

POSTER PRESENTATIONS

P01 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Physics & Instrumentation & Data Analysis: Instrumentation

P001

A Method For Clinical Protocol Optimisation On A High Sensitivity Time-Of-Flight PET Scanner

D. L. Bailey, E. A. Bailey, G. P. Schembri, P. J. Roach; Royal North Shore Hospital, St Leonards, AUSTRALIA.

AIM: To investigate scanning parameters (dose injected, time per bed position) to derive an optimal protocol for whole body FDG PET scanning on the Siemens mCT with extended axial field of view (FoV) and time-of-flight coincidence detection. **METHODS:** Just before acquiring a standard whole body FDG PET scan at 60 minutes after injection of c.250MBq in routine clinical patients, we acquire a single bed position dataset for 160 seconds in list mode with a cardiac gating input signal supplied by an ECG simulator set to 60bpm (externally triggered gating, ETG (Bailey and Kalemis, Phys Med Biol 2005; 50:N55-N62)). During image reconstruction the data are reframed into 10 sec time bins (16 in total) and then combined in varying combinations to give different total acquisition times (10 secs, 20secs, etc up to 160 secs). ROIs are defined over tissues of interest such as areas of assumed homogeneity (e.g., liver), lesions, blood pool, etc across all reformatted studies. Image coefficient of variation (CoV%), lesion target:background, SUVmax and visual assessment are then used to examine the optimal compromise between dose injected and time per bed position. Data are corrected for attenuation and reconstructed using a fixed EM algorithm with resolution recovery enabled. **RESULTS:** Using the injected FDG dose described, the scanning time per bed position appears to start to plateau based on CoV% in liver at around 80 secs per frame. The mean count in the ROIs did not vary greatly over the entire range and lesion target:background was stable from approx.30 secs acquisition time. SUVmax was invariant from c.60secs to 160secs acquisition time with a maximum deviation from the assumed correct value in the shortest time frames of <20%. **CONCLUSION:** ETG provides a convenient way to acquire data with which to assess varying parameters such as different acquisition times and injected doses to achieve an optimum between injected dose and scanning duration. For the Siemens mCT with extended axial FoV there appears to be little gained in acquiring for greater than 90secs per bed position with an injected dose administered of c.250MBq.

P002

Adaptation of Gammacamera performance evaluation tests to new portable minigamma cameras.

L. Brualla¹, D. Granero¹, T. Gracia¹, A. Vicedo¹, J. Rosello¹, J. Ferrer¹, N. Pavón²; ¹ERESA- Hospital Universitario General of Valencia, Valencia, SPAIN, ²Corpuscular Physics Department (CSIC), Valencia, SPAIN.

Aims: Nowadays it seems that the use of portable mini gamma cameras in the clinical use is expanding and attracting more clinical users. Actually there are several well established protocols as the National Electrical Manufacturers Association (NEMA), to carry out the quality assurance of a gamma camera. These standards can be used as a guide to evaluate camera performance and to compare different types of gamma cameras, but the issue with the new mini gamma cameras would be to set if NEMA tests for standard gamma cameras are directly applicable to a portable mini gamma camera, taking into account that the main use of the mini gamma camera is the detection of a lesion in the operating room. **Material and methods:** We have performed NEMA tests to analyze the portable mini gamma camera Sentinella from ONCOVISION. We have added particular tests to show the ability of the portable mini gamma camera to distinguish the small type of lesions to be detected in clinical surgery. We have reproduced features that usually happen in the clinical scenario as having a small lesion near the injection point, having several lesions of different size and activity very close, at a different depth etc. **Results:** We have developed new tests using the NEMA tests as a base. These tests allow to characterize the clinical performance of the camera for the special needs in the operating room such as the ability to detect nearby lesions. Image quality is similar to that of the standard gamma camera. **Conclusion:** NEMA standards for gamma camera need to be adapted to the size and operating conditions of a portable mini gamma camera. Particular tests need to be added to evaluate the mini gamma camera capabilities in the clinical scenario.

P003

Comparison of depth-contrast of a pinhole-collimator against a parallel hole-collimator for Tc-99m scintigraphy

R. Rodriguez¹, W. T. Kranert², C. Happel², M. Ricciardi¹, W. Kleinekofort¹, F. Grünwald²; ¹University Rhein-Main; Department of physical engineering, Rüsselsheim, GERMANY, ²Hospital of the Johann-Wolfgang Goethe University, Frankfurt / Main, GERMANY.

Aim: Compared to a parallel-hole-collimator (parC) the use of a pinhole-collimator (pinC) in nuclear medicine diagnostics is recommended especially for high definition imaging of small objects, due to its higher spatial resolution. Aim of the study was to compare scintigraphic contrast of a pinC to a parC. The suggestive clinical use of the collimators is evaluated and discussed. **Methods:** Measurements were performed using a double-head scintillation-camera Ecam 180 (Siemens), with a pinC (length of tube 19.5cm; hole diameter 4mm); and a parC (LEHR; septa length 24.05mm; septa thickness 0.16mm; spatial resolution 6.4mm). A Jaszack Phantom equipped with 3 spheres of different volumes (2ml, 5.5ml, 11.5ml) was used as test object. Contrast was determined using different mediums around the spheres: air, water and radioactive (Tc-99m) water with varied gradients of activity concentration (1:50, 1:30, 1:10, 1:5) and activity concentrations of 0.5 - 1 MBq/ml Tc-99m in the spheres. The sphere of interest was

