationary phase and 2-butanone as mobile phase to determine the amount of free $^{99m}\text{TcNaO}_4$ and $^{99m}\text{TcO}_2$. The whole TLC stripe was analyzed using the radio chromatograph MINIGITA (ELSE) instead of cutting it in two parts as described in the data sheet and counted its radioactivity with a dose calibrator as in the data sheet of the product. The labeling reaction and its Quality Controls were

repeated 3 times to validate the process. The radiochromatograms showed a retention time of 0–0.2 for ^{99m}Tc -Tilmanocept and 0.8–1 for $^{99m}\text{TcNaO}_4$ and $^{99m}\text{TcO}_2$. The CQs showed a mean RCP% of 95.97% for 85.9 MBq of Tc-^{99m} , 96.41% for 92.20 MBq and 95.48% for 96 MBq. The RCP% of ^{99m}Tc -Tilmanocept was determined successfully analyzing the whole TLC stripes instead of cutting them in two parts, defining the retention time of the radiopharmaceutical product ($T_r=0$) and its impurities ($T_r=1$) as required in the data sheet method. This different CQ method is simpler and faster than that described in the Lymphoseek data sheet, improving the Quality Control process of the radiopharmaceutical in the clinical routine.

E-TPW26

Nanocis®: Possible errors in the Summary of Product Characteristics method and an alternative method

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Background: After implementation of the radiopharmaceutical Nanocis® (^{99m}Tc -Technetium labelled colloidal rhenium sulphide) for use in gastric emptying examinations, discrepancies were observed between the Quality Control (QC) results using the QC procedure described in the Summary of Product Characteristics (SPC) and images obtained during camera acquisition. When performing QC in accordance with the SPC, radiochemical purity was always above 99%, indicating a total absence of free pertechnetate. These results conflicted with the image acquisition performed after administration of the radiopharmaceutical, in which free pertechnetate were observed in the patients thyroid gland. This discrepancy was investigated in cooperation with the Department of Nuclear Medicine and PET Centre, University Hospital Aarhus, Denmark, who reported the discrepancy to the Danish Health Authority. The aim of our study is to determine a correct QC procedure for Nanocis®. **Method and Materials:** After preparation performed, in accordance to the SPC, quality control was performed in four different ways, and results were compared. Method 1 (Number of preparations (N)=19): Stationary phase: Whatman No.1, Mobile phase: Methyl Ethyl Ketone, Application spot allowed to dry: Yes. Method 2 (N=10): Stationary phase: Whatman No.1, Mobile phase: Methyl Ethyl Ketone, Application spot allowed to dry: No. Method 3 (N=20): Stationary phase: Varian ITLC-SA, Mobile phase: Methyl Ethyl Ketone, Application spot allowed to dry: Yes. Method 4 (N=13): Stationary phase: Varian ITLC-SA, Mobile phase: Methyl Ethyl Ketone, Application spot allowed to dry: No. All TLC strips were scanned on a Scan-RAM radio-TLC scanner, using Laura® software (Scan length 20 cm, dwell time 0,1 sec.). **Results:** All QC's performed using method 1, resulted in acceptable labeling with a radiopharmaceutical purity over 99%. Methods 2, 3 and 4 resulted in radiopharmaceutical purities between 76 % and 99%. All results from the three different procedures resulted in comparable results. When comparing the results with imaging of the thyroid gland a clear correlation was seen between low radiochemical purity and thyroid uptake. The tests showed that

if method 1 is used, the free pertechnetate were retained near Retention front (Rf) 0. But method 2, 3 and 4 yielded comparable result, with free pertechnetate at Rf 1. **Conclusion:** Drying the application spot on Whatman No.1 paper will result in erroneous high labeling. To have a correct QC result, either Whatman No. 1 paper with no drying of the application spot, or using ITLC-SA paper, should be used.

E-TPW27

Nanocis®: Exchanging boiling water with a solid state heater: Is there difference in the radiochemical purity?

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Background: Correct preparation of a radiopharmaceutical is essential in order to minimise the amount of free pertechnetate in the final product. Any free pertechnetate administered to a patient will accumulate in the thyroid gland, the salivary glands and the ventricle, leading to possible erroneous diagnosis in examinations in which these regions are involved, for example ventricular emptying scintigraphy (VES). For VES, the radiopharmaceutical Nanocis® (^{99m}Techne- tium labelled colloid rhenium sulphide) is routinely used at our Department. But studies has shown that the radiopharmaceutical often have an unacceptable radiochemical purity. One theory is that the procedure for heating the radiopharmaceutical described in the summary of product characteristics (SPC) is erroneous. The SPC for Nanocis® preparation states that heating should be performed in a water bath with boiling water. We believe that due to heat dissipation, the optimal temperature of 100 degrees Celsius is difficult to maintain. We therefore exchanged the water bath with a solid state heater (SSH), during the heating step of preparation. The aim of our study is to determine if exchanging boiling water with a SSH will yield an acceptable radiochemical purity. **Method and Materials:** A number of kits were prepared according to the SPC, with the only deviation from the SPC being the heating procedure. After the initial steps of the preparation procedure had been completed, the prepared vials underwent heating in the SSH (ACCUBLOCK®, Labnet). Kits was heated to 130 degrees (Number of preparations (N)=8), 100 degrees (N=9), and 80 degrees (N=1 preliminary), for 30 minutes each. After performing the preparation and letting the vials cool, quality control were performed according to SPC (Stationary phase: Varian ITCL-SA paper, mobile phase: methyl ethyl ketone). All TLC strips were scanned on a Scan-RAM radio-TLC scanner, using Laura® software (Scan length 20 cm, dwell time 0.1 sec.). **Results:** All vials heated at 130 degrees were found to have a radiochemical purity of 99.9%. Vial heated at 130 degrees were not used for patient examination, due to the risk of structural changes to the kit, introduced by the high temperature. Vials heated at 100 degrees had a radiochemical purity of 95 - 99 %. All patient examination conducted with these kits showed a normal distribution. A single vial heated to 80 degrees as a control had an unacceptable radiochemical purity (88%). **Conclusion:** Replacing the water bath heating procedure, with a solid state heater, yields a more stable labeling with acceptable radiochemical purity.

E-TPW28

Bridatec®: Possible errors in the Summary of Product Characteristics preparation method

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Background: The radiopharmaceutical Bridatec® (^{99m}Techne- tium labelled Mebrofenin) has been in use for many years for various examinations, including cholescintigraphy and measurements of the splanchnic blood flow. In the past Bridatec® was prepared in the morning and allowed to stand at room temperature for at least 45 minutes before use. But due to an increase in the patient workflow this is no longer the case. Bridatec® is now drawn from the vial as soon as possible in order for the examination to start as rapidly as possible. According to the Summary of Product Characteristics (SPC), this is possible after 15 minutes incubation at room temperature. After a number of examination with signs of free pertechnetate in the patients, the validity of the SPC were questionable. According to the SPC, Bridatec® should be allowed to incubate at room temperature for 15 minutes, but the paragraph regarding quality control had stated that QC should be commenced after 20 minutes. This discrepancy lead us to start an investigation to verify the necessary incubation time in order to avoid free pertechnetate. The aim of our study was to verify the correct incubation time for Bridatec®.

Method and Materials: Preparation of the radiopharmaceutical was performed in accordance with the SPC. All samples were taken in 5 minute increments, starting after 5 minutes incubation after pertechnetate was introduced to the vial and ending after 30 minutes incubation. Quality control was performed on all samples, using thin layer chromatography (TLC) (Stationary phase: Varian ITLC-SA, mobile phase: Methyl Ethyl Ketone). All TLC strips were scanned on a Scan-RAM radio-TLC scanner, using Laura software (Scan length 20 cm, dwell time 0,1 sec.). **Results:** The radiochemical purity after preparation and sampling were as follow for N=5 (preliminary): 5 minutes incubation: 55 - 80% 10 minutes incubation: 75 - 88% 15 minutes incubation: 83 - 90% 20: minutes incubation: 93 - 96% 25: minutes incubation: 94 - 97% 30 minutes incubation: 96 - 97% **Conclusion:** After preparation, Bridatec® must be allowed to stand at room temperature, for at least 30 minutes before use.

E-TPW29

The Benefits of Producing in house Radiopharmaceuticals for Prostate Cancer PET-CT Imaging from an Economics & Business Perspective

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Aim: Total expenditure within the NHS is set to reach £123 billion by the year 2021, NHS trusts must devise ways to reduce spending and become increasingly cost effective whilst still allowing hospitals to deliver the highest quality of patient care. Within the oncology sector, early diagnosis and intervention is paramount when aiming to treat cancer efficiently and increase patient life expectancy. Prostate cancer is the most commonly diagnosed cancer in men with 45,000 new cases diagnosed in

2015. The aim of this study was to show the business and economic benefits of producing Ga-68-PSMA in house rather than buying externally. **Methods:** We reviewed externally purchased F-18 Choline data from January 2017–March 2018 to uncover the number of patients scanned (A), price of radiopharmaceutical (P) cost of scan (Cs), and NHS income per scan (I). The same patient numbers were applied to in-house Ga-68-PSMA and readjusted for differences in radiopharmaceutical price (P) and scan cost (Cs). $(I - (Cs - P)) * A = \text{Profit}$. The defective rate (d) of each tracer was calculated and used to formulate losses incurred by the trust through wasted man hours (Lm) and loss of potential profit (Lp). $(A * d) * Cs = Lm$, $(A * d) * (I - (Cs + P)) = Lp$. The profit figure was then adjusted to take into account these potential losses from defective product. $\text{Profit} - (Lp + Lm) = \text{adjusted profit}$. Further calculations were performed to demonstrate that the improved efficiency per week (E) could lead to cost savings for Ga-68-PSMA produced in house. $A / (E * d) = \# \text{ of week to perform A}$. Finally, a calculation was determined to show at which week Ga-68-PSMA would begin to be more cost effective than F-18 Choline. $\text{Choline Adjusted Profit} / (E * d) * (I - (P + Cs)) - (1.2(Lm + Lp)) = \text{Weeks until more cost effective}$. **Results:** 376 patients were scanned using F-18 Choline from January 2017–March 2018. $\text{£}48,702 / ((13.8 * 112) - (1.2(254 + 112))) = 43.6$ week until equivalent profit is reached. The same profit for F-18 Choline was achieved in 63 weeks. **Conclusion:** The results demonstrate that even though Ga-PSMA has a higher cost initially, over time you would benefit from technical economies of scale. The improved efficiency within the supply chain leads to more scans being able to be performed per week, and a significantly lower defective rate, resulting in increased profit. Other benefits of greater efficiency is improved patient satisfaction, decreased patient wait time leading to more rapid diagnosis and improved treatment and patient management.

E-TPW30

Comparison of QC Results of [^{18}F]FET Purified with SPE or HPLC Method

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Aim: [^{18}F]Fluoro-ethyl-L-tyrosine ([^{18}F]FET) is an amino acid derivative taken up into tumor especially brain tumors. Chiral radiopharmaceutical such as L-[^{11}C]methionine, [^{18}F]FET and [^{18}F]FDOPA have to be assessed the enantiomeric purity with HPLC before injection, in generally. We developed new chiral purity evaluation HPLC method to assess the enantiomeric purity and validated it. We also evaluated the quality of [^{18}F]FET synthesized different purification method. **Material and Methods:** [^{18}F]FET was synthesized with two types of chemistry modules: tracerlab MX module with SPE purification method using ABX cassette & reagent and all-In-One chemistry module with HPLC method using Trasis cassette & reagent. The quality control tests for the [^{18}F]FET was conducted as following the procedures described in the European Pharmacopoeia (EP) of “Fluoroethyl-L-tyrosine(^{18}F) injection” except enantiomeric purity. All experiment was conducted using chiral column (Astec CHIROBIOTIC, 250 x 10 mm, 5 μm) and mobile phase system (0.01 M

$\text{NaH}_2\text{PO}_4 \cdot \text{MeCN} = 20:80$). **Results:** For validation test, the HPLC analysis method was newly established. The reverse HPLC method separated L-FET and 3,4-dimethoxy-L-phenylalanine with R_s 8.5 (min R_s : 2.0) and the new chiral HPLC system separated L&D FET with R_s 1.7 (min. R_s : 1.5). Both the HPLC and SPE purification methods allows not only the synthesis of [^{18}F]FET with reasonable radiochemical yield (>15%, non decay corrected yield) but also high radiochemical purity (>98%) and enantiomeric purity (>99%). After purification, [^{18}F]FET shows one single fluoroethyl-L-tyrosine substance from HPLC and four impurities included fluoroethyl-L-tyrosine substance from SPE. The amount of each substance was <0.1 mg/V and the total amount of impurities was <0.5 mg/V. Ethanol contents was <10% (v/v) and residual reaction solvent was not detected. As a result, [^{18}F]FET met the EP QC acceptance criteria and showed high stability over 6 hr. **Conclusion:** The novel analysis method for the evaluation of enantiomeric purity of [^{18}F]FET has been established. The quality of purified [^{18}F]FET was assessed by the new QC method and the results from both methods met the EP criteria.

E-TPW31

Biodistribution of $^{68}\text{GaCl}_3$ in ^{68}Ga radiopharmaceuticals

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Gallium-68(^{68}Ga) has been widely used in Nuclear Medicine for diagnostic purposes as positron emission tomography (PET) radionuclide. The importance of ^{68}Ga radionuclide is increasingly used labeling with various molecules, such as peptides, proteins, antibody fragments. ^{68}Ga labeled peptides are today routinely used in clinical evaluation and many others are under investigation as clinical and preclinical. The purpose of this study was to investigate the organ distribution of ^{68}Ga in case of poor radiolabeling efficiency and dissociation of the radiolabeled molecule. This study evaluated distribution of Ga-68 radionuclide one hour after IV injection of ^{68}Ga in healthy female Sprague Dawley rats. ^{68}Ga is eluted from $^{68}\text{Ge}/^{68}\text{Ga}$ generator in the form of $^{68}\text{GaCl}_3$. One mCi $^{68}\text{GaCl}_3$ was injected to the rats via tail vein. Organs were removed and their radioactivity counted using gamma counter at 60 minutes after injection. Organ/background rates were calculated. The highest activity uptake was seen in small intestine and bone. There was also considerable uptake ovaries. The lowest activity was seen in kidney and large intestine at 60 minutes. The results show that bone and small intestine are mainly seen in the presence of free ^{68}Ga . Human biodistribution was estimated from the rat data.

E-TPW32

Efficacy and Toxicity of Lu-177 DOTATATE in Well-Differentiated Grade 3a Neuroendocrine Tumours

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Introduction: Lu-177 DOTATATE has been proven to be an effective treatment option in well-differentiated G1-2 neuroendocrine tumours (NETs). Many well-differentiated grade 3a NETs also strongly express somatostatin receptors. However the efficacy of Lu-177 DOTATATE in well-differentiated Grade 3a NETs is

not as clear. **Aim:** This study aims to assess the efficacy and toxicity of Lu-177 DOTATATE in Grade 3a NETs. **Methods:** We retrospectively searched our Lu-177 DOTATATE database for patients treated from 2013 to 2017. 7/278 (2.5%) patients were identified included in this study classified as Grade 3a NET based on WHO classification 2010. Patients were treated with approximately 7.4GBq of Lu-177 DOTATATE at an interval of 10–12 weeks. Response assessment was used via cross-sectional imaging (RECIST 1.1). Bone marrow and renal toxicity was assessed using CT-CAE 4.0. Progression free survival (PFS) was also evaluated using the Kaplan-Meier survival plot. **Result:** The primary was located in the pancreas in (3/7), midgut (2/7), presacral (1/7) and unknown (1/7). The ki-67 proliferation index ranged from 25–35% (mean 27%). 4/7 patients completed 4 cycles, 1/7 patient had 3 cycles (due to have a 4th cycle) and 2/7 patients had 2 cycles. 4/7 (57%) patients had a partial response and 1/7 (14%) patient demonstrated stable response. The 2 (29%) patients that had only 2 cycles had progressive disease on interim cross-sectional imaging. The median follow-up was 25.6 months. The median PFS was estimated at 22.4 months (range 5–34 months). There were no significant decrease in renal function and no grade 3/4 hematologic toxicity. **Conclusion:** Our small cohort of patients demonstrates that Lu-177-DOTATATE can be an effective treatment in Grade 3a NETs with relatively high partial response to treatment. This cohort of patients demonstrated a good median PFS of 22 months. Longer term follow-up is needed. No significant haematologic or renal toxicity developed.

E-TPW33

Lu-177 DOTATATE Retreatment: Efficacy and Toxicity

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Introduction and Aim: Lu-177 DOTATATE is an effective treatment for well-differentiated neuroendocrine tumours (NETs). Complete remission is rarely achieved but partial response or disease stabilisation is seen in approximately 80% of patients who have had progressive disease. However, invariably patients will develop future disease progression. The value of retreatment with Lu-177 DOTATATE is not clearly established. This study aims to assess the outcome and toxicity of Lu-177 DOTATATE retreatments. **Methodology:** This is a retrospective study of Lu-177 DOTATATE patients who received treatment from 2013–2017. 14/ 278 (5%) patients completed 4 cycles of Lu-177 DOTATATE, and were retreated with 2 cycles of Lu-177 DOTATATE following subsequent disease progression. Radiographic response was assessed using cross-sectional imaging (RECIST 1.1). Full blood count and renal function tests were assessed using CTCAE 4.0 to evaluate hematologic and renal toxicity. Progression free survival (PFS) was also evaluated using the Kaplan-Meier survival plot. **Result:** The mean administered activity at the initial 4 cycles was 29.8 GBq and the mean administered activity on the subsequent 2 cycles was 15 GBq. 1/14 had a partial response (PR) to initial 4 cycles and 13/14 demonstrated stable response (SD). The median PFS was 24 months. On the second course of treatment, 12 patients had evaluable data. 2 patients had PR, 5 patients had SD and 5 patients had progressive disease (PD). 1/14 patients

had Grade 3 renal toxicity during the initial course of therapy. This subsequently resolved. No renal toxicity was noted during the second course of treatment. 1/14 patients developed prolonged pancytopenia after second course of treatment. **Conclusion:** Lu-177 PRRT is an effective systemic treatment for NET. Favourable response can be achieved during initial treatment but prevention of disease progression is not a guarantee. However, resorting to retreatment can still elicit disease stabilization or partial response in a significant proportion of patients with minimal hematologic or renal toxicity. Longer term follow-up is needed to determine the durability of this response.

E-TPW34

Experience In The Treatment Of Neuroendocrine Tumors (TNEs) With Somatostatin-Like Peptides (SLP) Labeled With ¹⁷⁷Lu -DOTATATE

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Objective: The treatment with SLP marked with ¹⁷⁷Lu in patients with metastatic TNEs in progression is a therapy recently used in our country. The objective is to evaluate our preliminary results.