centered in the field of view. The distance between the central sphere and the collimator was 2.7cm or 14.1cm respectively, whereas the depth of the sphere in the surrounding medium was varied (5.4cm or 16.8cm respectively) as well. Contrast was specified visually and quantitative (counts/pixel) by ROI-evaluation of the whole sphere. The contrast c is defined as the mean number of counts in the sphere $[I]$ and in the background $[I_0]$ ($c = (I-I_0)/I_0$). The necessary count statistic to the secure determination of the contrast was determined using the 5.5ml sphere with an activity ratio of 1:30 by varying acquisition time (3 - 1,138s). **Results:** Despite their obviously decreased count rate pinC images showed better contrast compared to the parC images independent of detector-object distance between detector and sphere and the sphere volume. An increase of the time depending count statistic up to 10^5 counts/pixel did not improve contrast noticeably. The contrasts determined with the pinC were $1.55 \pm 20\%$ times higher. In contrast to the parC the smallest sphere (2ml) can be depicted with the pinC for an activity concentration of 1:30 in a depth of 16.8cm and 1:5 in a depth of 5.4cm respectively, while depiction failed with the parC. **Conclusion:** Due to its higher contrast and higher resolution in the depth, the pinC is superior compared to the parC especially in the high definition imaging of small structures. The disadvantage of the PinC compared to the parC is its low effectivity leading to decreased count statistics or increased acquisition time.

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Physics & Instrumentation & Data Analysis: NEMA performance measurements

P004

NEMA 2007 performance characteristics of the Siemens mCT PET/CT camera

J. R. de Jong¹, F. Schoenahl², R. Wiert¹, S. Lazarenko¹, M. Segbers¹, R. A. J. O. Dierckx¹, A. M. J. Paans¹, A. T. M. Willemsen¹; ¹Univ. Hosp. Center Groningen, Groningen, NL, ²Siemens Healthcare, Erlangen, GERMANY.

AIM: The Siemens mCT PET/CT camera is the first system to incorporate both high definition (HD) technology and time of flight (TOF). We performed performance measurements according to NEMA 2007 with special focus for the effect of HD and TOF on image quality. **METHODS:** Measurements were performed according to the NEMA NU 2-2007. Note that this means that the resolution measurements are done without taking advantage of HD or TOF. Data was analyzed using the NEMA 2007 software courtesy of Siemens Medical. In our hospital the Siemens mCT is a 4-ring system with a 64 slice CT. For image quality testing all images were reconstructed with a matrix size of 400, a gaussian filter of 2 mm and using 3 iterations with 24 subsets (OSEM / HD) or 21 subsets (HD + TOF). These settings are comparable to those used in clinical scans. **RESULTS:** Results of the NEMA measurements are summarized in table 1. The following findings are of particular interest: **Sensitivity:** Although the FOV has been increased to 78 cm, system sensitivity of the mCT is maintained. The reason is that a maximum ring difference for coincident detector pairs is no longer employed. Although this could also be the reason why the axial resolution away from the center of the FOV degrades faster for filtered back-projection, this latter effect will at least partially be countered by the inclusion of point-spread functions in the HD reconstruction. **Image Quality:** From the results for the image quality measurements there is a clear improvement in contrast recovery coefficient (CRC) and a slight improvement in background variability between OSEM and HD. For the smallest sphere diameter with 4:1 contrast there appears to be no difference indicating that HD may not have reached convergence yet. When employing the TOF capabilities of the mCT there is once again an increase in the CRC. This increase is largest for the smaller sphere and for the cold spot CRC's. This may be indicative of faster convergence for small lesions with TOF as well as lower amounts of noise, scatter and spill-over into colder regions. The latter observations concerning cold spot recovery are also supported by a decrease of residual errors in the lung insert with TOF. **CONCLUSION:** The combination of HD and TOF technology in the latest generation of Siemens PET/CT camera's brings about a marked increase in image quality and lesion recovery when compared to traditional 3D-OSEM.

Timing resolution	552 ps												
Energy resolution	11.20%												
Spatial resolution (FBP)	Radial r = 1 cm		Radial r = 10 cm										
	Transverse	Axial	Radial	Tangential	Axial								
FWHM	4.3	4.4	5.2	4.7	5.9								
FWTM	8.7	8.7	9.4	9.3	11								
Sensitivity	9.7 kcps / MBq		9.5 kcps / MBq										
	k = 1		k = 2										
Peak NEC rate (kcps)	185		130										
Scatter fraction (%)	35.5		34.6										
	Sphere diameter (mm)												
Reconstruction	10	13	17	22	28	37							
Hot sphere contrast	4:1	8:1	4:1	8:1	4:1	8:1	4:1	8:1					
	CRC (%)	46	48	56	62	64	68	70	74	75	74	77	79
3D-OSEM Variability (%)	9.7	8.4	7.5	6.4	6	5.1	4.9	4.2	3.9	3.6	3.1	3.1	
	Lung error (%)	17.2	17										
HD	CRC (%)	44	61	70	77	68	73	74	79	74	73	78	79
	Variability (%)	7.2	6.4	6	5.3	4.9	4.4	4	3.7	3.3	3.3	2.8	2.9
HD+TOF	Lung error (%)	16.7	16.8										
	CRC (%)	61	73	81	84	66	70	79	83	81	80	88	89
HD+TOF	Variability (%)	8.5	6.9	7.4	6.1	6.4	5.5	5.6	5.1	5	4.7	4.3	4.1
	Lung error (%)	8.5	8.6										

P005**NEMA NU4-2008 Comparison of Three Generations of Siemens Preclinical PET Systems**

A. L. Goertzen¹, Y. Tai², Q. Bao³, A. Chatziioannou³, R. Laforest²,
¹Department of Radiology, University of Manitoba, Winnipeg, MB, CANADA,
²Department of Radiology, Washington University School of Medicine, St. Louis, MO, UNITED STATES,
³Crump Institute for Molecular Imaging, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, UNITED STATES.

Objectives: The NEMA Standards Publication NU4-2008 for Performance Measurements of Small Animal Tomographs was recently published in final form. In this work, the NU4-2008 standard is used to evaluate five animal PET systems that span three generations of Siemens small animal PET system production. Data are presented for the P4, R4, Focus 220 and Focus 120 microPET systems along with the Inveon dedicated PET system. **Materials & Methods:** Data were acquired from each PET system according to the NEMA NU4-2008 methods. Measurements performed include: 1) Spatial resolution, as measured with data reconstructed using Fourier rebinning followed by 2D-FBP reconstruction; 2) System scatter fraction and count rate performance for the mouse and rat phantoms for all systems and the monkey phantom for the P4 and Focus 220 systems; 3) Sensitivity using a Na-22 point source; and 4) Image quality, accuracy of attenuation and scatter corrections and recovery coefficients using the NU4 image quality phantom, reconstructed with Fourier rebinning followed by 2D-FBP reconstruction. **Results:** Due to space limitations, we only include in this abstract a subset of the results comparing the oldest (P4) system against the newest (Inveon) system. 1) Spatial resolution: The spatial resolution (tangential/radial/axial) at the 5 mm offset position was 2.29/2.18/2.20 mm for the P4 and 1.63/1.62/2.45 mm for the Inveon. 2) Scatter fraction: For the rat phantom, the scatter fraction was 16.3% for the P4 with an energy window of 350-650 keV and 17.2% for the Inveon with an energy window of 350-625 keV. NECR: The peak NECR for the rat phantom was 173 kcps @ 280 MBq for the P4 and 590 kcps @ 110 MBq for the Inveon. 3) Sensitivity: The peak absolute sensitivity in the central slice was 1.19% for the P4 with an energy window of 350-650 keV and 6.74% for the Inveon with a window of 350-625 keV. 4) Image quality: The recovery coefficients for the P4 were 0.11 and 0.86 for the 1 and 5 mm rods, respectively. The corresponding values for the Inveon were 0.17 and 0.93. The spill-over ratio for the water and air filled cylinders (with attenuation and scatter correction applied) were 4.89% and 4.03%, respectively, for the P4 and 1.65% and -0.57% for the Inveon. **Conclusion:** NEMA NU4-2008 performance results are presented for three generations of Siemens animal PET systems. As expected, each generation has shown an improvement in performance relative to that of the earlier generation.

P006**Optimisation of I-124 acquisition parameters with the NEMA NU 4-2008 performances assessment for the Inveon PET system.**

N. Anizan¹, T. Carlier¹, C. Hindorf², M. Bardières¹; ¹INSERM, U892, Nantes, FRANCE, ²ONIRIS, Nantes, FRANCE.

Introduction: The use of I-124 in the context of radioimmuno therapy requires specific PET acquisition settings as I-124 has a complex decay scheme. The PET camera investigated in this study was the Inveon dedicated PET/CT system for small animal imaging. **Methodology:** The acquisition parameters were optimised based on the NEMA NU 4-2008 procedure. The Noise Equivalent Count Rate (NECR) was measured with mouse and rat-sized phantoms. The energy and timing windows were optimised with the maximisation of NECR curve and subsequent NEMA index were assessed with this set-up. The sensitivity and the spatial resolution were evaluated for the whole field of view (FOV) with a micro sphere and a capillary tube, respectively. Different reconstruction algorithms with and without scatter and attenuation corrections were assessed on the dedicated image quality phantom proposed by the NEMA protocol. **Results:** The upper energy threshold for the NECR maximum was determined to be 550 keV for the rat phantom, and 590 keV for the mouse phantom. The lower energy threshold (LLD) was 390 keV for the rat phantom. However, the peak NECR increased continuously for the LLD for the mouse phantom. As a consequence, we chose to evaluate two different LLD (250 and 400 keV) for this phantom. The NECR peak was found to be highest for the 250-590 keV window. This large energy window increased the sensitivity from 4.6% to 7.5% whilst the spatial resolution at the center of FOV was independent of the energy window. The activity concentration measured in the background of the image quality phantom was underestimated for both the 400-590 keV window (-13%) and the 250-590 keV window (-17%). **Conclusion:** The NECR maximisation with energy threshold variation was not enough to evaluate the best acquisition parameters for I-124 small animal imaging. A complete set of figures of merit must be acquired before choosing the optimal acquisition parameters for a given radionuclide.