Material and Method: From June-2016 to April-2018 we have done 35 treatments with ¹⁷⁷Lu-DOTATATE: 11 patients, 7 men and 4 women, mean age 60 years, with a range of 37–81, with TNEs (5 gastrointestinal, 4 pancreatic and 2 paragangliomas/1G1, 7G2, 3G3) disseminated and in progression. In 7 of them, 4 cycles of 200 mCi were completed. In 1 only two cycles by exitus and 1 doses pending; and in 2 only one dose (one exitus and one refusal to follow the therapy). In all patients, the therapeutic response was evaluated by means of CT, between the second and third doses and at the end of the fourth cycle. **Results:** In our treatment intention analysis, of the 11 patients, only one presented significant pancytopenia after the second and third cycles, but recovered before subsequent cycles. None of them presented renal toxicity. All of them confirmed a subjective improvement in their quality of life. Of the nine patients in whom a CT-interim was performed, in 4 there was a partial remission (PR), in 4 disease stability (DS) and in 1 progression (although it was later performed by PR). Of the 7 patients in which the 4 cycles were completed, in 4 PR was found and in 3 DS, although the first patient with PR, presented progression at seven months of the fourth cycle and died at 13 months of it). **Conclusions:** Treatment with ¹⁷⁷Lu-DOTATATE is well tolerated and controls the disease in the majority of patients, with limited and reversible toxicity, and with a subjective improvement in the quality of life.

E-TPW35

Treatment of liver neoplastic lesions with ⁹⁰Y radio-embolization

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Introduction: Malignant hepatic tumors, primary or metastatic, involve a huge amount of people in Italy, as worldwide. Liver

is the most common metastatic site of different cancer types, among which those of breast, gastro-intestinal and neuroendocrine origin. The radioembolization (TARE) consists in a new mini-invasive transcatheter endovascular therapy of the hepatic district, by which glass microparticles (TheraSphere) impregnated with the radionuclide Yttrium-90 (^{90}Y) are selectively injected in the hepatic artery. The ^{90}Y -loaded microspheres (20–30 micron in diameter) remain trapped in the smallest branches of the hepatic artery supplying the neoplastic lesion and finally irradiate the tumor with a high **beta** energy-**emission** in a super-selective way. The radio-embolization (RE) can be performed in place of the trans-arterial chemoembolization (TACE) in those HCC patients satisfying the criteria of Barcelona Clinic for Liver Cancer (BCLC) staging classification. Absolute contraindications to RE are essentially limited to the existence of an insufficient liver functional reserve and/or a severe pulmonary shunt. **Subjects and Methods:** at the reference center of IOV-IRCCS (Padua), from January 2016 till today, a total of 42 patients (38 Males, 4 Females) have been subjected to RE. The treatment process consists of three phases: 1. Selection of the candidate: patient day-hospital recovery, where contrast-enhanced abdomen computed tomography (CT) scan and liver angioscintigraphy with $^{99\text{m}}\text{Tc}$ -macroaggregated albumin (MAA) are performed for evaluating treatment eligibility. 2. Treatment: recovery in a single room, angiographic procedure, administration of ^{90}Y -TheraSphere, post-treatment monitoring of environmental contamination of angiographic room, control PET/CT 3. Follow-up: CT-scan exams to be performed at 1, 3, 6 and 12 months after the procedure for assessing the efficacy during time and for monitoring the global evolution of tumoral disease. The indicators of treatment effectiveness (patient survival, disease down-staging) permit also to select the patients that could successively benefit of a curative liver resection or transplant. **Results:** observation of treatment response/efficacy is relative to a 3–6 months period and results seem encouraging. **Discussion/Conclusion:** TARE represent a safe and reliable treatment for HCC. Technologist is an essential professional figure for realizing the whole procedure, having both Molecular Imaging and Interventional Radiology competences. Technologist takes care of radiopharmaceutical labeling (MAA- $^{99\text{m}}\text{Tc}$), quality control and scintigraphic exam in Nuclear Medicine, with tasks linked to CT scan execution and angiographic room assistance (both in the simulation and procedure phase) in Radiology.

E-TPW36

Lung Mass and Shunt Fraction Assessed by $^{99\text{m}}\text{Tc}$ -MAA SPECT/CT Predict Incidence of Imaging Radiation Pneumonitis After Liver ^{90}Y Radioembolization

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Aim: ^{90}Y -microsphere radioembolization (RE) is a promising hepatic intra-arterial therapy for patients with unresectable

liver cancer or metastases. The therapy was reported to be safe and well tolerated in most cases, but complications may arise when ^{90}Y - microspheres accumulated in organs other than liver through unwanted arteriovenous shunting. This is especially serious if significant ^{90}Y -micropsphere deposited in the lungs. Currently used partition model in predicting lung dosimetry assumes fixed lung mass of 1,000g and uniform distribution of ^{90}Y -microsphere. Our aim is to evaluate whether incorporating information derived from $^{99\text{m}}\text{Tc}$ -MAA SPECT/CT will better predict risks of pulmonary adverse events after RE. **Materials and Methods:** $^{99\text{m}}\text{Tc}$ -MAA imaging was performed in 143 patients prior to RE (SIR-Spheres®) at our institution during a 3-year period. $^{99\text{m}}\text{Tc}$ -MAA planar and SPECT/CT imaging of the entire lungs in 64 patients (46 men and 18 women, mean age: 63.8 ± 12.8) were retrospectively analyzed. Auto lung-segmentation with SPECT/CT was processed using PMOD software to estimate individualized lung mass. The measured lung mass was used to recalculate the estimated lung dosimetry given in each patient and correlated with incidences of pulmonary adverse events (AE). Clinical history of smoking or lung diseases were also recorded in all patients. **Results:** Forty-one (64.1%) patients had hepatocellular carcinoma (HCC), whereas 23 (35.9%) had liver metastases. Mean lung shunt fraction was greater in the patients with HCC than metastases (7.3 % vs. 3.7%, $P=0.032$). The mean lung mass estimated by SPECT/CT was 749.8 ± 207.2 g (range, 303.6–1280.9 g). RE therapy was precluded in five (7.8%) of 64 patients due to a lung shunting fraction of >20%. Among 59 patients received RE, the mean lung absorbed dose was significantly higher if individualized lung mass was used to estimate lung dosimetry (5.0 ± 4.4 Gy vs. 4.2 ± 3.7 Gy, $P<0.001$). Two of 64 patients (3.1%) demonstrated clinical and imaging radiation pneumonitis with no previous history of smoking or lung diseases. The mean lung mass and the lung shunt fraction of these 2 patients were 766.1 ± 79.8 g and $11.85 \pm 1.82\%$, respectively. The estimated mean lung doses were 19.0 Gy and 26.1 Gy using individualized lung mass. **Conclusion:** Estimating lung dosimetry prior to RE planning should incorporate individualized rather than a fixed lung mass to avoid pulmonary AE. Pulmonary threshold to cause clinical or imaging radiation pneumonitis can be as low as 20 Gy, as in our patients.

E-TPW37

Desing of Experimental Liver Phantom with Multifocal Tumor Implication for Use in Yttrium 90 Radioembolization Dosimetry

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Yttrium 90 (Y-90) treatment, which is called radioembolization for liver tumors, one of the Nuclear Medicine therapeutic applications, is the IV delivery of this radiopharmaceutical to the patient through the hepatic artery. In treatment, the radiopharmaceutical is highly localized in the tumor and radiates and destroys the tumor cells. This provides an effective treatment by ensuring that primer and metastatic tumors shrink or disap-

pear. Y-90 is also irradiated with normal liver tissue around the tumor due to high beta energy of 930 keV (maximum 2.2 MeV). Therefore, when an internal radiation dosimetry is performed for treatment, the critical tissue that determines the highest drug activity that can be given to the patient is normal liver tissue. At this point, the first problem that arises in the internal radiation dosimetry of the Y-90 radioembolization therapy is that it is not known how much of the radiation dose the tumor and normal liver tissue actually gets. In addition, the dosimetry operation is calculated by computer simulation using Monte Carlo method and the amount of activity to be sick is determined by trusting these results. The second problem is that it is not known how much the dosimetry calculations made in the virtual environment overlap with reality. **Aim:** In this study it was aimed to design and produce an experimental liver phantom with multifocal tumor imitation which can be filled with soft tissue equivalent material, cost effective, compatible with patient data via rapid prototyping technology with three dimensional printer to use in Y-90 radioembolization dosimetry. **Material and Methods:** The phantom was designed to be the closest to reality using the ZBrush 3D printer interface, due to hepatomegaly. Soft tissue mimicry was done using PLA material. Two tumor regions were formed at different diameters (3.3cm and 1.3cm). Two spheres of 1 mm wall thickness, with different diameters (3.2cm and 1.2cm), with an opening suitable for injection of radioactive material by means of a syringe, were used to imitate the tumor. Thanks to the presence of two tumor imprints, it is also possible to calculate the radiation doses that the sources have on each other. The actual radiation doses to be generated within the phantom were determined by TLDs placed at regular intervals around the tumor mimicry. **Results:** After obtaining the simulation results with Monte Carlo method, the results will be announced by comparing with the real experiment.

E-TPW38

^{99m}Tc-MAA SPECT/CT-based dosimetry in SIRT: Why personalized dosimetry matters - A retrospective study

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Introduction: The capacity to predict the distribution of ⁹⁰Y-Microspheres has been shown as a factor of improvement of SIRT efficacy. The similar distribution between ^{99m}Tc-MAA and ⁹⁰Y-Microspheres allows performing dosimetry simulation using ^{99m}Tc-MAA SPECT/CT co-registered with MRI, or CECT. In this study, we compare the activity to be administered obtained using a personalized dosimetry software with multi-compartment MIRD technique (Simplicit⁹⁰Y[®]) to the activity actually administered obtained from the classical non-compartmental MIRD dosimetry planning, using a target volume based only on the ^{99m}Tc-MAA SPECT. **Material and Methods:** 20 patients treated with ⁹⁰Y-TheraSphere[®] were included (19 HCC and 1 cholangiocarcinoma). For all of them, MRI, or CECT, ^{99m}Tc-MAA SPECT/

CT and ⁹⁰Y Bremsstrahlung Emission Computed Tomography (BECT)/CT were available. Radiological tumour response was correlated with the perfused tumour dose and the perfused fraction of the total tumour volume, using ⁹⁰Y BECT/CT and Simplicit⁹⁰Y[®]. We also calculated the activity needed to obtain 205 Gy [Garin *et al.*, 2016] in the perfused tumour, using ^{99m}Tc-MAA SPECT/CT and Simplicit⁹⁰Y[®]. We finally compared the activity based on this minimal tumour absorbed dose criteria to the activity actually administered, plotted the relative differences, and correlated these differences with the radiological tumour response. **Results:** Among the 20 patients, 10 patients responded. In this group, the ⁹⁰Y BECT/CT-based dosimetry showed 4 patients receiving less than 205 Gy (162 Gy on average) and 6 patients receiving more than 205 Gy (262 Gy on average) in the perfused tumour. For these 6 patients, the comparison between the administered activity and the recommended activity calculated by Simplicit⁹⁰Y[®] showed that 5 patients received an activity higher than recommended (70 % mean difference), but, with a dose to the normal liver staying below 70 Gy [Gnesin *et al.*, 2016] (49 Gy on average), except for 1 patient. Among the 10 non-responding patients, 5 patients progressed and 5 patients were stable. All of these patients received less than 205 Gy to the perfused tumour, based on a ⁹⁰Y BECT/CT-based dosimetry. Concerning the 5 patients who progressed, the comparison between the administered activity and the recommended activity by Simplicit⁹⁰Y[®] showed that all of them received less activity than recommended (50 % mean difference). **Conclusion:** These results indicate that reaching a minimal tumour absorbed dose criteria increases the efficacy of SIRT. They support the use of a more personalized dosimetry than the classical non-compartmental MIRD dosimetry for SIRT planning.

E-TPW39

Yttrium-90 microspheres treatment - Is admitting patients for radiation safety concerns justifiable?

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Introduction: Yttrium 90 (Y90) treatments are carried out by placing a catheter into the hepatic artery and delivering millions of biocompatible radiomicrospheres into the liver. Y90 is a pure beta-particle-emitter with a physical half-life of 64.2 hours, 0.94 MeV decay energy, and an average penetrative depth of 2.4mm in human tissue. The patients in our institution are administered with a mean activity of 0.92 Gbq (± 0.42). The study aims to verify if these patients can be safely allowed to be discharged on the same day if their clinical conditions are stable, and if so, what are the magnitude of radiation emitted from their liver. **Methods:** Readings were taken from a calibrated ionization survey meter measuring the external radiation exposure rates of 50 patients who had just undergone the Y90 treatment. The measurements were taken at 0.5 meters, 1 meter, 2 meters, and 3 meters, in a supine body axis position (liver to pelvis) as the patient are required to be rested in the supine position immediately post therapy and hepatic artery catheterisation. **Results:** Radiation dose rates of 25.1 (± 1.2), 16.6 (± 1.3), 8.5 (± 1.2), and 1.1 (± 1.1) µSv/hr were measured at 0.5, 1, 2, and 3 meters respectively immediately post therapy. The calculated assumption of a mem-

ber of the public or family member keeping at 1 meter distance from a patient at these dose rates for an average continuous 0.25 hours showed insignificant radiation exposure. The conservative assumption of a member of the public sharing public transport with the patient at a distance of 0.5 meters from a patient at these dose rates for a continuous 6 hours based on the measurements (at 2 hours post therapy) is less than 0.1 mSv of radiation dose exposure, with decay taken into consideration. Mean TEDE dose was 0.06 mSv. All patients had exposure rates below 1 μ Sv/hr by 24 hours at 1 meter from the liver. **Conclusion:** The Y90 microspheres beta dose delivery is mainly confined to the liver with minimal biologic elimination of Y90. Simple precautions such as making an effort not to maintain close contact (<1 meter) with pregnant women and limiting extended time (> 6 continuous hours) with family members, is advisable although not critical. Biologic elimination of Y90 from the patient's bodies is minimal, with only trace amounts detected. Y90 patients pose no reasonable radiation safety concerns to staff and public immediately post treatment.

E-TPW40

Technetium uptake prior to benign iodine treatment varies over time and scintigraphy should be repeated

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Aim: Before iodine-131 treatment for benign thyroid disease patients have a Tc-99m pertechnetate thyroid scintigraphy as part of the diagnostic workup. The scintigraphy is used to determine uptake, size and type (nodular or diffuse) of the thyroid gland and then used together with palpation to determine iodine dose (200, 400 or 600 MBq). If the scintigraphy is more than 3 months old it is repeated primarily to check uptake. We often noticed only little difference between the first and the repeated scintigraphy so we wanted to examine how much it changes over time and if the 3 month period could be prolonged and more patients could avoid the extra exam. **Materials and Methods:** Patients with thyroid scintigraphy and repeated scan during 2017 were identified. Patient data as sex, age, injected Tc-99m dose, iodine treatment dose, type of thyroid pattern, indication for treatment, duration and counts of the overview and zoom images were recorded. Differences in uptake, size and type between the two time points were scored visually on a 5-point scale by an experienced nuclear medical physician and uptake time ratio (UTR) of images was calculated and averaged in each 5-point group. **Results:** The 50 patients had the following demographics: Average age 62.6 years, 74% females, 98% nodular, 26% had goitre, 14% had hyperthyroidism, 60% had both goitre and hyperthyroidism. Average Tc-99m dose was 176 MBq. The distribution of selected fixed doses I-131 (200, 400 or 600 MBq) was 10%, 66% and 22%. One treatment was cancelled due to illness. The average time period (ATP) between the two scans was 159 days (range 50–271). No patients had visually notable change in size or pattern of the gland. The visually uptake was moderately lower in one patient (2%; ATP=152 days, UTR=0.7). 36 patients (72%, ATP=170, UTR 1.1) had unchanged uptake. 9 patients (18%, ATP=122, UTR 2.0) had moderately increased

uptake. 4 patients (8%, ATP=150, UTR 2.9) had clearly higher uptake. The visual uptake scores correlated as expected with UTR but not with ATP. **Conclusion:** Size and pattern of thyroid was stable in the one year period. No patients needed cancellation due to low uptake. 8% had so markedly increased uptake it could influence the choice of I-131 dose. Uptake varied over time but was not correlated with duration between scans and a specific cut off time could not be estimated and we decided to keep the 3 month period.

E-TPW41

Capsules versus liquid - evaluation of price and dose of iodine 131

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Aim: Radioiodine is commonly used in thyroid cancer and thyrotoxicosis treatment and it is distributed in form of liquid or capsules. Both forms have their pluses and minuses and this study aims to compare them, specifically we tried to make a comparison including radiation burden for operating staff and we also focused on the economical aspect. **Materials:** Radiation burden data were acquired from whole body and finger dosimeters and internal contamination of the thyroid gland was measured on four radiological assistants working with radioiodine. For the evaluation 2 years of data was used for each form and were assessed in relation to applied activity. Economical evaluation was made with price data in the Czech republic, personnel and manipulation costs and we also calculated costs of consumables which are used during the manipulation and per oral application. **Methods:** For the radiation doses we used basic statistics and the economical comparison was made using methods of health technology assessment (HTA). Results: Thyroid contamination and dose equivalent is lower for capsules in order of tens percents in the measured staff. It seems that liquid iodine is more suitable for diagnostic application because of its price, which nowadays is around fifteen times higher than the price of capsules for activity of 1 MBq. With growing activity, the price of capsules lowers and at the usual amount of activity used for therapy (3700 - 7400 MBq) the difference between the prices is not so tremendous. **Conclusion:** Contrary the fact that iodine in capsules is more expensive than the liquid form for therapy, the undeniable advantage of lower doses for staff seems to overcome this.

E-TPW42

Benefits of the poor iodine diet in patients that are treated with 131-Iodo for the treatment of thyroid neoplasms

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Aim: To optimize possibilities of the treatment of radioactive 131I received as a cure for the disease. **Material and Method:** Before receiving radioactive iodine treatment, it is necessary to reduce the levels of "endogenous iodine" ingested in the food. In this way, the remains of thyroid cells are avid of iodine and

are willing to capture the radioiodine that is administered. The most common way to achieve this is by avoiding medicines and products rich in this component and following a diet, at least for two weeks before. To this end, the health staff provides an explanatory document where they break down the foods they should stop consuming, those that they should not be abused and those that they are allowed. According to consulted articles it is recommended to continue with it during some days during the treatment. To do this, we contacted the nutrition and dietetics responsible of the hospital and we established a diet with low iodine content during the time patients stay in the hospital.

Results: After implantation the diet low in iodine, the patients admitted continued the diet while they were hospitalized. Example of menu was: Breakfast: infusion, sugar on, pure wheat bread and oil on. Lunch: pure wheat bread, spring rice, grilled tuna, steamed potatoes, lettuce salad and low iodine fruit. Afternoon snack: infusion, sugar, toast bread and jam. Dinner: pure wheat bread, vegetable cream, pork tenderloin, fried pepper, lettuce salad and low iodine fruit. **Conclusions:** The poor iodine diet can be the origin of an improvement in the effectiveness of the treatment and decrease of false negatives in the corporal tracking, essential for the follow-up and the early detection of possible recurrences. Appropriate dietary measures reduce the risk of blocking ^{131}I uptake. The determination of the udder would allow us to know the exact value existing in the patient.