P007**Performance evaluation of a hand held gamma camera MINICAM II according to NEMA standards.**

M. Constantinides; Theageneio Anti Cancer hospital, Thessaloniki, GREECE.

Introduction: A small field of view, hand held gamma camera, MINICAM II, has been developed for accurate location and visualization of tumors, sentinel lymph node and thyroid tissue during radiopharmaceutical guided surgery. The system utilizes fast signal processing electronics, allowing the display of the image and counting rate on an LCD screen. **Aim:** This study aimed to evaluate the performance of MINICAM II applying an acceptance testing and quality control protocol, according to the procedures of NEMA standards. **Materials & Methods:** The detector consists of 256 discrete CdTe elements (2.46x2.46x5mm³) mounted in 16x16 matrix, providing a FOV=40x40mm². One parallel-hole tantalum collimator (LEHR) 24 mm thick is provided. Images were recorded in a bitmap file on MMC memory card supplied. Display and data analysis were performed on a PC via MMC memory card reader. The following tests, included in the protocol, were performed according to NEMA standards: i. System extrinsic uniformity at the central field of view(CFOV), placing Tc-99m flat source phantom in front of the camera. ii. energy resolution, FWHM of the energy spectrum and iii. system sensitivity, placing Tc-99m source phantom of 37

MBq in front of the camera iv. contrast test (signal to noise ratio,SNR) and v. spatial resolution in air, using Tc-99m line source of 1.1 mm diameter vi. count rate characteristics and vii. dead time using Tc-99m sources in lead shielded vials, viii. side shielding, ix. system response for various source depths in tissue. **Results:** System uniformity at CFOV: 20.8 energy resolution: FWHM was not possible to be measured yet, because data was not in readable format. Sensitivity: 1.38 cps/MBq. Spatial resolution: FWHM at the surface of collimator: 2.4 mm Count rate characteristics: Maximum count rate 650 cps and 20% loss count rate 231 cps. Dead time: 0.9618 x 10⁻⁴ sec. Side shielding: leak sensitivity <0.1% of system sensitivity system response for various source depths in tissue. System response for various source depths in tissue: attenuation coefficient found equal to 0.42 cm⁻¹. **Conclusions:** MINICAM II performance is comparable with the existing hand held gamma camera. It can be of value for sentinel node detection, parathyroid radioisotope-guided surgery (Tl-201) and thyroid Tc-99m uptake measurements, since it can also be steady while fastened onto a probe holder.

P008**Comparative measurement of I-124 and F-18 on Siemens ECAT HR+ PET Scanner**

Y. Lee¹, J. Kim¹, K. Kim¹, A. Yu¹, J. Kim¹, J. Park¹, W. Lee¹, S. Woo¹, H. Kim², K. An¹, G. Cheon¹; ¹Molecular Imaging Research Center, Korea Institute of Radiological & Medical Sciences, Seoul, KOREA, REPUBLIC OF, ²Department of Radiological science, Yonsei University, Wonju, KOREA, REPUBLIC OF.

Objectives : Although I-124 has a complex decay scheme with higher gamma energy and poor positron abundance, I-124 PET was useful in radiation dosimetry of I-131. In this study, comparative measurement of I-124 and F-18 was performed using both 2D and 3D PET on Siemens HR+ PET scanner. **Methods :** For the comparison of spatial resolution and sensitivity of I-124 and F-18, measurement was performed using NEMA NU2-2007. For the comparison of image quality of I-124 and F-18, NEMA IEC body phantom which consisted of 6 hot spheres (inner diameter: 37, 28, 22, 17, 13, and 10 mm) were filled with I-124 or F-18 solution. The concentration of the background activity in the phantom was 5.3 kBq/mL and those of hot spheres were 4 times of the background. Image quality measurements were performed using both brain PET (pixel size: 0.51 x 0.51 mm²) and whole body (WB) PET (pixel size: 3.96 x 3.96 mm²) in both 2D and 3D PET for 320 sec, and reconstructed using OSEM algorithms (subset 16, iteration 2) with Hanning filter. %contrast and background variability were calculated. **Results :** Spatial resolution using brain mode at center was 5.20 mm in I-124 and 4.07 mm in F-18. Sensitivity was 0.02 and 0.09% (2D) and 0.17 and 0.50% (3D) in I-124 and F-18, respectively. %contrast of I-124 was 29, 38, 52, 72, 84, and 94% for 10, 13, 17, 22, 28 and 37 mm hot spheres using WB PET. %contrast of F-18 was 2, 16, 24, 59, 72, and 83%. Background variability was approximately 31% in I-124 and 15% in F-18 using 2D WB PET. In 3D brain mode PET, %contrast of I-124 was also lower than those of F-18. Background variability of I-124 was also two times higher than those of F-18. **Conclusions :** In this study, image characteristics of I-124 and F-18 was compared. For the consistency of image quality of I-124 PET compared to F-18 PET, optimal PET scan time should be considered.

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Physics & Instrumentation & Data Analysis: Image quality & correction**P009****Evaluation of two available fully 3D reconstruction algorithms implemented on a clinical PET-CT scanner**

F. Fioroni, E. Grassi, R. Sghedoni, M. Sarti, A. Versari, D. Salvo, G. Borasi, M. Iori; S. Maria Nuova Hospital, Reggio Emilia, ITALY.