E-TPW43

^{223}Ra -Dichloride therapy in Prostate Cancer: Portuguese reality

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Introduction: Prostate cancer is one of the most common neoplasms in Portugal and in other developed countries. The disease evolution is characterized by the appearance of bone metastases, causing degradation of patients' quality of life as well as their survival rates. ^{223}Ra -Dichloride mimetizes calcium and acts directly in bone metastases, being reported as the first radiopharmaceutical with an overall increase of patient survival benefit. This work aims at defining Portuguese reality concerning ^{223}Ra -Dichloride therapy in Prostate Cancer. **Materials and Methods:** Since January 2018, presentational questionnaires have been done to staff members of at least 8 Nuclear Medicine Departments involving more than 32 patients being treated with ^{223}Ra -Dichloride. Each questionnaire was divided into two parts: the former was meant to characterize the Departments and the latter referred to all of the procedures associated to this therapy. The staff members were asked questions about planning details as well as therapy implementation and even patient follow-up. Technical features were given special attention. **Results:** Result analysis has indicated that 100% of the Departments perform a Bone Scintigraphy prior to therapy in order to validate the existence of bone metastases, while visceral metastases are being screened with CT in the majority of the Departments, even considering that there are answers pointing the use of PET with

^{68}Ga -PSMA. Only 50% of the inquired mentioned imaging with ^{223}Ra -Dichloride. However, variations in technical parameters concerning imaging studies were found. Professionals involved and their role may differ significantly in each Department, while Nuclear Medicine physicians basically perform the same role in every Department, Nuclear Medicine Technologists' role presents considerable deviation (e.g.: participation restricted to the planning stage by performing bone scintigraphy and/or PET/CT imaging). As far as radioprotection issues are concerned it is also observed a variation because although dealing with an alpha emitter only 25% of the Departments use acrylic protections, while the remaining only use lead protections. All Departments recommend radioprotection against contamination, but procedures towards radioactive waste disposal vary and only 50% of the inquired seem to implement good practices. As a whole, similar results were found regarding administered activities, radiopharmaceutical administration and quality control. **Conclusion:** The use of ^{223}Ra -Dichloride therapy seems to have been increasing in Portugal lately. Obtained results demonstrate that optimization of technical aspects of this therapy seems to be related with the level of experience of Departments. Special attention should be given to the dissemination of good technical practices.

E-TPW44

Radiation Exposure (Un)Awareness amongst nuclear medicine patients - a systematic review

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Introduction: Medical imaging is the highest source of artificial radiation exposure and after natural sources it is the second largest source of exposure, accounting for 20% of overall exposure. However, it is still often a misunderstood subject amongst patients and public. The aim of this systematic review is to provide an overview of the literature on the awareness level of ionising radiation exposure from nuclear medicine patients.

Methods: A systematic review was performed using Medline, CINAHL, Embase, Web of Science and related articles (January - February 2018). Articles were screened according to: a) only studies ≥ 2010 were included; b) full articles only; c) subject/title must include at least 3 of the following: Ionising radiation/radiation; patient/s and/or public; awareness and/or knowledge and/or perceptions; medical imaging/imaging; radiology/radiologic; nuclear medicine; d) English only. All articles were critically evaluated using Joanna Briggs Institute Clinical Appraisal checklist tools. **Results:** 159 articles were identified, 24 critically evaluated, 4 studies included; 3 cross sectional studies and 1 qualitative study. The studies were conducted in Finland, USA, Australia and Hong Kong. No studies applied exclusively to nuclear medicine patients were found. However, studies selected included nuclear medicine patients (PET/CT patients = 3; conventional nuclear medicine patients = 1). All studies demonstrate a general lack of awareness among patients with regard to ionising radiation exposure from medical imaging, although one study reported that

patients who had nuclear medicine scans were better informed. In general, studies also highlighted a lack of communication between patients and professionals and the need for more effective communication, 2 studies reported patients' preferences for radiographers/technologists to be the source of information, 1 study reported radiologists and/or physicists as preferred source of information and 1 study reported referring doctors as preferred option. **Conclusion:** Overall, all studies critically evaluated demonstrate a need to better inform patients and public. However, given the wide range of procedures and radiation exposure associated, more studies specific to nuclear medicine are warranted to evaluate patients' awareness, knowledge and preferences in communication. This information in turn can guide the development of appropriate tools for effective communication on radiation exposure and risks associated with nuclear medicine imaging. This systematic review was undertaken as part of cross sectional study focused on nuclear medicine patients and their awareness of ionising radiation exposure ("Radiation Exposure Awareness from patients undergoing nuclear medicine diagnostic ^{99m}Tc -MDP bone scans and ^{18}F -FDG PET/CT scans"). ClinicalTrials.gov Identifier: NCT03458585

804-3 Monday, October 15, 2018, 11:30 - 13:00, Meeting Room 33

Technologists: Technologist e-Poster Walk 3

E-TPW45

Comparison of Side Effects and Number of Rescans with Adenosine and Regadenoson for Pharmacological Stress in Myocardial Perfusion Scintigraphy

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Aim: The aim of this study is to compare the differences of side effects using Adenosine and Regadenoson and the respective number of rescans for Myocardial Perfusion Scintigraphy (MPS).

Materials & Methods: A retrospective study was performed on 527 patients scanned between June 2015 and December 2017. Some patients were excluded due to insufficient information available or complications during the procedure. Patients were instructed to abstain from caffeine for 24 hours and medications that could interfere were reviewed. Stress was performed using either Adenosine or Regadenoson, depending on the patient's clinical history. ^{99m}Tc -Tetrofosmin was administered with activity of either 600 MBq (under 70 kg) or 800 MBq (over 70 kg). Additionally, a low level of physical stress was used for Adenosine. A record was kept of side effects and ECG changes recorded. Patients were asked to go for a walk, drink water and SPECT/CT was performed 40 min after injection. A trained Physicist assessed the pictures and determined if a rescans was needed. A retrospective study was created comparing the different side effects and number of rescans for each of the stressing agents.

Results: This study contained 475 patients, 82% stressed with Adenosine and 18% with Regadenoson, with ages between 39 and 88 years old. There were 42% males and 58% females. There was an average of rescans of 27% - Adenosine with 28% and

Regadenoson with 24%. Regarding side effects for Adenosine and Regadenoson, after analysis of symptoms recorded, we observed respectively: Chest Pain (7% vs. 6%); Chest Tightness (28% vs. 17%); Flushing (44% vs. 37%); Dyspnoea (62% vs. 12%); Headache (20% vs. 14%); Dizziness/Light Headed (27% vs. 31%); Hypotension (0.3% vs. 0%); Nausea/Vomiting (13% vs. 12%); Abdominal/Throat/Neck Discomfort (29% vs. 27%); AV Block 1st Degree (3% vs. 1%); AV Block 2nd Degree Type I (0.3% vs. 0%); AV Block 2nd Degree Type II (2% vs. 0%); AV Block 3rd Degree (0.5% vs. 0%) and ST Segment Depression (4% vs. 1%). **Conclusions:** A lower number of rescans was observed with Regadenoson but the difference is not very significant. Also, Regadenoson presents fewer side effects - generally self-limiting and of short duration - except for Dizziness/Light Headed where it is higher. These results are in agreement with the literature available. The high number of rescans may be explained with the patient's preparation. At this moment we are changing it and in the future we intend to compare the number of rescans with both methodologies.

E-TPW46

Quantification of the hepatobiliary clearance on myocardial perfusion imaging based on two factors: diet and biodistribution time of the ^{99m}Tc -tetrofosmin

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Aim: Myocardial perfusion imaging (MPI) is an important imaging modality in the management of coronary artery disease patients. However, physiologic uptake of the radiopharmaceutical in the liver and hepatobiliary system may impair image processing and interpretation. Some factors are known to influence hepatic clearance, the most relevant being the length and the diet during the biodistribution interval. In this sense, we aimed to quantify the influence of these factors on hepatobiliary clearance. **Material and Methods:** Data from 64 stress MPI studies was recorded (either physical or pharmacological stress). During the biodistribution interval, patients ingested either a lower lipid content meal or a higher lipid meal (2.5 vs 5g). The duration of the biodistribution interval was carefully recorded. After stress MPI acquisition, the sum of coronal slices was obtained and ROIs were drawn in the liver, muscle and subcutaneous adipose tissue. Hepatobiliary activity was corrected for muscle and subcutaneous adipose tissue uptake. **Results:** Of the 64 stress MPI studies analyzed, 47 ingested a higher lipid content meal and 17 a lower lipid meal. No statistically significant differences (Mann-Whitney U, $p > 0.05$) was found between the biodistribution time of the two different diet groups. Also, no statistically significant difference was found between the normalized hepatobiliary uptake in both groups (Mann-Whitney U, $p > 0.05$). Finally, a strong negative correlation between biodistribution time and normalized hepatobiliary uptake was found. **Conclusion:** In our small sample, the meal's lipid content did not seem to significantly affect hepatic clearance, contrary to the

biodistribution time, which was strongly correlated. Therefore, we argue, that patient with high hepatobiliary uptake, which impairs image processing and interpretation, may benefit from late image acquisition.

E-TPW47

The Effect Of Consistency Of Ingested Food On Intestinal Activity In Tc 99m-MIBI Myocardial Perfusion

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Introduction: Myocardial perfusion imaging is diagnostic method in the nuclear medicine. We quantitatively demonstrated the effect of the consistency of ingested food on intestinal activity in myocardial perfusion imaging at rest and during exercise.

Methods: We used descriptive method with review domestic and foreign literature and quantitative method. In the study we included the patients, which were made myocardial perfusion imaging in the stress or in the rest. When we analyzed scintigrams, we set up 3 regions of interest on the scintigram, on the inferior wall of the myocardium of left ventricle, on the intestines and on the liver. Then we calculated ratio between activity on the inferior wall of the myocardium of left ventricle and activity on the intestines. For each group of the patients we calculated the average and standard deviation. **Results:** With the patients, who consumed only liquid food before acquisition, was calculated a ratio between activity on the inferior wall of the myocardium of left ventricle and activity on the intestines for stress $1,30 \pm 0,24$ and for rest $1,13 \pm 0,23$. With the patients, who consumed liquid and solid food before acquisition, was calculated the ratio for stress $1,90 \pm 0,25$ and for rest $1,64 \pm 0,33$. **Discussion and Conclusion:** The ratios were higher with the patients, who consumed liquid and solid food before acquisition. With the patients, who made myocardial perfusion imaging in the stress, are ratios higher than the patients, who made exam in the rest. Eating solid food effectively contribute to the mobilization activities from the liver and intestines. Patients should consume liquid and solid food before acquisition and thereby reducing the occurrence of intestinal artefacts on scintigrams.

E-TPW48

Interobserver reproducibility for the quantification of global systolic left ventricular function with Equilibrium Radionuclide Angiography

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Aim: In breast cancer, the most common female malignancy in the world, the introduction of any effective drug has a major impact in clinical practice. Trastuzumab, a tumor growth inhibiting therapeutic, has significantly improved the survival of women with HER2-positive tumors. However, like any drug, side effects can compromise the quality of life and limit the use of the drug.

The cardiac effects of trastuzumab, which differ from the permanent myocyte loss associated with anthracyclines, give a special relevance to the Left Ventricular Ejection Fraction (LVEF) surveillance. The aim of this study was to evaluate the interoperator variability of the LVEF, obtained with Equilibrium Radionuclide Angiography (ERNA) in a multiprofessional setting. **Materials and Methods:** ERNA of 41 breast cancer women, aged 35 to 80 years, undergoing Trastuzumab therapy quarterly during the first year, were processed with the semi-automatic method. Each patient was submitted to four ERNA ($RNA_{baseline}$, RNA_1 , RNA_2 and RNA_3) and each one of the 164 ERNA were processed, with a semiautomatic method, by four different operators: one experienced Nuclear Medicine Physician (NMP), one experienced Nuclear Medicine Technologist (NMT) and two inexperienced Nuclear Medicine Students (NMSa and NMSb). The LVEF results obtained by each operator were analyzed and compared. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS 24.0). **Results:** Regarding to $RNA_{baseline}$, homogeneity, correlation and concordance were verified in LVEF values obtained by the four operators (t-Student, $p > 0.05$), ($r = 0.9-1$) and ($CCC \geq 0.9$). In RNA_1 , the results between operators were homogeneous ($p > 0.05$), correlated ($r = 0.9-1$) and concordant ($CCC \geq 0.9$), with the exception observed in the pairs NMP/NMSb and NMT/NMSb ($p < 0.05$). In RNA_2 and RNA_3 , good values of homogeneity, correlation and concordance were obtained ($p > 0.05$), ($r = 0.9-1$) and ($CCC \geq 0.9$), respectively. There was a slight decrease in correlation and concordance comparing the LVEF values obtained by the NMP and the NMT with the NMSa and NMSb, in $RNA_{baseline}$, RNA_1 , RNA_2 and RNA_3 ; although it was not statistically significant. **Conclusions:** The semi-automatic processing method of ERNA can be considered a reliable and reproducible technique, because it's not entirely dependent of the qualified operator responsible for its processing. The minor professional experience of the operator has also proved to be a conditioning factor for the heterogeneity of the results obtained.

E-TPW49

Development method of extra-cardiac activity removal that influence on false negative image using artificial intelligence

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Aim: Cardiac nuclear medicine using ^{99m}Tc -radio-pharmaceuticals sometimes produces false negative images on the lower wall due to the influence of the cardiac accumulation and there was a possibility of misunderstanding of image findings. In past studies several methods have been developed to remove regions other than myocardium. However, when the distance between the myocardium and the cardiac accumulation was short, it could not cope well. Therefore, we report on the development

of the basic technology for eliminating the false negative image by removing the pixel size using artificial intelligence image detection technology. **Material and Methods:** We classified a trans-axial image include three areas by using the deep learning algorithm “Adam” in artificial intelligence. We classified them as pixel size level as myocardium, extra-cardiac and background. The algorithm of “Selective Search” was used as the program for that image classification. About 800 images containing only the myocardium and liver and gallbladder area of about 350 images and 1234 images only including the background were learned using these images as teaching-data. For verification, we used 900 images (include all area) apart from learning, and verified the detection rate of three areas for each image. **Results:** As for the detection of the heart part of this study, a learning result with a detection rate of about 80% was obtained when the number of learning was 100 or more. Regarding the detection accuracy of areas such as the liver and background, the results of the detection accuracy exceeding 80% were obtained by this study as in the case of the cardiac. However, there were a few cases in which some liver and other extra-cardiac were close distance were not successfully detected. **Conclusion:** In the examination of this time, generally good results were obtained. However, when myocardium and extra-cardiac are completely in contact with each other, it is difficult to remove it, and a method such as removal based on the myocardial shape model is necessary. Furthermore, by removing the extra-cardiac activity at the pixel level, it is possible to reconstruct an image in which there is no extra-cardiac activity, and in the future it is possible to create a tomographic image without artifacts.

E-TPW50

When clinical audit does not go to plan: Comparison of predictive post-operative FEV1 using SPECT/CT lung lobar quantification and post-operative measured FEV1 and impact on patient management

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Lung resection requires removal of an entire lobe, and at times a bilobectomy or pneumonectomy. Many patients also have severe emphysema, limiting extent of the surgery to avoid making the patient oxygen dependent. Pre-operative assessment includes predicted post-operative forced expiratory volume in 1 second (ppoFEV1), since ppoFEV1 <40% predicts significantly increased perioperative mortality. The ppoFEV1 can be estimated by multiplying the pre-operative FEV1 by the residual perfused territory percentage as predicted on planar perfusion scintigraphy (PPS). PpoFEV1 using PPS has shown variable correlation with the spirometry-measured post-operative FEV1. PPS can estimate the relative perfusion contribution of both whole lungs however, it cannot account for the obliquity of pulmonary fissures leading to underestimation of the ppoFEV. Quantitative SPECT/CT lung imaging allows assessment of pulmonary perfusion at the lobar or where possible segmental level. It also provides treatment planning images for surgical assessment. **Aim:** - Compare the ppoFEV1 predicted from SPECT/CT lung lobar quantitative imaging with the mea-

sured ppoFEV1; - Assess the impact of SPECT/CT lung lobar quantification on surgical planning and patient management. **Methodology:** SPECT/CT lung lobar quantitative imaging of 29 patients (scans performed between June 2016 and October 2017) was retrospectively analysed. Using Hermes Medical Solutions HYBRID 3D® the perfusion contributions of each lobe were calculated. Measured ppoFEV1 results and follow up data were obtained from patient records. Feedback was sought from consultants on the value of SPECT/CT imaging compared to the previous PPS service. **Results:** Only 1 patient underwent a measured ppoFEV1 test making it impossible to perform any correlation between predicted and measured ppoFEV1. 6 patients underwent lung reduction surgery, 6 patients were found to be unsuitable for surgery and 1 patient refused surgery. 10 patients are still being monitored with a view to possible future surgery. The remaining 6 underwent non-surgical interventions. Preliminary feedback from consultants showed that SPECT/CT lung lobar quantification does influence patient management. **Conclusion:** Clinical audit is used to assess quality of service provision and is an important part of service development. This well planned audit was designed to assess the move from PPS to SPECT/CT lung quantification. Unfortunately the parameters identified and agreed for audit were not routinely recorded post-surgery. The rate of surgical intervention anticipated was also not reflected in patient numbers. Preliminary feedback obtained from Respiratory Medicine consultants confirmed the value of this scan and how it improves the patient management although it was not possible to establish any quantitative correlation.

E-TPW51

Useful parameter using only MAG3 Instead of using combined MAG3 and DMSA renal studies in the investigation of urinary tract infection in children

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Introduction: Urinary tract infection (UTI) in children is a common cause of morbidity and hospitalization. Nuclear medicine renal study using (99mTc -MAG3) and (99mTc-DMSA) have become an integral part of the investigations of a child with UTI. The Renal study using the tubular agents Tc-MAG3 document morphologic and functional changes, while DMSA demonstrates morphologic changes and gives accurate differential renal function. Both MAG3 and DMSA studies document changes that are characteristic for acute UTI and the long term complications of UTI in children. Sometimes both MAG3 and DMSA studies are performed in the investigation of UTI assuming that the studies are complementary in evaluating morphologic and functional changes associated with UTI. In performing both studies, the child receives combined radiation doses from the MAG3 and DMSA. There is also inconvenience of long hospital stay for the 3 hours between injection and DMSA imaging. The purpose of this study was to test the hypothesis that the early (1-3min) images of renal shows similar finding to the DMSA study in children with UTI and thus combined studies may not be necessary. **Material and Method:** Between 2016

and 2017, 300 children were referred to the nuclear medicine department Fujairah hospital for the investigation of UTI. Both renal ^{99m}Tc -MAG3 and ^{99m}Tc -DMSA were performed with a mean age of 60 months (Range 2 to 144 months) **Results:** Our study showed that the composite picture of 1-3min image of ^{99m}Tc -MAG3 gives similar information as the ^{99m}Tc -DMSA in 75% of cases. **Conclusion:** A single tubular tracers such as ^{99m}Tc -MAG3 study could replace the dual approach of ^{99m}Tc -MAG3 plus ^{99m}Tc -DMSA.