Purpose: The aim of this study was to evaluate the performances of the new VUE Point High Definition (VP HD) reconstruction algorithm implemented on our GE Discovery STE 16 (DSTE) scanner, with particular reference to lesion detectability in oncologic applications. **Material:** The 3D VUE Point High Definition algorithm, an evolution of the previous 3D VUE Point (VP), incorporates the crystal efficiency, detector deadtime, the native block-based detector geometry and volume scatter correction. In this study the impact of different parameters of iterative reconstruction were evaluated. According to the NEMA 2001 standard, spatial resolution and image quality tests were performed. All the measurements were performed using a complete set of NEMA NU-2 2001 PET phantoms provided by Data Spectrum Corporation (Hillsborough, NC, USA). To control the results obtained with the standard GE package and to allow the calculation of different parameters (in particular the signal-to-noise ratio) a new software program was developed. The image quality characteristics of VP and VP HD algorithms were also analyzed by a visual experiment performed by trained Nuclear Medicine clinicians on total body oncological images. **Results:** The new VUE Point HD algorithm, thanks to the new detector geometry modeling, showed an improved resolution in transverse plane (FWHM 1cm off-axis transaxial spatial resolution 4.32 mm for VP and 3.61 mm for VP). The VP HD gave higher Hot Sphere Contrast Recovery Coefficients than the values obtained with the previous algorithm (for the smallest sphere, the Hot Contrast Recovery Coefficient was 17.4 for VP and 22.5 for VP HD). The use of a homemade image evaluation program revealed very useful to complement the Company standard program, implementing the NEMA protocol. This tool allowed the calculation of important parameters to characterize the IQ performance of the scanner in particular the background noise and, most importantly, the signal-to-noise ratio. This latter parameter is probably the most meaningful for IQ evaluations and, in our case, accounts for the clinicians' preference for the new VP HD algorithm. **Conclusion:** The studies showed that iterative reconstruction VUE Point HD provided better results than VUE Point in terms of spatial resolution, contrast image and signal-to-noise ratio, making this new this reconstruction algorithm suitable for oncological practice.

P010**Influence of High-Definition and Time-of-Flight Reconstruction Techniques on Recovery Coefficients of PET Images**

R. Wierts, S. V. Lazarenko, J. R. de Jong, M. Segbers, A. M. J. Paans, R. A. J. O. Dierckx, A. T. M. Willemssen; University Medical Center Groningen, Groningen, NETHERLANDS.

Aim: With the introduction of time-of-flight (ToF) and high-definition (HD) reconstruction techniques in the current generation of PET/CT scanners, image quality has improved significantly. In this study, the influence of HD and HD+ToF reconstruction techniques on the recovery coefficients (RC) of PET images is investigated. **Materials and methods:** The NEMA IEC body phantom is measured with a 64 slice Biograph mCT scanner (Siemens). All spheres, with inner diameters of 10, 13, 17, 22, 28 and 37 mm, are homogeneously filled with an ^{18}F -Fluorodeoxyglucose solution with an activity concentration of 21.5 kBq/ml. Measurements are performed with different background activity concentrations corresponding to signal-to-background ratios (SBRs) of infinity, 8.7, 5.4, and 2.6. The acquisition time per scan is 10 minutes. The obtained PET data are reconstructed to a 400x400 matrix, corresponding to a 2.0 mm transaxial pixel size, and a slice thickness of 2 mm using different reconstruction techniques: OSEM3D (3 iterations, 24 subsets), HD (3 iterations, 24 subsets) and HD+ToF (3 iterations, 21 subsets). Images are reconstructed using both a 3 mm and a 5 mm Gaussian filter. For each reconstructed image, a region is drawn for each sphere using a region growing segmentation technique with a 40% (background corrected) activity concentration threshold. **Results:** For both the 3 mm and 5 mm reconstructed images, the HD and HD+ToF reconstruction algorithms result in a significant increase in RC for each sphere compared to the OSEM3D algorithm without any significant differences between the HD and HD+ToF algorithms. For the HD and HD+ToF reconstructed images with 3 mm post-filtering, the RC is independent of both SBR and sphere diameter (except for the smallest sphere) and are 0.88 ± 0.05 for the HD and 0.87 ± 0.04 for the HD+ToF reconstruction techniques. For the 3 mm post-filtered OSEM3D reconstructed images, the RC increases with increasing sphere diameter and decreasing SBR due to the relatively low spatial resolution of the OSEM3D algorithm. For the 5 mm filtered images, the RC decreases with decreasing sphere volume and slightly increases with increasing SBR as a result of decreased spatial resolution compared to the 3 mm post-filtered reconstructed images. **Conclusions:** The HD and HD+ToF reconstruction algorithms result in a significant improvement of the RC and decrease in partial volume effects compared to the OSEM3D algorithm using the NEMA IEC body phantom. No significant difference in RC is found between the HD and HD+ToF algorithm.

P011**Correction for Scatter Using Modified Beam Stopper Method Integrated with The Dual Energy Method**

C. Lin, H. Lin, K. Chuang; Biomedical Engineering and Environmental Sciences, National Tsing Hua Univ., Hsinchu, TAIWAN.

Aim: Fully three dimensional (3D) positron emission tomography (PET) can achieve higher sensitivity of coincidence events, but the absence of inter slice septa inevitably leads to an increase of scatter events. The scatter contributes 30~50% of the total events in 3D data and it decreases the image contrast and underestimates the radioactivity. Therefore, a robust and flexible scatter correction method is necessary to remove the contamination of scatter. In this study we describe an improved dual-energy window (DWE) method which can provide a better estimate of scatter distribution. **Materials & Methods:** The DWE method was applied to scatter correction in 3D brain PET by Grootoontk et al. This method assumed that the spatial distribution of counts in lower energy window was proportioned to counts in upper energy window. However, in reality, the scatter in upper energy window (dominated by single scatter) is spatially less related to the distribution in the lower window (contributed by multiple scatter mostly). The conventional beam stopper (BS) method can accurately estimate the shape and amplitude of scatter distribution. Using dual scans, with and without BS, this technique is able to corrections of multiple scatter events and scatter events contributed from out of FOV. In this work, we propose a hybrid scatter correction method that integrated the DWE method and the one-scan BS method. Note that in this research, the BS method needs one scan (with BS) only, and information of without BS scan can be calculated from a simple interpolation. The scatter fractions at those blocked lines of response were measured through the one-scan BS method directly, and then the entire scatter fraction was restored based on the information provided by the DWE method. **Results:** SimSET (Simulation System for Emission Tomography) Monte Carlo (MC) simulations of a HR+ PET scanner on asymmetric and inhomogeneous phantoms were performed to validate the proposed approach. Preliminary results demonstrated that the proposed method provided more accurate prediction of scatter distribution and achieved a better image restoration compared to the DWE method. **Conclusion:** The hybrid method provided an accurate way to correct the scatter in 3D PET, taking various kind of scatter into account, including the scattered events from outside of FOV and multiple scattered events. Furthermore, it can improve contrast-to-noise ratio and yield better uniformity compared to the DWE method.

P012**Scatter correction for PET image with beam stoppers in one single scan**

S. C. Chen¹, K. Chuang², C. Lin², H. Lin², M. Jan³; ¹Kaohsiung Medical University, Kaohsiung, TAIWAN, ²National Tsing-Hua University, HsinChu, TAIWAN, ³Institute of Nuclear Energy Research, Taoyuan, TAIWAN.

Aims: Modern PET scanners generally perform 3D counting with septa retracted to improve the counting statistics. The scatter fraction can surge to as high as 40%. Scattered radiation reduces contrast and leads to the overestimation of reconstructed radioactivity concentrations. Scatter correction is important for accurate quantitative analysis study. In our previous study, we successfully use beam stopper (BS) device for scatter correction. However, the method requires dual scans (with and without the BS) to estimate the scatter component in the sinogram that might cause misregistration error. This study uses only one single scan with BS for scatter correction. **Materials & Methods:** The missing part (at the position where the BS intercepting primary beams) in the sinogram without BS is estimated from its neighboring pixels via

interpolation. Once the missing data was recovered, we can process the scatter correction as previous method described. The scatter component at the location blocked by each BS can be estimated. Assuming that the scattered radiation has a spatially slow-varying distribution, the whole scattered sinogram can be obtained from curve fitting of these local measurements. **Results and Conclusion:** Simulated data using the SIMSET simulation package and clinical data of a PET/CT scanner were employed to demonstrate the effectiveness of this algorithm. Preliminary results indicated that this technique enhances the image contrast and quantitative accuracy. The proposed method is a direct, fast, and simple technique for scatter correction. The main error comes from the interpolation of missing scan without BS.

P013**Factors influencing the PET image quality of the Siemens Biograph mCT**

R. Wierts, J. R. De Jong, S. V. Lazarenko, M. Segbers, A. M. J. Paans, R. A. J. O. Dierckx, A. T. M. Willemssen; University Medical Center Groningen, Groningen, NETHERLANDS.

Aim: Two factors influencing PET image quality of the Siemens Biograph mCT are investigated for the OSEM3D, HD and UHD reconstruction algorithms: 1) the effect of low-mAs CT scans used for PET attenuation correction, 2) the number of iterations applied for image reconstruction. **Materials and methods:** The NEMA IEC body phantom was scanned with a Siemens Biograph mCT scanner with TrueV PET and a 64 slice CT. All spheres, with inner diameters of 10-37 mm, were filled with an ^{18}F -Fluorodeoxyglucose solution with an activity concentration of 13.6 kBq/ml in a background of 1.56 kBq/ml. Six CT scans of the phantom were acquired using effective reference values of 5, 10, 20, 30, 50 and 100 mAs with 100 kV tube voltage. Subsequently, a single PET data acquisition scan of 16 minutes was performed. Each CT scan is reconstructed using the Siemens B19f low dose kernel with a slice thickness and increment of 2 mm. PET reconstruction was performed with 3 iterations and 24 (OSEM3D/HD) or 21 (UHD) subsets for each CT mAs. PET images were smoothed with a 5 mm Gaussian filter. The effects on the recovery coefficient (RC) of each sphere, determined by a 40% threshold region growing segmentation technique, and the signal-to-noise ratio (SNR) are investigated. For the 30 mAs CT scan, additional reconstructions, using 4, 5, 6 and 10 iterations, were performed for each reconstruction algorithm. The effect of the number of iterations on the RC is investigated. **Results:** No significant differences for both the RC and SNR were observed with varying CT mAs values for any of the reconstruction algorithms. For the HD and UHD reconstruction algorithms, increasing the number of iterations from 3 to 10 iterations results in a steady increase in RC for the smallest sphere from 0.48 to 0.59 (+23%) for the HD and from 0.53 to 0.59 (+11%) for the UHD algorithm, whereas no increase in RC is observed for the OSEM3D algorithm. Note however, that the RC for OSEM3D remains lower than for HD and UHD due to resolution effects. **Conclusions:** For the NEMA IEC body phantom, the PET image SNR and the RCs are independent of the CT mAs value for effective mAs values larger than 5. Image reconstruction convergence is slower for the HD and UHD algorithm than for the OSEM algorithm. This is particularly evident for the smallest sphere although values of the RC are still superior to OSEM.