E-TPW52

Diuretic decision seven minutes post ^{99m}Tc -MAG3 administration in a renography

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Aim: The F+10 method in supine position, which has been implemented at our Nuclear Medicine department since 2015, involves a 30- minute long dynamic acquisition. The diuretic is only administered when necessary and decision is taken by the radiographers in a semi-automated fashion without consulting a physician, by calculating the remaining activity in the kidneys seven minutes post ^{99m}Tc -MAG3 injection and comparing the value with an arbitrary threshold of 75 %. If needed, the diuretic is injected three minutes later. The aim of this study was to correlate our method with the established previously used F+20 protocol in adults. Is the currently used threshold of 75% of activity left in any kidney at seven minutes the optimal cut-off value for diuretic administration? **Material and Methods:** This is an ongoing retrospective study which include 320 F+20 examinations of adult patients performed during 2013-2015. They were all re-evaluated according to the currently used F+10 method, categorized as requiring diuretic or not and correlated to the original F+20 examination. A ROC-curve was drawn to delineate the best cut-off value for remaining renal activity. Sensitivity, specificity and accuracy were calculated. **Results:** preliminary results indicate that the F+10 re-evaluations with the currently used cut-off value of 75% did not correlate with the original F+20 examinations. In 80% (255 examinations) of the F+10 re-evaluations diuretic would have been considered necessary while only 52% (167 examinations) received diuretics in the original F+20 renographies (sensitivity 1.0, specificity 0.42). However, all the patients who required furosemide in the original F+20 renographies would have received diuretic if they had been imaged with the F+10 protocol. Furthermore, examination time is considerably reduced. After an evaluation of the ROC-curve the optimal cut-off value was 94% (sensitivity 0.92, specificity 0.84, accuracy 0.88). However, by implementing this value, 13 patients (4%) would have been falsely categorized as not requiring diuretic. **Conclusions:** The ^{99m}Tc -MAG3 renography with the F+10 protocol in supine position is a feasible and acceptable method in clinical practice.

E-TPW53

Incidence of asymptomatic nephroptosis detected by ^{99m}Tc -MAG3 renogram

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Purpose/Introduction: Nephroptosis is a condition in which the kidney descends more than two vertebral bodies ($>5\text{cm}$) during a position change from supine to upright. The kidney might move into an abnormal position but is capable of moving back into a normal anatomical site. The aim of this study was to evaluate the incidence of asymptomatic nephroptosis by renal scintigraphy with ^{99m}Tc -MAG₃. **Subjects & Methods:** Twenty-five adult and cooperative patients (18y-79y; median age: $50\text{y} \pm 18\text{y}$; 17 women, 8 men) referred to our department for a ^{99m}Tc -MAG₃ renography, gave their consent to make one-minute additional upright static image (Up-image) obtained after the standard supine one-minute post-micturition image (Supine-image). Those two images were performed after a small radioactive hot-source were fixed on the skin of the patient, at right iliac-crest level. In both, Up-image and Supine-image, the distance between the source and the lower pole of right and left kidneys we carefully measured, and the movement of the kidneys were calculated. The patients were divided in three groups: G1-kidneys descends $<3\text{cm}$; G2-kidneys descends between 3-5cm; G3-kidneys descends $>5\text{cm}$. All relevant data was recorded, including the gender, age, clinical indication for ^{99m}Tc -MAG₃-scintigraphy, height and weight and number of children. **Results:** All 25 patients underwent ^{99m}Tc -MAG₃ scintigraphy to evaluate renal obstruction. In G1 we found 8 patients (2 men, 6 women; median age: $43 \pm 20\text{y}$; median weight: $64 \pm 15\text{kg}$; median height: $160 \pm 5\text{cm}$). From 6 women included in this group, 5 had 1-4 children. In G2 we found 10 patients (3 men, 7 women; median age $56.2 \pm 18\text{y}$; median weight: $66.2 \pm 7\text{kg}$; median height: $161 \pm 9\text{cm}$). Five women had 1-6 children. G3 includes 7 patients (2 men, 5 women; median age: $50 \pm 17\text{y}$; median weight: $63 \pm 12\text{kg}$; median height: $162 \pm 7\text{cm}$). Bilateral nephroptosis ($>5\text{cm}$) was found in 8% of the patients (one man and one women) and 20% had unilateral left nephroptosis (two men and three women). We found no relation between nephroptosis and gender, weight, height and number of births/woman. However, patients in G1 were younger than in the G2 and G3 patients. **Discussion/Conclusion** In our small sample, a significant number of patients, 28%, had asymptomatic and unexpected nephroptosis. That condition cannot be predicted by variables like gender, number of birth per women and neither by the weight and height. Only age seems to have some influence in the incidence of nephroptosis. However, due to the small sample size more studies are warranted.

E-TPW54

Gravity versus Bladder Emptying: which is the mightier?

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Purpose/Introduction: ^{99m}Tc-MAG₃ scintigraphy is widely used to evaluate urinary tract obstruction. In well hydrated patients, it's assumed that drainage from the renal pelvis can be physiologically promoted by gravity and by an empty bladder. Both justify the acquisition of post-micturition images, after the standard dynamic renogram. However, for several reasons for some patients, an adequate micturition is not possible. The aim of this study was to evaluate which, **gravity** or the **emptying bladder**, have more impact in the drainage. **Subjects & Methods:** Forty-one adult and cooperative patients (18–76y; median age: 50±16y; 29 women, 12 men), referred to our department for a ^{99m}Tc-MAG₃ renography, gave their consent to make one-minute additional supine static image, obtained after the standard one-minute post-renogram static image (bladder-image). That additional image, the gravity-assisted drainage (GAD-image), starts just after a short period of patient's upright position and before the standard post-micturition image (PM-image). The time gap between images were controlled and appointed and regions of interest (ROIS) were drawn in both kidneys, in the three static images: bladder-image, GAD-image and PM-image. The counts obtained in each ROI were collected and the difference between the total counts of GAD-image and bladder-image and between the total counts of PM-image and GAD-image were calculated and then divide by the respective time-gap, obtaining respectively the slope-G1 and the slope-G2. Descriptive and inferential statistics were applied (IBM-SPSS software, version-25). Significant differences were considered for p-value<0.05 (Wilcoxon test). **Results:** All 41 patients underwent ^{99m}Tc-MAG₃ scintigraphy to evaluate renal obstruction. Six patients were excluded because there was no reduction in counts, between the three static images. Between bladder and GAD-image, patients assumed an upright posture during 4.2±1.7 minutes and need more 5.3±1.4 minutes to go to the bathroom (time between GAD-image and PM-image). A statistical significant difference was founded, for both kidneys, between slope-G1 (-34.2±66.2cont/seg for right kidney and -21.9±31.7cont/seg for left kidney) and slope-G2 (-9.3±10.4cont/seg for right kidney and -8.0±14.0cont/seg for left kidney): Wilcoxon test, p<0.001 for right and left kidneys. **Discussion/Conclusion:** Frequently, in our daily routine, we come across patients who have urinary disorders that compromise an adequate bladder emptying. Our results suggest that, for the same time period, gravity is enough, and the bladder emptying have no significant additional impact as demonstrated by the slope reduction after voiding.

E-TPW55

Bone Scintigraphy usefulness for the diagnosis of Osteoporosis

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Introduction: Osteoporosis is a chronic disease that affects 80% of the population upward 60 years old. It is a metabolic disease with predominant osteoclastic activity, causing a progressive bone density decrease, which raises the risk of fracture. The aim of this study is to evaluate the usefulness of bone scintigraphy on the diagnosis of osteoporosis **Methods:** A retrospective study was performed with 49 patients who were referred for clinical reasons for bone scintigraphy (^{99m}Tc-HMDP) and bone densitometry within, at most, one year. All bone scintigraphy studies were carried out using a double detector gamma camera (GE® INFINIA™ II) equipped with low energy high resolution collimators; energy window 140 keV +/- 10% and an image matrix of 1024 x 256. Bone scintigraphy studies were processed with Xeleris™ III. Bone densitometry studies were acquired with a HOLOGIC® equipment and images were processed with QDR™ software. Regions of interest (ROI's) at L1-L4 vertebral group and the femoral neck were defined, representing trabecular and cortical bone tissue, respectively. The femoral bone middle third was selected as a control region. The mean counts per ROI were obtained. ROI ratios were calculated (ROI/control area) and the results were compared with Bone Mineral Density values of the bone densitometry for the respective regions. Since this study is ongoing, preliminary results are presented. 16 patients were evaluated forming a total of 27 ROI's (13 of lumbar spine and 14 of femoral neck). To evaluate the association between the variables bone scintigraphy counts number and bone densitometry BMD values, the Spearman correlation test was used. **Results:** A weak correlation between the variables was found. Particularly for the lumbar spine area, a **Spearman** correlation factor of 0.2 was found, suggesting a non-correlation; at the femoral neck, a **Spearman** correlation factor of 0.5 was obtained, indicating a good correlation between femoral neck BMD and radiopharmaceutical uptake at the same area. **Conclusion:** Despite preliminary results suggest lumbar spine quantification in bone scintigraphy to have no correlation with bone density decrease, femoral neck quantification might predict BMD values and could be used for referral bone densitometry. Nevertheless, further investigation on this field proved to be necessary.

E-TPW56

Quantification: A New Standard In Diagnosing Unilateral Condylar Hyperplasia (UCH)?

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Aim: Unilateral condylar hyperactivity is the most common benign disorder of the postnatal growth of the temporo-mandibular joint. UCH is presented by an unilateral, progressive asymmetry of the mandibula and secundaire of the maxilla. Until 2010 patients underwent a condylectomy based upon anamneses, CBCT, facial photos and x-rays. With the extracted tissue examined at the pathology department it showed that a major part of patients did not have a UCH at all. There was a need for more objective surgery criteria. This abstract describes the process of quantification in diagnosing UCH. **Method and Materials:** 50 percent of all the patients the maxillofacial surgeon sees in practice suspected for UCH are indicated for a

condylectomy. These patients are referred to the department of nuclear medicine and undergo a 3-phase skeletal scintigram and SPECT/CT of the skull and mandibular joints. The radiotracer that is used is Tc99m-Osteocis. 2,5 hours after injection the images made in the dynamic phases are repeated. In addition a SPECT/CT is done. The dynamic and planar images are processed and stored for visual interpretation. SPECT/CT fusion images will be evaluated to exclude tumors, arthritis and other differential diagnoses. To calculate the semi-quantitative results, the non-AC dataset frames showing the condyles, will be composed to one frame. Two similar ROI's are drawn in the condyles in the transverse composed image. The percental difference in activity between the left and right condyle is calculated using the following formula: $([\text{countsR}] / [\text{countsR} + \text{countsL}]) * 100\% = \%R$. Count rates that are used are the 'mean count', the 'max count' and the 'average count' value. A condylectomic surgery is indicated based on a significant $\geq 10\%$ left/right difference in activity. Patients with non-significant results $>6\%$ and $<10\%$ will be followed in clinical practice and if showing signs of further progression, still get an indication for surgery. **Results:** 95% of the referred patients show a difference in condylar growth activity. In general half of the patients (49% in years 2012-2017) show a significant difference in growth activity. Now only these patients will be offered an condylectomic surgery. **Conclusion:** Using Quantification for diagnosing UCH reduces the number of patients who are unnecessarily operated on. Therefore we know that semi-quantification is an important value in reducing the amount of unnecessary condylectomies.

E-TPW57

The Role of Three-Phase Bone Scintigraphy in Management of a Patient with Extraordinary Bone Metastases

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Introduction: Three-phase bone scintigraphy is sometimes of great value in the detection of uncharacteristic metastases and assists the management of patients in terms of primary focus detection. While evaluating the skeletal system with whole-body bone scintigraphy, other system pathologies may also be detected incidentally. In this case, we present the extraordinary findings on the three-phase bone scintigraphy imaging of the complicated bone metastases in a patient with thyroid carcinoma. **Case Report:** A 69 year-old female patient without a previously known disease, who had a complaint of back pain for a year and a fracture of the L3 vertebrae on X-ray, admitted to our department. We performed three-phase bone scintigraphy, on which an increased activity was observed in the left pelvic region in the dynamic blood flow and the blood-pool phases of the study. Late images revealed an increased radioactivity uptake in the left sacroiliac joint area and an hypoactive region with a periferic relatively increased activity. A similar appearance was also observed in the sternum. Moreover, there were increased uptake of radioactivity in the cranial bones, L3 vertebrae and pelvic bones. MRI showed pathologic fracture of L3 verte-

brae and a mass lesion (95 mm) with a heterogeneous contrast enhancement, which extends into the sacral joint space and left iliac crest, and a pathologic fracture of the left superior pubic ramus. The presence of the mass and hypoactive lesions on bone scintigraphy suggested that the bone metastases were originated from a thyroid or a renal malignancy. FDG PET/CT, which was performed to investigate the primary focus of the metastases, revealed a mass located in the left thyroid lobe (SUVmax: 10.3), an irregular bordered mass in the right lung, with a maximum diameter of 17 mm and SUVmax: 4.4. The FNAB of thyroid nodule was reported as malign cytology and the true-cut biopsy of the mass in the left iliac crest, as metastasis of thyroid carcinoma. **Conclusion:** The lytic metastases may be overlooked on the late phase of the bone scintigraphy. The blood flow and blood-pool phases of three-phase bone scan may be needed to evaluate the vascularity of the primary tumor or metastases and to demonstrate the lytic metastases may be missed on the late phase bone scan. Early phases of bone scan may also be a guide for the prediction of origin of the metastases, on accounts of osteoblastic or osteoclastic dominance of the lesion.

E-TPW58

Importance of lymphoscintigraphy to find sentinel ganglion in the context of malignant neoplasm of breast: case reports

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Aim: To assess the importance of the sentinel ganglion (GS) detection technique by lymphoscintigraphy in order to avoid lymphedema of the upper limbs in malignant neoplasms of the breast. The sentinel ganglion is the first ganglion of the lymphatic chain to drain the lymph from the primary tumor. The lymphoscintigraphy allows to identify this ganglion, to facilitate its removal by the surgeon and to be analyzed by the pathological anatomy through an extemporaneous analysis in order to avoid axillary emptying in case of negative analysis for metastases. **Materials and Methods:** All lymphoscintigraphy were performed with the BrighView Philips model camera. All of these studies followed the same protocol according to the EANM guidelines. An anamnesis of the patient was carried out, the explanation of the procedure and the positioning of the patient according to the protocol in force. A dynamic study was performed immediately after administration of the radiopharmaceutical and then static, anterior, oblique and lateral images. After processing the acquired images and marking GS on the skin with the aid of the Europrobe3, clinical reports were performed. For the analysis of the data, we selected female patients with breast neoplasia, who underwent the examination between June 23, 2017 and March 22, 2018, aged between 33-88 years. **Results:** Through the evaluation of the sample of 56 users we can verify that this technique allowed to avoid axillary emptying in 39 patients. Of the 56 patients, 2 had bilateral breast neoplasia, 33 right breast neoplasm and 21 left breast cancer. Of the 2 patients with bilateral malignant neoplasia, one presented both negative ganglia and the other presented negative right GS and positive left GS and consequent axillary emptying. Of the 33 patients with neo-

plasia of the right breast 8, they emptied, and of the 21 patients with left breast neoplasia, 9 performed emptying. **Conclusion:** According to the data obtained in Nuclear Medicine study, it was verified that lymphoscintigraphy allowed to avoid axillary emptying in 39 patients, which corresponds to 70% of the sample. It is confirmed that this diagnostic technique is an asset in the preservation of the lymphatic chain. The availability of this technique in a hospital regimen for the detection of sentinel ganglion is considered important to avoid the limitations associated with axillary emptying and consequent improvement in the quality of life of these patients.

E-TPW59

Can [^{123}I] FP-CIT SPECT using the Japanese normal database improve diagnostic accuracy of Parkinson's disease?

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Purpose: I-123-ioflupane single photon emission computed tomography (FP-CIT-SPECT) has been used to assess dopamine transporter (DAT) loss in Parkinson's disease. The specific binding ratio (SBR), quantitative parameter of DAT density in striatum, may be affected by the difference of age, sex, SPECT system. This purpose of this study was to evaluate the utility of FP-CIT-SPECT using the Japanese normal database (NDB) in the diagnosis of Parkinson's disease. **Materials and Methods:** To standardize quantitative outcome measures of DAT density obtained with different SPECT systems, striatal phantom filled with striatal to background ratios between 8:1 to 1:1 were measured using a gamma camera (ECAM) in our institute. Totally 50 patients with Parkinson's syndrome (PS), 28 with Parkinson's disease (PD) and 22 without PD (N-PD), were blindly chosen (23 men and 27 women; age range, 40–86 years). SBRs of the patients were calculated using either new (Japanese database with different age and sex; NEWver) or old (non-Japanese database regardless of age and sex; OLDver) version software (AZE Virtual Place Hayabusa [DaT-View], AZE, Ltd. Tokyo, Japan). To test the diagnostic accuracy between old and new versions, McNemar test was used. **Results:** Based on this phantom study, calibrated SBR was calculated by the formula: $Y = 1.25 \times \text{Measured SBR} + 0.78$. The sensitivity for OLDver and NEWver were 100% and 93%, respectively ($p=0.5$), and the specificity were 55% and 100% ($p=0.002$). The diagnostic accuracy of NEWver (96%) was better than OLDver (80%, $p<0.001$). **Conclusion:** FP-CIT-SPECT using Japanese NDB improved the diagnostic accuracy of PD by decreasing false positive finding.

E-TPW60

^{123}I MIBG SPECT to evaluate patients with Parkinson's disease

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Introduction: Since ^{123}I -meta-iodobenzylguanidine (MIBG) is a sympathomimetic, it is taken up by the norepinephrine transporter, stored in vesicles at postganglionic sympathetic nerve terminals, and released into the synapse by nerve stimuli. Whereas norepinephrine is degraded after release by monoamine oxidase or catechol-O-methyltransferase, MIBG is unaffected, allowing visualization of the function of sympathetic nerves noninvasively. The degree of MIBG uptake reflects whether the postganglionic sympathetic nerve is damaged. Several studies using this technique showed that ^{123}I -MIBG is useful for differentiating PD from atypical parkinsonism, especially multiple system atrophy (MSA). In this study, we compared the results of cardiac-MIBG imaging in patients to demonstrate its usefulness in differentiating Parkinson's disease (PD) from atypical parkinsonism. **Subjects and Methods:** ^{123}I -MIBG (111 mBq) was injected intravenously into each subject. Three hours later, the image of cardiac uptake was taken using a dual-head γ -camera SPECT. The region of interest consisted of the entire heart and mediastinum in the frontal image. The ratio of ^{123}I -MIBG uptake in the heart to that in the mediastinum (H/M ratio) was calculated.

Results: MIBG is not metabolized by catechol-O-methyltransferase or monoamine oxidase. Two uptake systems for MIBG have been identified in adrenergic tissues. The first system involves diffusion in non-neuronal and neuronal tissues. Scanning during the first 15 min postinjection mainly reflects the greater influx of MIBG into the extraneuronal space in myocardial tissue, rather than into the neuronal component. The second system is uptake by neuronal tissue using the sodium and ATP-dependent transporter at low concentrations. The neuronal accumulation of MIBG reaches its maximum at 3–4 h after injection, so a delayed MIBG scan reflects the neuronal uptake of MIBG more specifically. Therefore, myocardial MIBG uptake was assessed 15 min and 3–4 h postinjection. A decreased MIBG uptake suggests the loss or destruction of cardiac sympathetic nerve endings.

Discussion/Conclusion: This study demonstrates that cardiac-MIBG is a clinically powerful tool to differentiate PD from other parkinsonian syndromes.

E-TPW61

Dual-Time-Point PET/CT with 18F-FDG for Differentiation of Malignant and Benign Lesions

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Purpose/ Introduction: According to Chen *et al.*, (2016), dual-time-point (DTP) improves the specificity of PET using the change in maximum standardized uptake value (SUV_{max}) between early and delayed scans to help differentiate benign and malignant solitary pulmonary nodule, improving accuracy in classifying several lesions. The purpose of the present study is to evaluate the clinical value of 18F-fluoro-2-deoxyglucose (^{18}F -FDG) to differentiate malignant from benign lesions; it was also important to compare the diagnostic power of single and DTP when interpreting a clinical positron emission tomography /computed tomography (PET/CT). **Subjects and Methods:** The subjects were 247 lesions (primary and metastatic lymph nodes)

in 155 patients associated with several pathologies. 18F-FDG PET-CT scan was performed at 60 minutes (early scan) and at 90 minutes (delayed scan) post-administration. The evaluation was based in SUV_{max} , average SUV (SUV_{avg}) between the early and delayed images and retention index (RI). Furthermore, cut-off values were evaluated using receiver operating characteristic analysis (ROC curve) and the areas under the curve (AUC) for each parameter. A RI of 10% or higher was chosen as a cut-off for differentiating malignant from benign entities. **Results:** The 155 patients with an average age of 59.91 years presented higher SUV_{max} and SUV_{avg} in the delayed scan compared with the early images. A $SUV_{max}=8.62$ and $SUV_{avg}=5.03$ were obtained in the early images and $SUV_{max}=9.58$ and $SUV_{avg}=5.65$ in the delayed images ($p=0.023$ and $p=0.027$ for SUV_{max} e SUV_{avg} , respectively). A comparison between benign and malignant lesions reveal that the last has a higher SUV_{max} and SUV_{avg} in the early images (10.16 and 6.46, respectively) than benign lesions ($SUV_{max}=6.11$; $SUV_{avg}=3.66$). Benign lesions increase both of the values in the delayed images ($SUV_{max}=6.76$ and $SUV_{avg}=4.04$) and decrease in malignant lesions ($SUV_{max}=9.56$ and $SUV_{avg}=6.02$). The RI is 15.30% reveals that lesions retain 15.30% of the radiopharmaceutical until 90 minutes post administration. The AUC varies between 0.607 and 0.611 meaning that a complete separation between them is poor. The sensitivity, specificity, positive and negative predictive values were calculated and it was obtained 97.74%, 70.59%, 78.26% and 92.31%, respectively. **Discussion/Conclusion:** The data show that DTP 18F-FDG PET-CT is useful to distinguish between malignant and benign processes in lesions. It is important to determine the therapeutic approach, especially in the follow-up of oncological patients considering that some therapies can induce inflammation, leading to high glucose consumption; in these cases, the comparison between images at different times is definitely worth.

E-TPW62

Weekly low dose FDG PET/CT during chemoradiotherapy for NSCLC

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Aim: Tumour response monitoring over the course of concurrent chemoradiotherapy (CCRT) with serial ¹⁸F-fluorodeoxyglucose (FDG) PET/CT has the potential to dynamically adapt radiotherapy to biological parameters. However, frequent FDG PET/CT scanning is demanding for patients, personnel and data evaluation. The aim of this study was to evaluate the logistics, safety, patient burden, image quality and data consistency of weekly low dose FDG PET/CT during CCRT.

Materials and Methods: Stage II-III Non-Small Cell Lung Cancer (NSCLC) patients scheduled for CCRT, consisting of radiotherapy (66 Gy in 24 fractions) combined with daily low dose cisplatin, were eligible for inclusion. Five weekly PET/CT scans (Philips Gemini Big Bore ToF) of the tumour and regional lymph nodes were made over the course of treatment and at 3 months af-

ter CCRT. Each in treatment position, with 50 MBq FDG, 2 bed positions and a total acquisition time of 14 minutes. Procedure logistics were evaluated in all involved departments, radiation exposure was assessed for patients and for staff, image quality was evaluated visually, and the changes over time of various PET parameters were determined. **Results:** Thirty-eight patients were included, of which 28 completed the treatment and all imaging. Reasons for drop-out included changed treatment (1), withdrawn informed consent (2), progressive disease on serial PET (2), availability of FDG (2), scanner malfunction (1), and patients indicating high burden (2). Two patients with complete imaging are shown in figure 1. Planning logistics of 6 PET/CT scans linked to CCRT required close collaboration and dedicated imaging time slots. Patients typically spent 1.5 hours longer in hospital on days of PET/CT scans. The radiation exposure of patients was about 20 mSv for the six scans in total, and involved staff received < 1 μSv per complete treatment. The image quality of low dose FDG PET at baseline and during treatment was visually identical to routine diagnostic procedures, with similar spatial resolution and signal-to-noise levels. PET parameters all showed differences in timing and extent of their response over time. **Conclusion:** Weekly PET/CT with low dose FDG is promising for tumour response monitoring during CCRT, with good image quality and with acceptable radiation dose and costs. However, multidisciplinary protocol development is essential to derive safe and efficient workflows with acceptable patient burden. The selection of optimal PET parameters and time points to derive clinical decisions will require additional scientific research.

E-TPW63

Standardised Uptake Value & Hounsfield Unit in lumbar spine & head of the femur for Alkaptonuria measured from 18F-NaF PET/CT bone scan

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Alkaptonuria is a genetioarthritic disorder caused by a deficiency of homogentisate 1-2 dioxygenase (HGD) enzyme leading to increasing homogentisic acid (HGA). Over time HGA deposits in connective tissue forming cartilage pigmentation and arthritis specifically in the spine and large joints called ochronosis. The role of positron emission tomography combined with computed tomography PET/CT in management and evaluation of bone disorder is increasing. The primary aim of this study is to assess bone involvement in lumbar spine and hip region for AKU patient by measuring Hounsfield units (HU) from CT and standardised uptake value (SUVmax) from PET. The secondary aim was to determine if SUVmax and HU obtained from PET/CT correlate with each other and with age and bone mineral density.

Methods: A total of 25 AKU patients who involved in the SONIA2 trial and underwent the whole body 18F-NaF-PET/CT and DEXA

scans were enrolled in our study. The patients were grouped into four groups stratified by decade of life. A HERMES software was used to measure an average HU from CT image and SUVmax from PET image for lumbar vertebrae L1-L5 and head of the femur. For each measurement, the largest possible elliptical region covering the ROI was drawn, excluding the cortical margins to avoid volume averaging. The quantitative values were compared between age groups, and correlation of SUVmax value with HU and bone mineral density were determined. **Results:** In our study, the mean SUVmax values were not changed significantly between the groups of age. The range of lumbar vertebrae SUVmax was between 1.5 to 15. There was no correlation coefficient of SUVmax with age, HU and bone mineral density (low r , $p > 0.05$). HU values showed no correlation with increasing age in most of the lumbar vertebral bodies and head of the femur except in L4 which showed a decreasing tendency with increasing age ($r = 0.68$ and $p < 0.005$). There was a significant correlation coefficient of HU and bone mineral density in lumbar and femur region (low r , $p < 0.05$). **Conclusion:** SUVmax and HU values are not correlated with age for AKU patients. SUV can be used as a quantitative method to quantify bone PET/CT studies. HU values from PET/CT can be useful in measuring bone mineral density based on the strong correlation between HU and bone density. The current study supports further finding investigating quantitative radiographic methods using ^{18}F -NaF PET/CT which convey bone metabolism and structural information.

E-TPW64

Orbital Uptake findings in ^{68}Ga -DOTA-TATE PET/CT - retrospective study

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Introduction: Neuroendocrine Tumours (NET) is heterogeneous group of tumours that have a diverse presentation and incidence is increasing. The well differentiated NETs may be present for a long time without producing significant clinical symptoms. Subsequently, they are diagnosed later, usually expressing several metastases at this time. The common sites of metastatic disease include liver, skeletal and lymph node metastases. Orbital metastases are rare. Although the incidence is quite low, orbital NET metastasis can result in morbidity causing diplopia and proptosis. ^{68}Ga -DOTA-TATE PET/CT scans are sensitive for the detection of orbital metastases. **Aim:** To evaluate the incidence and characteristics of patients with orbital metastases in NETs. **Materials/Methods:** A database of ^{68}Ga -DOTA-TATE PET/CT studies done in the Nuclear Medicine Department of the Royal Free Hospital, NHS Foundation Trust (London, UK) from 2010 to 2018 was created. A search was done over the 1100 reports present in the database for the term "orbit" or "orbital". Seventeen cases (1.5%) matched the search criteria (age average of 68 years - 9 male and 8 female patients). A second database for better characterization of these 17 cases was created (e.g. with the patient gender, primary tumour localization, laterality of orbital uptake, soft vs bone uptake, other metastasis sites). A statistical analysis was done to verify any correlation between the orbital lesions and any other of the other variables.

Results: From the 17 cases selected, the primary site of disease was midgut in 54%, pancreatic in 31% and pulmonary in 15%. Regarding soft vs bone uptake, 77% of the orbital uptake was in the soft tissue with equal ratio of left and right sided metastases. When evaluating patient characteristics, the distribution of metastatic disease was as follows: liver (53%), lymph nodes (41%) and skeletal (35%). **Conclusion:** Orbital metastases are an uncommon site of metastatic disease found in 1.5% of our patients. From the 17 cases reviewed in our retrospective study, we can state that the majority of the patients with orbital uptake had the primary tumour site in the midgut. The majority of patients did not have extensive metastatic disease, with liver metastases found in 53% and skeletal metastases in 35%. The incidence of orbital metastases was equal for left and right orbit.

E-TPW65

^{18}F -Fluorodopa PETCT accurately identifies neuroendocrine malignancies

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Aim: To evaluate the diagnostic value of ^{18}F -Fluorodopa whole-body PET/CT in an initial cohort of patients with clinical suspicion on a neuroendocrine tumor (NET). **Patients and Methods:** A total of 90 patients who were referred for ^{18}F -Fluorodopa PET/CT from January 2015 to March 2018, were included in this retrospective study. All patients, except those evaluated for a pancreatic lesion, received carbidopa preadministration before injection of 200-350 MBq ^{18}F -Fluorodopa. A PET/CT scan was acquired from head to mid-thigh at 1 hour post injection (p.i.) of the tracer, using a Siemens Biograph 16 Truepoint PET/CT system. An additional early scan at 5 min p.i. and/or late scan at 2h p.i. was acquired, when indicated. Scan results were compared with histopathological follow-up, when available. **Results:** Of the 90 patients included in this study (60.3 ± 14.4 years [mean $\pm$ SD]), male:female 41 [45.6%]:49 [54.4%]), pathology reports were available at follow-up for 30 patients. Pathologic diagnosis confirmed the findings of the previously performed ^{18}F -Fluorodopa in 27 of these patients. NET (not otherwise specified) was detected in 25.9%, pheochromocytoma in 18.5%, carcinoid in 11.1%, and insulinoma in 7.4%. Another 37.0% of the patients were histopathologically diagnosed with either benign or non-neuroendocrine malignancies. ^{18}F -Fluorodopa PET/CT was unable to identify the tumour localisation in three patients; one due to the small size of the tumour (< 2 mm) and two due to an atypical character of the tumour. For two histopathologically confirmed pancreatic NETs, the early scan at 5 min p.i. showed intense ^{18}F -Fluorodopa uptake, which was less noticeable 1h p.i.. For one histopathologically confirmed intestinal carcinoid, the scan at 2h p.i. revealed ^{18}F -Fluorodopa uptake in a lesion, which was not detected at 1h p.i.. **Conclusion:** In 27/30 patients who were subjected to ^{18}F -Fluorodopa PET/CT and in whom histopathological follow-up was present, scan results were histopathologically confirmed. An additional PET/CT acquisition at either an early or late time-point should at least be considered for patients with suspected pancreatic NET or carcinoid of the digestive tract, respectively.

E-TPW66

Contribution Of Delayed Imaging Of The Abdomen And Pelvis On PET-CT Studies

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Objectives: Describe the importance of delayed images when focal uptakes are seen in the abdomen or pelvis in ^{18}F -FDG PET-CT studies. **Materials and Method:** All ^{18}F -FDG PET-CT studies performed in 2016 were retrospectively reviewed. They were all performed in a SIEMENS Biograph 6 camera, using the usual and recommended acquisition protocol (images from the base of the skull to the upper thighs; low dose CT with mAs modulated with CARE Dose4D; 130kV; 4mm slices; 3 min/bed position; 50-60min after the intravenous injection of 5MBq/Kg of ^{18}F -FDG), after 4-6 horas of fasting, adequate hydration, glucose control and removal of any metallic object. Images were acquired from the thighs to the head, to avoid urinary bladder artefacts. After initial scanning images were reviewed. If any focal metabolic uptake was seen in abdomen and/or pelvis, delayed images (90-150min after injection) were obtained, with 3 min/bed position scanning time. **Results:** During 2016 a total of 132 delayed images were performed. After analysis, the following results were obtained: In 48.5% of cases (64 studies) focal uptake remained and increased activity in the delayed images, therefore additional complementary studies were suggested to rule out pre- or malignant lesions. In 36.4% of cases (48 studies) malignancy was ruled out as the focal uptake disappeared, suggesting an initial physiologic uptake or due to elimination of the tracer. In 15.1% of cases (20 studies) the focal uptake remained but significantly decreased its activity, therefore considered as probably infectious or inflammatory. **Conclusion:** The acquisition of delayed images, when focal uptakes in abdomen or pelvis are seen in the initial scan, facilitates and improves their interpretation.

804-4 Monday, October 15, 2018, 11:30 - 13:00, Meeting Room 34

Technologists: Technologist e-Poster Walk 4

E-TPW67

Effects of Furosemide administration on the interpretability of ^{18}F -DCFPyL PET/CT

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Aim: Relatively high concentrations of ^{18}F -DCFPyL are excreted via the kidneys in the urine. This may cause interpretation difficulties due to activity in the ureters. Focal ureter activity may be falsely interpreted as lymph node metastasis and the occurrence of halo artefacts near the kidneys and bladder may obscure metastases at those locations. This study examines whether the administration of Furosemide and the timing of its administration affect the interpretability of ^{18}F -DCFPyL PET/CT. **Method:** Eighty patients that received ^{18}F -DCFPyL PET/CT

were retrospectively included in the study. 40 of these patients received Furosemide simultaneously with the administration of ^{18}F -DCFPyL and another 40 patients received Furosemide 85 min after ^{18}F -DCFPyL administration. PET/CT images were acquired 60 and 120 min p.i. The frequency of occurrence of activity depositions in the ureters and halo artefacts near the kidneys and bladder was determined, as well as intensity of ^{18}F -DCFPyL uptake in kidneys and bladder. **Results:** The acquisition at 60 min p.i. of ^{18}F -DCFPyL revealed no differences between both groups in occurrence of activity depositions in the ureters, occurrence of halo artefacts and uptake of ^{18}F -DCFPyL in the kidneys. A significantly lower concentration of ^{18}F -DCFPyL is found in the bladder in the cohort that received Furosemide at ^{18}F -DCFPyL administration. At 120 min p.i. of ^{18}F -DCFPyL a significantly lower number of ^{18}F -DCFPyL depositions in ureters was found, both focal and linear, when Furosemide was administered at 85 min p.i. of ^{18}F -DCFPyL. In this cohort the ^{18}F -DCFPyL uptake in kidneys and bladder is also significantly lower; however, the occurrence of halo artefacts is similar in both groups. **Conclusion:** Administration of Furosemide may improve the interpretability of ^{18}F -DCFPyL PET/CT by reducing activity depositions in ureters. However, the effect depends on the timing of the Furosemide administration in relation to administration of ^{18}F -DCFPyL and the acquisition time of the PET/CT images. When PET/CT images are acquired 120 min p.i., administration of Furosemide at 85 min p.i. shows a positive effect as compared to administration simultaneously with ^{18}F -DCFPyL. Further studies are needed to identify the best time point for Furosemide administration.

E-TPW68

Low-Radiation Heart Inflammation PET-CT Acquisition Protocol

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Synopsis: The primary objective of the study is to test the (CT) ionization dose reduction of an improved Heart-Inflammation PET-CT acquisition protocol. The primary goal is to reduce of 50% the dose of the patient. **Purpose:** Heart Sarcoidosis disease is an inflammation that can be well detected with FDG PET-CT acquisition. Imaging modalities that can both identify disease and predict response to therapy are paramount to improve management of cardiac sarcoidosis. ^{18}F -FDG PET has many practical advantages in assessing disease activity and monitoring treatment response in patients with cardiac sarcoidosis. Accumulating data support the growing role of ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET in the diagnosis and risk stratification of patients with cardiac sarcoidosis. The patient will come several time and dose monitoring is needed. **Methods:** The study was conducted on a GE MI PET-CT scanner. The protocol Acquisition was composed of two PET-CT acquisition. One acquisition over the heart, composed by a low dose-CT scan (detector coverage 40mm, helical thickness 3.75 mm, pitch e speed 0.516:1 20.62 mm/rot, rotation time 0.8 s, 120 KV, min 15 max 100 mA) and a 20 min gated PET acquisition and one PET-CT over the thorax, composed by a low dose-CT (detector coverage 40mm, helical thickness 3.75 mm, pitch e speed 0.984:1 39.37 mm/rot, rotation

time 0.8 s, 120 KV, min 15 max 100 mA) and a 2x2min PET static Frames. The new Protocol will be composed by Only one Low dose-CT scan (detector coverage 40mm, helical thickness 3.75 mm, pitch speed 0.984:1 39.37 mm/rot, rotation time 0.8 s, 120 KV, min 15 max 100 mA) over all the area of interest (with a small cardiac dedicated CT-retro recon) followed by the 20 min cardiac-gated PET acquisition and 2x2min PET static acquisition.

Results: As we changed the Acquisition Protocol we noticed a dose reduction of almost 50% of the DLP an adequate image quality. **Discussion:** As we noticed such a reduction, we did permanently change the acquisition protocol with the help of our application specialist. **Conclusion:** With this small change we have given a huge dose DLP reduction to those Patient that comes regularly to evaluate the response to the Heart-Inflammation sarcoidosis therapy with a PET-FDG Scan.