P014**Comparison of SUV for Time-of-Flight (TOF) and non-TOF reconstructions on the 128-slice mCT**

L. Wen, S. Eberl, A. Waugh, A. Brewer, J. Brackenreg, A. Mohamed, J. D. Verschuer, M. J. Fulham; PET & Nuclear Medicine, Royal Prince Alfred Hospital, Sydney, AUSTRALIA.

Aim: To compare SUV for Time-of-Flight (TOF) and non-TOF reconstructions on the Siemens 4-ring 128-slice mCT PET-CT. **Methods:** We analysed 52 consecutive whole body FDG PET-CT patient studies; the studies extended from the vertex to the upper thighs. Each study was reconstructed with TOF (4 iterations, 21 subsets) and non-TOF (3 iterations, 24 subsets) High-Definition reconstruction algorithms supplied by the vendor. Attenuation, randoms and scatter corrections were included and a 4 mm FWHM Gaussian post reconstruction filter was applied. Spherical volumes of interests (VOI) with diameters of 20 mm were defined for brain, liver, lung, and areas superior and lateral to the bladder. The region size and locations were chosen to minimize partial volume effects due to potential differences in resolution between the two algorithms. The same VOI size and location were used to derive average SUV for TOF and non-TOF reconstructed images. **Results:** The absolute difference of SUV between the reconstructions was calculated as $SUV_{TOF} - SUV_{non-TOF}$; results are shown in Table 1. The differences in SUV were site dependent. The TOF reconstruction led to slightly lower SUV in the brain and liver as well as the areas superior to the bladder and slightly higher SUV were observed in areas lateral to the bladder. The mean bias is small (<0.3 SUV units for all regions) and maximum difference reaches 1.0 SUV units in the brain. Table 1: SUV difference between TOF and non-TOF reconstructions

	Brain	Liver	Lung	Bladder-S*	Bladder-L*	Bladder-R*
Mean	-0.21	-0.08	0.01	-0.04	0.13	0.11
SD	0.18	0.08	0.04	0.11	0.14	0.14
Max	0.16	0.11	0.14	0.25	0.46	0.55
Min	-1.02	-0.37	-0.08	-0.30	-0.20	-0.28
Mean SUV	6.43	1.77	0.31	0.81	0.58	0.60

* Bladder-S: superior to the bladder; Bladder-L: lateral to the bladder (left); Bladder-R: lateral to the bladder (right) **Conclusion:** We found region dependent differences in SUV between the different reconstruction algorithms. The mean and maximum differences were generally small; we suggest that the same reconstruction algorithm is used for repeat studies.

P04 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Physics & Instrumentation & Data Analysis: Reconstruction

P015

Somatostatin receptors' detectability: the role of SPECT acquisition modality

F. Voltini, G. Marotta, C. Canzi, M. Schiavini, F. Zito, P. Gerundini; Nuclear Medicine Department Fondazione IRCCS Cà Granda - Ospedale Maggiore Policlinico, Milan, ITALY.

Aim Various SPECT acquisition modalities are available in several γ -cameras to improve image quality. The aim of this work was to study, for three SPECT systems, the effects on the performance in somatostatin receptors' detectability due to different acquisition orbits: body-contour and circular orbits. **Materials and Methods** The γ -cameras SYMBIA (Siemens), IRIX (Philips) and Millennium-VG (G&E) were all equipped with medium energy collimators with planar resolution respectively: 11.4, 10.7 and 10.4 mm. The comparison was performed simulating SPECT examinations on patients, using an anthropomorphic Alderson phantom containing lungs, heart, liver and 8 spherical inserts ($0.3 \pm 1.8 \text{ cm}^3$) to simulate tumoral foci in lung, liver and abdomen. The heart was filled with water and the lung with styrofoam beads. The mediastinal, abdominal, liver and lesion cavities were filled with water solutions of ^{111}In of different concentrations. SPECT scans were performed with step and shoot over 360° , $3^\circ/\text{step}$, with 4.7 mm pixel. The body contour orbit for SYMBIA and VG followed the body profile by an automatic device while for IRIX was defined by the operator before the acquisition. The anthropomorphic phantom was acquired with both circular and body-contour orbits for each γ -camera. Data were reconstructed by FBP and Butterworth filter utilizing the software provided by each gamma-camera. The images were analyzed to calculate: a) the contrast to quantify the detectability for each of the eight lesions in the phantom acquired both with circular orbit (Contrast-CO) and body-contour orbit (Contrast-BC) b) a paired t-test between corresponding Contrast-CO and Contrast-BC values. **Results** The table reports the mean of contrast values of measurements performed for both orbits by each γ -camera and the results of paired t-test.

	M.-VG	IRIX	SYMBIA
Mean-Contrast-CO	54.5	44.3	49.0
Mean-Contrast-BC	58.1	45.0	52.1
p	0.02	N.S.	N.S.