E-TPW69

Identification of Brown Adipose Tissue in adult men using Hounsfield Units

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Aim: The common method to visualize brown adipose tissue (BAT) is by ^{18}F -FDG PET/CT. Although ^{18}F -FDG PET/CT is sensitive to visualize activated BAT it has several limitations. It is expensive, the radiation dose is relatively high and it is labour-intensive. Therefore, there is a constant search for alternative methods which could localize BAT. In this study we investigate if we could differentiate activated BAT from white adipose tissue (WAT) based on Hounsfield units (HU) of a low dose CT scan in healthy subjects. Additionally we investigated the association of HU and the activity of BAT. **Methods:** Thirty five healthy men underwent an ^{18}F -FDG PET/CT scan after 2 hours rest in a mildly cooled room (17°C). Approximately 200 MBq of ^{18}F -FDG was administered intravenously after 1 h of cold exposure and PET/CT acquisition was performed 1 h after ^{18}F -FDG administration. ^{18}F -FDG PET/CT was made from the base of the skull to the groin. In each patient with active BAT 20 ROIs (when possible) were drawn. In the subcutaneous fat of the pelvic region 10 ROIs were drawn, as a reflection of WAT. In subjects without activated BAT on ^{18}F -FDG PET/CT 10 fixed ROIs (diameter 1cm) were placed in supraclavicular fat. When activated BAT was present on ^{18}F -FDG PET/CT the mean standard uptake value (SUV) was calculated. In all subjects the HU of both BAT and WAT was determined. **Results:** ^{18}F -FDG uptake in BAT was observed in 23 of 35 subjects. The mean HU of these activated BAT regions was significantly higher compared with the mean HU of WAT (respectively -64.4 ± 20.5 and -94.6 ± 12.1 , $p < 0.001$). In the 12 subjects without activated BAT the HU of the supraclavicular fat was significantly lower compared with the HU of those with activated BAT (respectively -102.3 ± 16.0 and -64.4 ± 20.5 , $P < 0.001$). In addition, in those subjects with activated BAT there was a positive correlation between HU and SUV ($R = 0.33$, $p = 0.0041$). **Conclusion:** Activated BAT has a higher HU compared to WAT. In addition, a higher SUV is positively correlated with HU. Therefore, low-dose CT might be an alternative method to detect activated BAT.

E-TPW70

Validity of the Temperature of the Skin in the Supraclavicular Area as an Indirect Marker of Adipose Brown Tissue in Young Adults

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Aim: The aim of the study is to analyse the possible relation between skin temperature in the clavicular area and the activity and quantity of Brown adipose tissue (BAT) in young healthy adults. **Material and Methods:** An overall of 88 participants (57 women) underwent a protocol of cooling down by means of a vest irrigated with water at controlled temperature until they reported shivering (i.e. shiver threshold). Between 48 and 72 hours later participants were exposed during 2 hours to a 4-5 Celsius degrees higher temperature over shivering threshold, right before PET/TAC implementation. One hour before PET/TAC 5mCi of FDG were injected. TAP was quantified through SUV threshold of 1.2% lean mass determined by dual X-ray absorptiometry and a range of radiodensity of -190/-10 Hounsfield Units. While cooling down all participants carried a iButteon (cutaneous thermometer) placed in the right supraclavicular fossa. This served to average the last 5 minutes of the thermoneutral period prior to cold exposure and the two hours of exposure to cold. **Results:** Supraclavicular temperature at the end of the thermoneutral and cold period was not found associated to TAP quantity (all $p \geq 0.05$). However, a positive and significant association between supraclavicular temperature both before and after cooling and the TAP average activity (average SUV $R^2 = 0.097$; $p = 0.007$) and maximum (SUV peak; $R^2 = 0.084$; $p = 0.006$). Moreover, when the analysis was adjusted by body composition (body mass index), the results remained without change. **Conclusions:** Supraclavicular Skin temperature seems to be an indirect indicator of BAT activity. Hence, it is possible to use it as a cheaper and non-invasive alternative to estimate the BAT activity in young healthy adults.

E-TPW71

Renal Function's Effect On Exposure Rate Of Patients Undergoing 18F FDG PET/CT

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Aim: The purpose of this research study is to clarify if renal function has an effect on the exposure rate between patients with adequate, moderately compromised, and severely compromised renal function who have undergone 18F FDG PET/CT imaging. **Methods:** Patients were divided into three groups based on their estimated glomerular filtration rate (eGFR): 15 patients with adequate renal function ($\text{eGFR} > 60$), 15 patients with moderately compromised renal function ($\text{eGFR} 45 - 60$), and 15

patients with severely compromised renal function (eGFR < 45). Patients injected with ^{18}F FDG (0.1 mCi/Kg body weight) and underwent imaging at 45 ± 5 minutes post injection. Exposure rate was measured prior to imaging using a radiation survey meter at 1 meter distance, after emptying the urinary bladder. In patients with (eGFR < 45), diuretic injection (Frusemide) 40mg was given intravenously at 45th min and exposure rate was again measured after 15 minutes. Patients with extensive disease were excluded from the study. **Results:** The average exposure rate increased as the patients' renal function worsened. However, there was no statistically significant difference between the two groups of patients i.e. (eGFR > 60) and (eGFR 45 - 60). The exposure rate is high in patients with severely compromised renal function when compared to patients with adequate renal function. However post diuretic injection, exposure rate in patients' with (eGFR < 45), significantly decreased. **Conclusion:** In general, exposure rate in patients' undergoing ^{18}F FDG PET/CT is influenced by renal function. In patients with (eGFR < 45), we observed diuretic injection at 45th min post ^{18}F FDG injection, (i.e. after uptake phase of FDG) significantly reduced the exposure rate in this group of patients, resulting in decreased radiation exposure to technologists and health care professionals while handling the patient during imaging.

E-TPW72

Feasibility of ^{18}F -Choline PET/CT to detect hyperfunctioning parathyroids in case of inconclusive scintigraphy and radiological imaging

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Aim: To evaluate the feasibility of ^{18}F -Choline PET/CT in the localization of hyperfunctioning parathyroid glands in patients with negative or equivocal results at MIBI scintigraphy and conventional radiological imaging modalities. Furthermore, this study wants to assess the usefulness of an early acquisition at 5 minutes compared to an acquisition at 60 minutes to localize the hyperfunctioning parathyroid glands. **Materials and Methods:** We enrolled 18 consecutive patients with hyperfunctioning parathyroid glands between September 2017 to February 2018 who completed the diagnostic imaging and had negative or doubtful findings at the ultrasound of the neck and $^{99\text{mTc}}$ -sesta MIBI scintigraphy. PET/CT Philips Gemini TF Big Bore has been used for the acquisition scans and as radiopharmaceutical 2.5 MBq/kg of ^{18}F -Choline. The PET/CT protocol foresaw an acquisition from the neck to the mediastinum in high resolution (HR) at 5 minutes (early acquisition) and at 60 minutes (late acquisition) post-injection of ^{18}F -Choline. CT parameters were: 120 KV, 70 mAs, pitch 0.813, $16 \times 1.5\text{mm}$ collimation, thickness 2, FOV 600. Two bed positions in HR were acquired in each acquisition for a total of 12 minutes (6 min per bed position), FOV 576 mm. SUVmax and its variation (ΔSUV) between the two acquisition was registered for each patient. **Results:** Pathological parathyroid glands were clearly seen in 11 patients by ^{18}F -Choline PET/CT with little change of SUVmax and ΔSUV values between the two acquisitions. In

our cases ^{18}F -Choline PET/CT seems to be a promising new imaging tool in patients with suspected hyperparathyroidism and negative/equivocal results at conventional imaging techniques. ^{18}F -Choline PET/CT also showed a higher sensitivity than the $^{99\text{mTc}}$ -sesta MIBI scintigraphy. Our preliminary results displayed no significant interpretative difference between early and late acquisitions. **Conclusion:** In our small group of patients, ^{18}F -Choline PET/CT seems to be a promising new imaging tool, able to reveal and guide the side of surgery when the ordinary techniques have failed to. In the future, additional patients are necessary to consolidate these results.

E-TPW73

Optimisation of the protocol for Cardiac Sarcoidosis using ^{18}F -FDG

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Aim: The presence of Cardiac Sarcoidosis can be determined using ^{18}F -FDG PET-CT scans. Imaging quality can be improved with the optimisation of both the fasting period and the diet patients undergo prior to the scan as well as the uptake time after administration of the tracer. The aim of this study is to compare the changes that were made to the protocol in order to obtain the best diagnostic result. **Materials and Methods:** The patients included in this study had a suspected diagnosis of cardiac sarcoidosis. Following the administration of 300-400MBq of ^{18}F -FDG, patients underwent a PET/CT cardiac scan with either an uptake time of 60 minutes or 90 minutes. The scans analysed were from patients that followed a fasting period of 12 hours with no diet restrictions and from patients that followed a fasting of 15 hours with changes in diet (low carbohydrate, high fat and high protein). All the cardiac scans had an acquisition time of 30 minutes. A visual assessment of these scans was then performed. **Results:** A comparison of scans was made between patients who performed 12 hours of fasting with no modified diet and patients who performed 15 hours of fasting with a low carbohydrate diet. A visual assessment of the scans showed that the uptake of FDG in the heart was significantly decreased given the changes applied to the diet which altered the metabolism in the heart. This provided an easier assessment given the decrease in physiological activity. A comparison was also made between patients who had 60 minutes of uptake period and those who had 90 minutes uptake. The increased uptake time resulted in a decrease in background activity which also improved the image quality. **Conclusion:** The optimisation to a protocol with a fasting period of 15 hours with a low carbohydrate diet and a 90 minute uptake period resulted in an improvement in image quality and enhanced diagnostic interpretation.

E-TPW74

The effect of a carbohydrate free diet as patient preparation for a ^{18}F -FDG PET scan to assess the detection of cardiac sarcoidosis or endocarditis

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Introduction: ^{18}F -FDG PET scan is a commonly used imaging technique to diagnose cardiac sarcoidosis (CS) or endocarditis. Previously patients who underwent FDG PET scan for the indication CS or endocarditis were prepared by following a carbohydrate low diet twenty four hours prior the ^{18}F -FDG injection. Unfortunately, some PET scans did not show the desired suppression of the ^{18}F -FDG uptake in the myocardium. As a result, no distinction could be seen between positive uptake and physiological uptake of ^{18}F -FDG in the myocardium. The aim of this study is to evaluate the effect of a carbohydrate free diet for twenty four hours prior the PET scan on ^{18}F -FDG uptake in the myocardium in comparison to a carbohydrate low diet for twenty four hours prior the PET scan. **Method:** This was a retrospective study. Twenty patients with the indication infection detection are divided into two groups: one group of patients followed a carbohydrate free diet twenty four hours prior the PET scan (group A, $n = 10$) and one group of patients followed a carbohydrate low diet twenty four hours prior the PET scan (group B, $n = 10$). All remaining preparations before the assessment are the same for both groups. Patients with diabetes mellitus are excluded. Patients with a glucose level >10 mmol/L were excluded, and patients with CS and endocarditis were excluded. All the images were interpreted and visual analysis was performed by an experienced nuclear medicine physician. **Results:** Ten patients which followed a carbohydrate free diet and ten patients which followed a carbohydrate low diet were included. All patients received intravenous heparin before the ^{18}F -FDG injection and the glucose level of each patient (mmol/L) was measured before ^{18}F -FDG injection. Patients from group A which followed a carbohydrate free diet showed a reduction in 10/10 exams (100%) of FDG uptake in the myocardium. Patients from group B showed a reduction in 7/10 exams (70%) of FDG uptake in the myocardium. **Conclusion:** A total dieting restriction of carbohydrates twenty four hours prior ^{18}F -FDG injection shows a notable suppression of myocardial FDG uptake (100%) in addition to a carbohydrate low diet twenty four hours prior ^{18}F -FDG injection (70%). Therefore the interpretability of ^{18}F -FDG PET scans are improved or the detection of CS. ***Results are preliminary**

E-TPW75

Alteration of Breast SUV according to the Menstrual Cycle in ^{18}F -FDG PET/CT

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^{18}F -FDG PET/CT is a useful modality for identifying high-glucose-consuming cells, such as cancer cells by the glucose metabolism of ^{18}F -FDG. ^{18}F -FDG is taken in by cancer cells and inflammatory diseases but occasionally, there is some unusual ^{18}F -FDG uptake on normal tissues depending on patients' individual physiological characteristics. In particular, in fertile females, unusual ^{18}F -FDG uptake in the breast changes according to the stages in the menstrual cycle, which can cause misdiagnosis. Therefore, this study examined the change in ^{18}F -FDG uptake of breast in the menstrual cycle on ^{18}F -FDG PET/CT. One hundred and sixty females (34 ± 3.5 years old), who had not

undergone a gynecologic anamnesis and had a regular menstrual cycle over the previous 6 months. The subjects were divided into the following 4 groups (each with 40 patients): flow phase, proliferative phase, ovulatory phase and secretory phase using Pregnancy Calculator 0.14 and patients' medical history. Discovery STe (GE Healthcare, USA) was used as the PET/CT. The SUVs on the ^{18}F -FDG-accumulated lesion on the breast were analyzed, and 3 nuclear medicine specialists performed a blind test. The SUVs on the breast were 1.64 ± 0.25 in the flow phase, 0.93 ± 0.28 in the proliferative phase, 1.66 ± 0.26 in the ovulatory phase and 1.77 ± 0.28 in the secretory phase. The highest uptake value was observed in the secretory phase ($p < 0.05$). The accumulated SUVs on the breast was divided into the following 3 grades comparing to the lung and liver: The image density of the breast uptake was equal to that of lung (Grade I); between that of the lung and liver (Grade II); and equal to or greater than that of liver (Grade III). These results showed a high uptake value in the secretory, ovulatory phase and flow phase ($p < 0.05$). In fertile females, the ^{18}F -FDG uptake of the breast showed changes according to the menstrual cycle. The result of the study can be used to improve the diagnosis of breast disease. Therefore, the false-negative findings of breast disease can be reduced by performing an examination at the appropriate period based on patients' medical history and considering the individual menstrual cycle.

E-TPW76

Association of Wrist and Room Temperatures With Levels of Captation of ^{18}F -FDG Induced by cold Through Brown Adipose Tissue in Young Adults

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Aim: The aim of this study is to analyse the link between wrist and room temperatures on the one hand and the activity and quantity of Brown Adipose Tissue (BAT) on the other. Both measurements are gathered by F-FDG PET/TAC through exposure young healthy patients to moderate cold. **Material and Method:** A total of 75 individuals had 2 iButtons (thermometers) over 7 days. One of them placed at the ventral part of the wrist of the non-dominant hand, while the second one at the waist level, to measure room temperature. On the 8th it was measured TAP activity and quantity through ^{18}F -FDG-PET/TAC. The shivering threshold of the participants was determined 48-72 hours before. Participants were exposed to individualized cold (4-5 Celsius degrees over the shivering threshold) about 2 hours before. One hour before PET/TAC, 5mCi of ^{18}F -FDG were injected to each individual. TAP was quantified through one SUV threshold of 1.2% lean mass determined through Dual Energy X-ray Absorptiometry and a range of radiodensity of -190/-10 Hounsfield Units. **Results:** It was found a negative relation

between wrist temperature and BAT activity and quantity (all $p \leq 0.012$). Moreover, it was found a negative relation between room temperature and all TAP variables (all $p \leq 0.002$). **Conclusion:** Wrist and room temperatures registered during all daily life are associated to BAT activity and quantity in young and healthy adults.

E-TPW77

Worklist Organization at Department of Nuclear Medicine Unit of AOUI Verona: optimisation of the examination timing in the execution of ^{18}F -FDG PET/CT for Radiotherapy Planning

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Aim: This study wants to analyze the organization of the work lists in two years, 2016 and 2017, in order to choose the best organisation to optimise the time necessary for the execution of the metabolic planning with ^{18}F -FDG PET-TC in patients who have to undergo radiation treatment. **Materials and Methods:** In our department there is only one PET/CT, Philips Gemini Big Bore, which was installed to run approximately 4000 PET/CT per year, both for diagnostic and radiotherapy metabolic planning purposes. The analysis was conducted by comparing the organization of the work lists and the number of PET/CT carried out in two different years 2016 and 2017 having made some changes in the setting. In 2016 the work list provided the weekly availability of 9 places from Monday to Friday for the bringing about the metabolic planning with PET/CT. The performance was randomly distributed on the basis of requests sent to our department from the Radiotherapy Dept and according to the availability of the PET/CT equipment. The positioning procedures and immobilisation options require extra time compare to the ordinary techniques for PET/CT staging, respectively 30-40 minutes compared to 12-20 minutes for each patient. As a consequence, in 2017 the work list was organized with the same number of dedicated spaces for metabolic treatment planning (9 patients) but all consecutively concentrated in two mornings, exactly on Monday and Thursday morning. **Results:** In 2016, we performed a total of 215 PET/CT scans in the radiotherapy treatment position compared to 262 in 2017, we registered an increase of 47 cases (22%). The available PET/CT space for treatment planning in 2016 was used up to 46.7% and up to 56.9% in 2017. The eventual free spaces not completely occupied by patients for metabolic treatment planning were suddenly booked with either patients for staging or re-staging purposes. **Conclusion:** Thanks to the new organization of the work list proposed and implemented in 2017, it was possible to obtain an optimisation of the time spent to perform the PET/CT in treatment position so we could carry out a greater number of PET/CT examinations. Last but not least, the concentration in two mornings allow us to obtain the collaboration of the technicians of the Radiotherapy Dept which contribute in decreasing the time spent in patient immobilization and positioning, and in a reduction of the absorb dose due to a prolong exposure of the staff.

E-TPW78

Evaluation of the influence of a visual design of an examination guide on patient comprehension and testing accuracy

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Aim: An examination guide is a useful medium to provide the patient with an overview, pre- and post-test preparation, and precautions of nuclear testing. The design and arrangement of existing written texts and announcements were evaluated to elucidate the comprehension of patients undergoing testing. **Materials and Methods:** Informational material describing bone scanning and ^{201}Tl myocardium perfusion single-photon emission computed tomography (SPECT), as a secondary examination, which accounts for the largest portion of gamma imaging at Asan Hospital (Seoul, South Korea), was selected as an improvement target in consultation with a national innovation center. Existing informational material was dispensed to patients scheduled for bone scans from November 2016 to February 2017 and the revised material was issued from March 2017 to May 2017. A survey was conducted of 200 patients who underwent ^{201}Tl myocardium perfusion SPECT before and after the revisions ($n = 100$ each time period) to assess the patients' understanding of the material. **Results:** When comparing the use of the conventional vs. revised material, the number of patients who received treatment before bone scanning had decreased from 130 to 60, while the number of those who required additional imaging decreased from 53 to 14. Prior to the revision, 43% of patients underwent testing before preparation and 18% underwent additional testing. The decreased need for additional image acquisition after revision of the informational material resulted in a decrease in acquisition time of about 2 min, from 16.5 to 14.2 min. In the case of ^{201}Tl myocardium perfusion SPECT, patient comprehension of all five items surveyed had increased, while the number of patients who had repeatedly asked about various facets of the procedure pre- and post-testing had decreased from 36% to 16% and 31% to 14%, respectively. **Conclusion:** Lower patient comprehension is accompanied by a decrease in image quality due to non-compliance during pre-testing and may lead to repetitive questions from the patient, which may also negatively affect the fatigue and work efficiency of the examiner. Improved readability and visibility of informational material through visualization was correlated with greater patient comprehension as well as improved image quality and acquisition time.

E-TPW79

Distraction and communication before and during PVK insertion and/or injection of tracer on children at Section for Pediatric Nuclear Medicine

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Aim: At every referral of a child to the hospital there is a risk of a traumatic experiences; it is therefore very important to minimize the risk of traumatizing the child as much as possible. The

child does not only bring his or her own experiences to the examination but is also influenced by the parents in all aspects. The use of distraction for the child, can prevent restraining and reduce the assistance from the Department of Anaesthesiology. **Method:** To reduce the use of restraining the examination must be demystified as much as possible. Ideally in the safe environment at home, where the parents explain the examination based on the material received from the Section for Pediatric Nuclear Medicine (SPNM) When the child is being welcomed at the SPNM; it is distracted to order to temporarily forget what is going to happen and through communication the child is assisted to master the examination. The SPNM has provided basic training in balloon animal making for the staff, and during insertion of a PVK or injection of tracer, the child is told a story and at the same time participating in creating a balloon animal and assisting in building the story of e.g. how the worm became a tiger. Children also love soap bubbles - they are magical and are perfect for anxious children entering an examination room. Parents are active participants and their enthusiasm is reflected to the child. Suddenly the surroundings are no longer dangerous, and it is much more fun to look at soap bubbles and focus is shifted from a technologist injecting a tracer/inserting a PVK to a parent blowing soap bubbles. **Results:** Following the balloon course and implementing the method we have had a lot of positive feedback. It is easier to distract the children when your college are making op a story while forming a balloon animal. The children's focus is mostly on the balloon and they often discover that they could master the examination and that it didn't hurt. The soap bubbles have the same effect, and we can get help from the parents. We can make competitions - who can pup most bubbles, and before you know it, the examination has finished. **Conclusion:** With a few simple tricks it is possible to reduce the stress levels and distract the children in a very effective way, so that no restraining is used under the examination.

E-TPW80

How to build a large database for PET/CT research

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Aim: Region Skåne, Sweden, recently installed three silicon photomultiplier-based positron emission tomography with computed tomography (PET/CT) systems and three more will be installed in the upcoming years. We want all clinical PET/CT patients to be included in a research study and since more than 6000 patients will be enrolled annually, a good infrastructure is required. An interdisciplinary research group was formed. The Regional Ethical Review Board approved our application and all patients who agree to participate are enrolled. The aim of this study was to find out how to handle both inclusion and data of a large number of patients admitted for PET/CT, that are enrolled in research studies. We also wanted to decrease the pa-

perwork and store the same data in a research database and in the clinical radiology information system (RIS). **Material and Methods:** In order to handle this amount of data we chose to use REDCap, a research database developed at Vanderbilt University (Nashville, Tennessee). The company Molnify (Stockholm, Sweden) developed a program to transfer patient data, a questionnaire and the written informed consent to the research database by using an application for iPad. The questionnaire is also copied to RIS. All data are handled within the hospital's intranet. The patients receive a web-address in their patient call, with information about the study, both as a written document and as a short movie. They also receive information at the department before the examination, and sign the informed consent at an iPad. **Results:** The infrastructure is set up and the inclusion of patients started May 2017. As of april 2018, 3100 patients have given their consent to participate and are included in the database. The first study is completed and the manuscript submitted and other studies have started. Along the way, there have been different challenges, such as how to get a good work flow in the department without creating additional work for the staff and how to sort the data in an easily accessible way. **Conclusions:** The infrastructure simplifies extraction of patients and patient data for future studies.

E-TPW81

Clinical Practice in Nuclear Medicine - Learning by taking responsibility (LTR)

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Aim: Aim of the study was to provide information and to evaluate the new training method related to nuclear medicine clinical practice from the radiographic students' point of view. **Background:** LTR-model is based on the Dutch Learning Department environment model. In which students run the activity in the department independently. They can consult and advise each other and still have opportunity to ask help from radiographer supervisor, who is responsible for quality of examinations and patient safety. **Subjects and Methods:** During the third and the fourth academic year students' clinical practice was fulfilled under radiographer supervision in nuclear medicine department. The goals for five weeks (8 ECTS) clinical practice included: as a member of the team, students were able to plan, implement and evaluate the most common nuclear medicine procedures related to the holistic care of patients in accordance with the quality requirements. And they were able to implement appropriate radiation protection for patients, personnel and other people in the nuclear medicine department. In the LTR -model the pair of students took responsibility on planning and implementing the nuclear medicine examinations in one single examination room during one week. The radiographer supervisor from the department of the NM had the ultimate responsibility for patient safety and quality of examinations. The material included written feedback from 15 students, 5 supervisors and 2 teachers. The data was analyzed with content analysis technique. **Results:** From students' perspective LTR-model is better

way to learn compared to traditional clinical practice, rehearse initiative, creativity, self-confidence and belief in your own making, promote the skills of co-operation as a team and decision making which leads to better problem solving skills and responsibility. From supervisors' and teachers' perspective LTR-model offers an effective and inspirational way to learn. LTR model also serves an opportunity for a holistic assessment of students' practical skills. It seemed that the students could integrate theoretical knowledge to practice better than in traditional internship.

Conclusions: The LTR model requires that effective learning processes and versatile learning conditions are available before LTR-model week. We agree as in earlier research has found that at traditional clinical practice a student follows a supervisor, but at LTR-model a supervisor follows a student.

E-TPW82

Reduction of CT radiation dose in PET-CT: evaluation of low dose CT scan protocols

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Background: In the past decade, the great advances in computed tomography (CT) technology and applications have increased the clinical utilization of CT also in Nuclear Medicine. Attentions of radiation exposure dose increase recently and it become a crucial issue in PET-CT. **Aim:** In our diagnostic center, at the moment, CT acquisition is only used for attenuation correction and for anatomical localization. In this study, in order to reduce the CT exposure dose of a patient in PET-CT scans, we controlled current (mA) e voltage (kV) factor related CT dose and we checked image quality obtained. **Material and Method:** For this study we used an Alderson RANDO phantom, moulded of tissue-equivalent material. To acquire CT images we utilized a PET-CT scanner Discovery STE, GE Healthcare. Our baseline CT acquisition protocol for Total Body FDG PET-CT (vertex-inguinal region) consisted of a helical CT scan with these parameters: 120 kV, 30-150 modulated AUTO-mA, index noise 25, 3,75 mm thickness. We acquired phantom using standard protocol CT and we tried to perform other scans adjusting AUTO-mA from 150 mA to 40 mA and decreasing voltage from 120 kV to 100 kV. We analysed CTDIvol (mGy) as dosimetric CT parameters obtained by scans with different protocols. We investigated the effect of lowering CT parameters (mA and kV) in terms of signal-to-noise ratio (SNR) analysing CT images on the liver, lung, bone, brain and heart. Finally, we correlated SNR and CTDIvol to evaluate low dose CT acquisition protocol. **Result:** Using a voltage of 120 kV CTDI value changed from 2,43 mGy (low dose CT with 40 mA) to 6,65 (Auto-mA 30-150). Using a voltage of 100 kV CTDI value changed from 1,47 mGy (low dose CT with 40 mA) to 4,55 (Auto-mA 30-150). Lowering CT parameters have an effect on CT image quality in terms of SNR. **Conclusion:** Adjusting mA and kV values is possible to have a considerable CT dose reduction. Obviously, the CT images quality decreases in relation to the current value and voltage parameters especially. However, exposure dose CT reduction doesn't influence emissive PET attenuation corrected images.

E-TPW83

Reduction of Radiation Exposure to Patients for Repeated PET/CT Scans

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Aim: Due to increased clinical indications, the patients undergo PET/CT examination multiple times at various stages of the disease management. Also, it is important to reduce the radiation exposure to the patient, staff and relatives of the patient. The purpose of our study is to assess the image quality by reducing the administered activity of 18F FDG and by increasing the acquisition time, thereby the reducing the radiation exposure.

Material and Methods: We evaluated 24 patients in this study (15 males, 9 females). All patients were divided two groups. First group of patients (12 patients) were injected with 18F-FDG the standard dose (3.7MBq/kg) and the second group of patients (12 patients) were injected with 18F-FDG equivalent to half the standard dose (1.85MBq/kg). All patients were scanned at 60 min after injection on PET/CT (Philips True Flight Select, Medical Systems), Group 1 and group 2 patients were imaged at 1.5 min and 3 min per bed position, respectively. The dose rate at 1 m distance from the patients were measured immediately and 1 h post injection. The measurements of dose rate were acquired by using Geiger-Muller (GM) probe (Ludlum, 14C, USA). **Results:** The mean dose rates of immediately and 1 h post injection for patients of Group 1 were 16 µSv/h and 8.02 µSv/h and for group 2 were 5 µSv/h and 2.44 µSv/h. Two trained Nuclear Medicine Physicians reviewed the imaging quality. All images were assessed as qualitatively on visual interpretation and dose reduced images are found quite good. **Conclusion:** We suggest that the reduction radiation exposure by decreasing the injected dose and increasing the acquisition time is applicable for repeated PET/CT scans.

E-TPW84

Comparison of the EANM paediatric dose card and the Administration of Radioactive Substances Advisory Committee (ARSAC) for I¹²³mIBG

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Aim: Currently the UK Administration of Radioactive Substances Advisory Committee (ARSAC) states; the EANM paediatric dose card requires further research prior to implementation. The aim of this study was to determine the practicability of harmonising the EANM paediatric dose card with the current UK guidelines for I¹²³mIBG imaging for neuroblastoma, and to further investigate the image quality of scans under the new dosing scheme.

Method: 22 patients were retrospectively selected at random (age 3-15 years, weight 12-50kg). All patients had undergone a wholebody scan on a Siemens Symbia Intevo equipped with MELP collimators 24 hours post I¹²³ administration according to ARSAC guidelines. Anonymised scans were processed with an IDL user script using a Poisson resampling method simulating the image quality expected from the reduced activity proposed

in the EANM scheme. 2cm ROIs were drawn at the dome of the liver, directly above the liver in the lung for background and over any metastases noted in the clinical report. Patients with multiple metastases had one ROI drawn over the metastasis with the lowest number of counts. Liver-to-Background ratios were calculated for mean ROI counts. **Results:** The average EANM dose card guidelines are 18% lower than that of the ARSAC: the largest difference in administered activity would receive 38.85MBq less than with ARSAC. Using this difference in administered activity generated a mean liver/background ratio of 2.02, against the EANM dose card of 2.01. Despite the lower administered activity, liver-to-background ratios remained very similar, paired t-test found no significant differences in the means ($p=0.4521$); the mean liver/background ratio for ARSAC was 2.62 compared 2.65 for EANM. Meanwhile, the mean lesion/background ratio was 3.02 for both ARSAC and EANM. With a standard deviation of 0.23, this tells us that there is very little difference when comparing the scan quality for the separate doses. There was a cross-over point at weights of 64kg or more receiving higher than the ARSAC limit. These were not included in the study as doses will not exceed the adult dose of 370MBq $\pm$ 10%. **Conclusions:** Despite administering less activity with the EANM dose card, the difference in image quality between dosing schemes was minimal. The Royal Marsden Hospital (NHSFT) will discuss adopting the EANM dose card up to 64kg or ARSAC limits. This study was limited to ^{123}I MBG but further study is planned across all categories of the EANM dose card.

E-TPW85

Patient radiation dose estimates: Implementing EURATOM 59/2013 in our Department

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The Aim of this study was to compare the averages of patient radiation dose estimates for the most frequent nuclear medicine (NM) diagnostic procedures performed at Clinical Department of Nuclear Medicine, Clinical Hospital Center Rijeka, with the values mentioned in the literature. Furthermore, the aim was also to emphasize the important role of NM technologist in the procedure. **Materials and Methods:** Estimation of effective dose to patients due to nuclear medicine procedures was introduced in our Department from February 2018, when the EURATOM 59/2013 directive was scheduled for implementation. Effective dose to the patient was estimated by the medical physicist based on the relevant, study-specific data obtained from the technologists (patient age, gender, applied activity, renal function, time of bladder emptying etc.). In order to facilitate the procedure, a worklist containing the above data relevant for the estimate was written in collaboration with physicists and completed by NM technologists. In this work, effective dose estimates were collected from most frequent NM diagnostic procedures: $^{99\text{m}}\text{Tc}$ HDP skeletal imaging (100 studies), $^{99\text{m}}\text{Tc}$ Tetrofosmin myocardial perfusion imaging (stress and rest, 100 studies) and $^{99\text{m}}\text{Tc}$ MAG3 dynamic renal scintigraphy (85 studies). Altogether, there were 285 studies included, all performed on adult patients, without "low dose" CT. The averages of effective dose estimates

were then compared with values mentioned in literature. The **Results:** showed that average applied activity for skeletal imaging was 502 MBq ($N=100$), for myocardial perfusion imaging it was 679 MBq for stress and 673 MBq for rest study, 1345 MBq for both ($N=100$), and for renal scintigraphy it was 165 MBq ($N=85$). For the mentioned procedures average effective dose estimates were as follows: skeletal 2.5 mSv, myocardial perfusion (stress and rest) 10.1 mSv and renal 0.8 mSv. **Conclusion:** Average patient radiation exposure due to NM procedures at our Department was lower than values mentioned in relevant literature (skeletal imaging 2.9 mSv to 4 mSv, myocardial perfusion imaging 16.3 mSv, renal scintigraphy 3 mSv). This is primarily due to lower activities applied to the patients in accordance with the ALARA principle and due to refinement of ICRP biokinetic models and mathematical phantoms over the years leading to different estimated values. In this work, the importance of close collaboration of NM technologists, physicians and physicists is emphasized.

E-TPW86

$^{99\text{m}}\text{Tc}$ -Octreotide (Tekrotyd) uptake in accessory spleen: A case report

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Introduction: Accessory spleen, seen in 16% of the normal population, is a potential pitfall in radiologic and radionuclide evaluation of oncologic patients. It may show physiological increased of $^{99\text{m}}\text{Tc}$ -Octreotide uptake and mimic malignancy in somatostatin receptor scintigraphy (SRS). **Case report:** We present a 41-year-old male patient with neuroendocrine tumor in the tail of the pancreas underwent partial pancreatectomy, which was requested SRS with Tc-Octreotide (Tekrotyd) for suspected hepatic metastasis detected on CT. SRS was performed after administration of 740MBq $^{99\text{m}}\text{Tc}$ -Octreotide using a dual-head gamma camera with low-energy parallel hole collimators. Planar whole body images with abdomen single photon emission CT (SPECT) images were obtained at 1h and 4h. **Results:** Hepatic lesions detected on abdomen CT were not visualized and did not show increased tracer uptake. In addition to physiological uptake in liver, spleen, and kidneys, a focus of increased tracer uptake was detected adjacent to spleen. In the retrospective assessment of abdomen CT, well demarcated round lesion which was isodense with spleen suggesting accessory spleen. These lesions were matched with the focal increased tracer uptake on SRS. **Conclusion:** Accessory spleens are congenital focus of healthy splenic tissue, mostly localized in splenic hilum, but may be seen in any locations in the abdomen. In the literature, majority of the reported cases related with accessory spleen were based on false positive evaluation, especially in splenectomized patients. It's important to make a definitive diagnosis in the suspicion of accessory spleen in any imaging modalities for an accurate clinical management in patients with malignancies.

E-TPW87

PET/CT in the evaluation of hypoxia for Radiotherapy Planning of Head and Neck Tumors: Systematic Literature

Review

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Introduction and Aim: The PET allows evaluation of various molecular pathways, metabolism, cell proliferation, oxygen consumption, receptor expression and genes. Performing a PET/CT, with the administration of a radiopharmaceutical that allows the identification of cells of high and low degree of oxygenation, allows to increase the precision in the treatment of the planned target volume. The aim of this study is to identify the most suitable radiopharmaceuticals for the detection of cellular hypoxia through PET/CT images and recognize the benefits for radiotherapy treatment planning through IMRT and VMAT techniques. **Material and Methods:** The present work consists in a systematic literature review, in which the literature search was performed using the databases PubMed, b-on, Free Medical Journals, BioMed Central and Google Scholar. We included articles and books in Portuguese and English, dated from 2004 to 2018. The following Boolean logic was used for the search: “radiotherapy planning treatment AND hypoxia”, “Hypoxic cells AND radiotherapy treatment AND PET”, and “PET/CT AND hypoxia cells AND radiotherapy”. The choice of articles was made considering if they approached the radiotherapy treatment planning with PET/CT and excluding all those who did not approach the hypoxia evaluation. **Results:** The reduced oxygen rate affects the probability of tumor healing, reducing the success rate, especially in head and neck tumors. Specific radiopharmaceuticals such as ^{18}F -FMISO, ^{18}F -FETNIM and ^{18}F -HX4 allows the detection of hypoxia, that is relevant to the optimization of radiotherapy treatment, as it serves to delimit hypoxic subvolumes within the target volume of treatment. The IMRT and VMAT uses X-rays, where the indirect effect of radiation on DNA is of importance, and the oxygen interacts with free radicals to form organic peroxides. In cases of head and neck allows a reduction of xerostomia, increases the probability of tumor control and the quality of life. **Conclusion:** With the use of PET/CT, the interobserver variability is decreased. The GTV PET/CT volume of the primary tumor is, on average, smaller than the one defined by CT with contrast. The identification of hypoxic areas with PET/CT imaging allows the scaling of radiation dose to radioresistant subvolumes. The non-invasive technique presented translates itself into a high increase of disease free survival and a decrease of recurrence.

E-TPW88

Utility of both FDG PET/CT and DPD SPECT/CT in the diagnosis of infiltrative cardiomyopathies: 2 case reports

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Aim: Sarcoidosis and amyloidosis are multi-system infiltrative diseases, which carry a poor prognosis. This project aims to describe the utility of scintigraphic techniques in sarcoidosis and amyloidosis using ^{18}F -fluorodesoxyglucose Positron Emission Tomography/Computed Tomography (^{18}F -FDG PET/CT) with specific pre-scan preparation and Single Photon Emission

Computed Tomography with 3,3-diphosphono-1,2-propanodicarboxylic acid (DPD SPECT) in two case reports. **Materials and Methods:** Cardiac sarcoid specific protocol ^{18}F -FDG PET/CT and DPD SPECT/CT scans were performed at Barts Heart Centre to investigate the aetiology of their cardiomyopathy in two patients. Patient preparation for cardiac sarcoid specific PET includes 24 hours no carbohydrates diet, 12 hours fast and heparine injection 15 minutes prior to ^{18}F -FDG administration, and 60 minutes uptake. On the other hand, no specific patient preparation is needed for DPD scintigraphy. Acquisition conditions for FDG PET/CT for sarcoid include: 2 minutes/bed position; a low dose CT for attenuation correction and, at the end, a high-resolution computed tomography (HRCT) of the chest. Regarding DPD scintigraphy, two whole body scans are performed: one immediately after $^{99\text{mTc}}$ -DPD injection and another 3 hours post-injection, followed by chest SPECT/CT. **Results:** Findings in the both patients' heart Magnetic Resonance Imaging (MRI) show signs of cardiomyopathy. SPECT DPD of one patient revealed heart uptake, whereas, PET/CT FDG any were seen. On the second patient, SPECT DPD revealed no cardiac uptake, but PET/CT FDG for sarcoid appeared to have focal septal uptake in the heart. **Conclusion:** The diagnostic work up of infiltrative cardiomyopathies often requires a multi-parametric, multi-modality approach. Both scintigraphic techniques are very sensitive and have additive and complementary value over non-ionising imaging modalities.

e-Posters Technologists

ETP-1

e-Poster Area

4. SPECT & SPECT/CT Physics & Instrumentation & Data Analysis -> 1. General Instrumentation, Quality Assurance, Performance and Standardization

EP-0285

Measurement accuracy of BCF used in quantitative analysis of bone scintigraphy

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Aim: In order to perform quantitative evaluation using quantitative analysis software of bone scintigraphy, GI-BONE (AZE, Japan), it is necessary to calculate Becquerel calibration factor (BCF). BCF was calculated as the ratio of radioactivity concentration (Bq/ml) in the phantom at the time of scanning to the measured SPECT count density per scan duration (count/ml/sec). BCF should be a constant value regardless of the radioactivity concentration filled with the cylindrical phantom at the time of scanning. Generally, when calculating BCF, it is recommended to enclose the radioactivity concentration of about 15 to 20 kBq/ml into the cylindrical phantom. In this study, we determined the measurement accuracy of BCF when we changed the radioactivity concentration of Tc-99m enclosed into the cylindrical phantom. **Material and Methods:** A cylindrical phantom was filled with 7 kinds of Tc-99m solution; 0.9, 2.1, 4.0, 4.9, 8.2, 17.6, and 40.5 kBq/ml. SPECT/CT acquisition was performed for 360° rotation with low-energy high-resolution (LEHR), and SPECT data were reconstructed under the same conditions as used in bone scintigraphy at our hospital. Attenuation and scatter correction (AC+SC+), non-attenuation correction and scatter correction (AC-SC+), and non-attenuation and non-scatter correction (AC+SC-) were used for the image correction methods. Circular region of interest were drawn on 11 images around the center of the cylindrical phantom, the mean BCF, the standard deviation of BCF, and the coefficient of variation of BCF were calculated in each Tc-99m concentration, respectively. **Results:** When the Tc-99m concentration were 8.2 kBq/ml or more, the mean BCF calculated using the data with any image correction methods showed almost constant value. However, when the Tc-99m concentration were 0.9, 2.1, 4.0, and 4.9 kBq/ml, the mean BCF varied. The standard deviation of BCF were large at any Tc-99m concentrations. The lower the Tc-99m concentration were, the larger the coefficient of variation of BCF calculated using the data with any image correction methods were. **Conclusion:** When the Tc-99m concentration enclosed into the cylindrical phantom were 0.9, 2.1, 4.0, and 4.9 kBq/ml, the measurement accuracy of BCF were low.

EP-0286

Usefulness Assessment of a Manufactured Phantom Using 3D Printing Technology in PET/CT

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The purchase of PET / CT has increased for each hospital, and accordingly, the necessity of quality control is also highly recognized. However, additional correction of standard quality control guidelines and continued development of efficiency test of performance evaluation are required, and research on phantom development is necessary for efficiency of inspection. Thus, through this study, it is necessary to investigate the usefulness of a phantom made using the advantages of 3D printers. We acquired images using PET / CT (GEMINI TF 64, Philips, USA) for Step wedge made of Aluminum, PMMA, ABS. Comparing the difference between the change in the counts value and the change in the measured SUV value coefficiented for each substance using 4.1 mCi of 18F-FDG, the change was compared. According to the results of this study, when comparing Aluminum, PMMA and ABS phantom, the count value decreased as all steps increased and the SUV value was also approximated. However, due to the cost issues and technical limitations of 3D printing technologies, the research was conducted using only the ABS phantom, and PVA with its material being widely used as the material for 3D printers, and PVA with its limits. It is said that when the cost and technical challenges of 3D printing technology are resolved, a wider range of materials could be followed up. Based on this research, we confirmed that 3D printing technology can be usefully used in terms of PET / CT accuracy control. In the case where 3D printing technology developed in the future is actually applied to PET / CT accuracy control, it can be considered that it can contribute not only to the efficiency check of performance evaluation but also to radiation dose.

ETP-2

e-Poster Area

4. SPECT & SPECT/CT Physics & Instrumentation & Data Analysis -> 2. Image Reconstruction & Data Analysis

EP-0287

The Investigation of Movement Artifacts in Myocardial Perfusion Scanning in PET/CT: Phantom Study

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Aim: The aim of this article is to investigate the artifacts based on the patient movement while myocardial perfusion scanning with PET/CT, to determine the size of the defects which patient movement causes, to research at which shooting time phase these defects would occur. **Material and Method:** Anthropomorphic SPECT cardiac phantom is used to simulate the movement of the patient in this study. As soon as one day protocol rest study was started, cardiac phantom was repeated 10 times; at the beginning, mid and end of shooting time without motion and 4mm, 12mm and 20mm with motion creating. After analyzing each image one by one, polar map was based on the results of statistical analysis. **Results:** According to the PET/CT study; there was no statistically significant difference between 4mm, 12mm

and 20mm of movements generated at the beginning and mid of study. A statistically significant difference was found between the movements created in the end of shooting time ($p < 0.05$). It was understood in post hoc analysis that; this difference was derived from 20 mm group generated motion and 12mm group with motion. **Conclusion:** Based on Myocardial Perfusion Scanning studies in PET/CT, it was clearly understood that axial patient movements were unable to cause any artifact up to 12mm.

EP-0288

Evaluation of basic needs for Pet-CT patients

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Aim: To identify the most usual basic needs of the patients that come for PET-CT test. **Material and Method:** Retrospective study of patients who came to our unit between July 5, 2017 and January 31, 2018, where data of 102 patients were collected. The nurses do an initial interview and they has attached a model assessment sheet with a basic pattern of elimination, safety, communicate emotions, needs and fears, collaboration problems and nursing diagnoses. **Results:** The average age was 63.4 years. In the elimination pattern highlighted constipation with 15.6%, it followed by alteration in urinary elimination with 12.7%. Disorientation and / or intellectual abilities were assessed at 10.7%. Safety pattern: to the 7.8% it was necessary to facilitate the transfer to the home (ambulance) and only 1.9% had presence of drug allergies. Anxiety, fear and risks of falls were also collected. Between 1 and 3% demanded information about therapies or side effects and had a negative / defensive coping attitude. Collaboration problems: collaboration with the doctor, teaching: procedure / treatment, surveillance, intravenous puncture, administration of intravenous medication and environmental management: worker safety. Nursing diagnoses: 34.3% fear, 27.4% willing to improve urinary elimination, 26.4% risk of falls and most were willing to improve knowledge with 78.4%. **Conclusions:** Although the sample is small, we can make an idea of the needs that we can most find in a PET patient. The importance of the initial nursing interview detecting the most frequent problems and acting on the possible appearance of anxiety / fear, alteration in urinary elimination / constipation, risk of falls and transfer to home, makes healthcare more fluid. Finally, it is worth highlighting the great collaboration with which patients come to carry out this study.

EP-0289

Variation of the indices in analysis software for PET/CT using digital phantoms

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Aim: For PET/CT, indices such as standardized uptake value (SUV), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) are used to evaluate tracer accumulation. Differences

in these indices may occur even with the use of the same PET scanner because different algorithms are used in different analysis software programs. In this study, we examined the causes for differences among 6 analysis software programs using digital phantoms. **Material and Methods:** Six software programs were used in this study, namely, syngo.via (Siemens), GI-PET (AZE), Metavol (Hokkaido University + University of California, Los Angeles), VOX-BASE II (J-MAC SYSTEM), Advantage Workstation (GE), and PMOD (PMOD). We made 2 types of digital phantoms. The first type of phantom was used to examine whether MTV included voxels with lower values than the threshold. The center voxel has a SUV of 2.5, and SUVs of slices were made to gradually decrease by 0.1 as going to the outside. A rectangular phantom was made by piling up these slices. The second type of phantom was aimed to imitate real clinical accumulations. Four kinds of cubic accumulations having different sizes were made in background, noise was added into them and they were smoothed with 5mm Gaussian filter. The slice thicknesses of the phantom were 3mm, 4mm and 5mm. A region of interest was drawn on PET images, and each index was obtained with 6 software programs. **Results:** In case of the first phantom, MTV obtained with Metavol was lower than the true value by two slice volumes. This seemed due to the fact that Metavol does not measure the outermost data. In case of the second phantom, almost the same values of SUVmax, SUVpeak, and SUVmean were obtained with each software program. The maximum difference in MTV and TLG among them was 15.3%. Each program deals differently with the voxels close to the threshold values. **Conclusion:** The differences in indices obtained with the 6 software programs are attributable to varied handling of each program to the voxels close to the threshold.

ETP-3

e-Poster Area

7. Cardiac Imaging -> 4. Other topics

EP-0290

Relevant Specific Simulation Parameters (ReSSiP) for validating the “true” device-simulated outcomes: A Handheld Gamma Camera System

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Purpose: For gamma cameras, most Monte-Carlo simulations are used to account for energy distribution, radiation interactions, spatial resolution, collimation, acquisition settings and sensitivity with acceptable results. However, an accurate simulation aggregating the device degradations and enhancements state-values is still far from reach. To accurately simulate the energy linearity or system sensitivity after major changes of the gamma camera could be impossible using the default manufacturer's values. The aim of this study is to highlight some relevant parameters

for an optimal molecular imaging simulation while encompassing the specific camera system characteristics and settings of a handheld gamma camera. **Subjects & Methods:** An explicit prototype description of the simulation method is considered. The simulation model is structured as discrete-stochastic (probability distribution of distinct events), dynamic (time-dependent changes in the system state), explicit (output is determined with a finite set of input parameters), linear (representation of objective functions and constraints by linear equations) and inductive (parameters are based on empirical findings). The relevant modelling parameters for the handheld gamma camera system (the CrystalCam), consist of the following (not in the exact order): Collimator-Detector-Response; Intrinsic- and System uniformities; Spatial resolution; Energy resolution; Energy-Channel calibration; Dead time; Sensitivity; Pixel size; System-Cross-Calibration; Background; Energy window settings; Attenuation correction; Scatter correction; Partial volume effect; Lesion overlapping effect; Count duration; Energy Spectrum; Total Counts; Photomultiplier tube gains; Acquisition modes and Minimum detectable activity. The parameter-value pairs are determined empirically. Due to the relatively large state-value set, a semi-supervised simulated model is used. Performance and reproducibility of the simulated outcomes are verified and validated using new sets of parameter-value pairs. **Result Analysis:** Objective comparisons of the simulation and measurement data are listed. Significant dependencies between measured data and simulations are weighted and corrected accordingly. Detailed configuration of the simulations and actual measurements are listed. Graphical interpretations are used to display the accuracy and correlation of the simulations to the actual measurement values. **Conclusion:** This study presents an advanced simulation technique using the ReSSiP to “truly” account for the state-values of the CrystalCam. The ReSSiPs can be used as a baseline standard to accurately simulate the CrystalCam by accounting for degradation and enhancement parameters-values. Taking the numerous parameters into account for investigations and validations, it is clear that it is a time and resource consuming process to carefully record the correct parameter-value pairs. However, successful simulations making use of the ReSSiPs will greatly improve digital models of gamma cameras.

ETP-4

e-Poster Area

9. Oncology, diagnosis -> 2. FDG PET-CT/MR

EP-0291

The Impact of Blood Glucose Testing in 18F-FDG PET Imaging

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Aim: My colleagues attended a course in PET/CT and experienced a difference in practise among departments in selecting patients for blood glucose testing. Blood glucose testing of patients prior 18F-FDG PET Imaging is recommend in the EANM procedure guidelines for FDG PET/CT tumour imaging version

2.0. I therefore decided to examine the impact of our procedure where every patient is tested. Does it affect the number of cancellations? Would it be enough to test only patients with known diabetes? How many undiagnosed patients will we find in risk of diabetes? Will the numbers be so high it would make glucose correction of SUV a possible outcome? **Materials and Methods:** In a 3 month period (Jan-Mar 2018) we registered all 962 refereed FDG-PET/CT patients' sex, age, cancellation status and asked if they had diabetes. Blood glucose level was measured on all attending patients, with a laboratory accredited and calibrated Accu-chek Inform II bedside glucose meter using venous blood. A value of 7.0 mmol/L or above was defined as increased. Patients with a blood glucose level above 11.0 mmol/L was cancelled and rescheduled. Patients were asked to be fasting 6 hours for calories. Blood glucose levels are stated as average +/- standard deviation and compared with t-test. **Results:** Of the 891 attending patients (average age 66.3 years and 50.8% females) 105 patients (11.8%) stated they had diabetes. 52 (49.5%) of the these diabetic patients had increased fasting blood glucose (Average 8.7 +/-2.1mmol/L, range 7-15.7) and 9 patients (8.6%) had a blood glucose above 11 mmol/L and was cancelled. 39 (5.0%) of the 786 patients without known diabetes had increased fasting blood glucose (Average 7.7 +/-0.7mmol/L, range 7-9.5) and none got cancelled due to high glucose level. In the group with increased fasting blood glucose (N=91, 10.2%) the known diabetic patients had significantly higher glucose level (p=0.01). **Conclusion:** We recommend measuring blood glucose levels at all patients as a large proportion had increased levels and some needed rescheduling. Among patients without known diabetes we actually suspected diabetes in 5%, which have important impact on future patient care. The suspected diabetes is reported and could actually be the reason for unspecific symptoms in a patient with a negative PET-scan. Also the variation in blood glucose is so high it would be valuable to know when interpreting the SUV-values and correction for glucose levels is sometimes done manually in selected cases.

ETP-5

e-Poster Area

15. Musculoskeletal Imaging -> 1. Bone Scintigraphy

EP-0281

One Year Imaging of cancer patients at Nuclear Medicine centre, Ibadan, Nigeria

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Introduction: Cancer imaging in University College Hospital (UCH), Ibadan with Gamma Camera started in April, 2006 to cater for staging, treatment and assessment of metastases. This presentation is aimed at analysing the number of patients, age group, treatment progress report, cancer preponderance among cases like cancers of the cervix, prostate, breast and most common scan performed as well as the challenges and contribution of radiographers in nuclear medicine. **Methodology:** A total of 637 Radionuclide bone scan patients during the period were

presented. The diagnosis, biodata and results were analyzed using descriptive means. Patients for other scans were excluded. Tc-99m injected intravenously, doses ranged between 15–20mCi. Whole body delayed bone scan imaging was done 2–4 hours post injection. **Results:** skeletal metastases, the commonest clinical indication for radionuclide bone scan. 95% of patients were females with preponderance of left breast cancer. Larger numbers of men are for metastatic prostate cancer. affected age group is the productive age range of Nigerians (41–50) **Conclusion:** No effective cancer management can be achieved without Nuclear Imaging. Ability to use this imaging modality by Radiographers for imaging and staging cancer will go a long way in contributing positively in cancer prevention/management.

EP-0282

Role of planar whole-body scintillation gamma-camera imaging in Radium 223 biodistribution evaluation on bone metastases

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Introduction: Radium 223 dichloride (Ra223) is the only targeted alpha therapy able to extend survival in patients with bone metastases from prostate cancer. Mechanism of action and data currently available focused on high activity on bone metastases.

Material and Methods: In our institution, a patient with bone metastases was treated with Ra223, after obtaining informed consent. The evaluation of the deposit areas of Ra223 was assessed with a planar whole-body scintillation γ -camera imaging.

Results: After the first administration we performed a planar total body scintigraphy using the gamma photon of the Ra223. This procedure was repeated after each administration, highlighting a maximum retention percentage of Ra223 after the first administration and close to zero at the end of the treatment, in accordance with the complete remission of the lesions detected with technetium 99 scanning. Images showed the preferential uptake of Ra223 in gamma scintigrams overlapped the same lesions previously identified by computed tomography and technetium-99 scans. Currently the patients show to follow up the complete remission of bone disease. **Conclusions:** This report is the first document attesting Ra223 deposit metastases opening new opportunity of activity monitoring for this radiopharmaceutical. Authors conclude that the described technique is useful to have an immediate evidence of Ra223 uptake in bone lesions, presupposing subsequent therapeutic effect.

ETP-6

e-Poster Area

16. Radiation Exposure & Protection -> 4. Staff radiation protection

EP-0283

Optimization of Radiation Protection in the Preparation and Application of 18-FDG

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Background / Aims: Preparation and application of radiopharmaceuticals are activities that are associated with the exposure of workers to ionizing radiation. Mobile device KARI100, on the transport of radiopharmaceuticals 18-FDG for PET, and RAD-INJECT, for its application, offer the possibility to reduce the doses of radiation exposure to staff and the optimization of radiation protection in the workplace. Aim of the presentation is to compare the results of personal dosimetry before and after the installation of mentioned equipment. **Methods:** To compare was used the value of the collective dose for the years 2015 and 2016 for staff of Pharmacy Department (preparation of radiopharmaceuticals) and Nuclear Medicine Department (application of radiopharmaceuticals). The collective dose is here means the sum of doses of all staff a given section during 6 months. The collective dose $H_p(10)$ determines the personal dose equivalent at a given point beneath the surface of the body at a depth of 10 mm, taken as the value for the whole body dose; the collective dose H_T is the equivalent dose for hand. **Results:** From dosimetry measurements of Pharmacy Department is evident dose reduction on finger dosimeter by more than 40% after the installation of the device KARI100. The results of the measurement of whole body dosimetry are balanced both before and after the installation of the device KARI100. On Nuclear Medicine Department get from the beginning only to drop the values on the finger dosimeter, but a slight rise in the whole body dosimetry of doses as a result of the job training of staff with new technology. Both doses decreased of about 50% after training. **Conclusion:** By comparing the data from the years 2015 and 2016 get to reduce the values of collective doses for staff of the Pharmacy Department on finger dosimeter, the values of whole body dosimetry have remained at the same level, despite their slight increase assumption. For staff of Nuclear Medicine Department get to reduce the values of collective doses to the finger and whole body dosimeters.

ETP-7

e-Poster Area

17. Logistic -> 1. Patient Care

EP-0284

Effects of web-based information on patient satisfaction and image quality in patients undergoing an 18F-FDG PET/CT examination - a randomized controlled trial

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Purpose: The aim was to investigate the effect of web-based patient information on patients' satisfaction with care during an ¹⁸F-FDG PET/CT examination, their knowledge about the examination and the image quality, compared with standard care, and to explore the use and satisfaction with web-based information. **Subjects & Methods:** One hundred-forty-eight patients were recruited and randomly assigned to a Standard Care Group (SCG) or an Intervention Group (IG). Patients in SCG

received information about the ^{18}F -FDG PET/CT examination according to standard care and IG also received access to web-based information about the examination. A questionnaire was used to evaluate patient satisfaction, knowledge and discomfort and a blinded image quality assessment was conducted.

Results: The overall satisfaction was high in both IG and SCG. More patients in IG than SCG knew how the ^{18}F -FDG PET/CT examination was conducted. Descriptive data suggest that image quality was slightly better in IG than SCG but there were no statistically significant differences between the groups regarding any of the outcomes. Also, only 54 of 75 patients (72%) in IG used the web-based information. However, those who used the web-based information were satisfied and found it helpful.

Conclusion: Effects of web-based information need to be investigated in a larger sample of patients. Improved information before an ^{18}F -FDG PET/CT examination may increase patient knowledge and help them to prepare and undergo the examination. It may also improve image quality. However, this needs to be investigated using image quality as the primary outcome. The results may be used to improve patient information and care and thereby optimize the ^{18}F -FDG PET/CT examination procedure.

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