Conclusion The shape of the orbit differently affects the contrast values in fact the mean values for body-contour orbit is higher than corresponding values obtained with circular orbit for all the SPECT systems. However the paired t-test is significant only for Millennium-VG, this indicates that the differences between the Contrast-BC and Contrast-CO values depend on the type of gamma camera used. Only Millennium-VG seems to guaranty better somatostatin receptor detectability, for all the lesions, when SPECT acquisition is performed with body contour orbit rather than with circular orbit probably because of its particular technical features.

P016

Segmentation of PET volumes: effect of LOR-RAMLA reconstruction parameters

A. Martineau¹, J. M. Rocchisani², D. Groheux¹, J. L. Moretti¹; ¹Saint Louis Hospital, Paris, FRANCE, ²Avicenne Hospital, Bobigny, FRANCE.

Aim The purpose of this study is to assess the effect of reconstruction parameters of Line-Of-Response Row-Action Maximum Likelihood Algorithm (LOR-RAMLA) on a Signal-to-Background Ratio (SBR)-based adaptive thresholding of 18FDG PET images. **Materials & methods** The study was performed on a Gemini XL PET/CT scanner (Philips Medical Systems). We used the NEMA IEC/2001 image quality phantom to establish three calibrations curves of the optimal thresholding for adequate sphere volume segmentation versus the measured SBR on reconstructed slices. The calibration curves were deduced from five 2-minutes per bed acquisitions and three different relaxation parameter values of the LOR-RAMLA reconstruction: 0.025 ('smooth'), 0.05 ('normal') and 0.1 ('sharp'). The experimental SBR was between 8.8 to 1.8 and the spheres volumes were between 0.5, 1.1, 2.7, 5.2, 10.9 and 26.4 mL. For each sphere volume, the optimal thresholding was iteratively calculated to reach the actual volume of each sphere. The plots of the optimal thresholding versus the measured SBR were fitted using an inverse function already described by Daisne *et al* ($y = a + b/x$). An experimental study was conducted with the same phantom and a SBR value of 10 in order to validate the calibration curves for the three different LOR-RAMLA reconstructions. **Results** The fitting parameters (a,b) of the inverse function are (30.11%, 72.43%), (29.35%, 74.12%) and (32.44%, 59.44%) respectively for 'smooth', 'normal' and 'sharp' LOR-RAMLA reconstruction. Curves mainly differ for measured SBR values less than 3. In the experimental validation study, the maximal error on segmented volumes were 1.5 mL, 1.8 mL and 2.3 respectively for 'sharp', 'normal' and 'smooth' reconstruction. We found similar performances except for a measured SBR value less than 3 where the 'sharp' LOR-RAMLA reconstruction has better results. **Conclusion** The calibration curves for SBR-based adaptive thresholding have been computed for three relaxation parameters value of LOR-RAMLA reconstruction and have been validated on a phantom study. 'Sharp' LOR-RAMLA reconstruction performs better for measuring volumes than the two others reconstructions. More intensive experimental validations are needed to confirm these results with a larger range of SBR.

P017

An application of motion blur filter to continuous mode acquisition in SPECT imaging

J. Sato, N. Nakagami, A. Okizaki, Y. Ishikawa, Y. Kusano, K. Watanabe, M. Shiba, T. Aburano; Asahikawa Medical College Hospital, Asahikawa, JAPAN.

Objective: In single-photon emission computed tomography (SPECT), a continuous mode acquires the projections with rotational motion. Therefore, motion blur can occur in all projections unidirectionally. In this study, a restoration filter is dealt to improve the projection images with motion blur. **Methods:** Wiener deconvolution method has widespread use in image deconvolution applications, as the blurred image restoration. We implemented a new restoration filter to compensate for the motion blur using the Wiener deconvolution method on the basis of the direction-dependent. To evaluate the validity of the filter effect, computer simulation with numeric digital phantom was performed. Simulated projection images of the continuous mode were generated as brain simulated data. This simulation study was calculated using the software "Prominence Processor" developed by Maeda. The projection datasets of continuous mode were processed by this proposed filtering method using MATLAB. After the reconstruction with FBP, the transaxial images of the conventional and proposed methods were compared to the static mode SPECT using Normalized Mean Square Error (NMSE) method. Furthermore, image contrast of the practical brain SPECT was compared with the proposed filtered image. **Results:** The results showed that the images of continuous SPECT acquisition could be improved visually by the application of motion blur filter. In the simulation study, the average values of NMSE slightly improved from 0.123 to 0.116 by the proposed method. The contrast of the brain SPECT images was increased from 0.60 to 0.73 with this filter. **Conclusion:** In continuous mode acquisition of SPECT, the application of motion blur filter could improve the image quality.

P018

A practical device-dedicated whole-body PET reconstruction method: impact on standardized uptake values in clinical studies

J. Daouk, P. Bailly, L. Fin, M. Meyer; CHU Amiens, Amiens, FRANCE.

Aim 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET) has proven relevance in oncological diagnosis, staging and follow-up. The standardized uptake value (SUV) is one of the most widely used criteria for image interpretation. However, factors such as noise and image resolution affect the measurement of this value. We previously reported a device-dedicated projector based on point-source measurements used in attenuation-weighted ordered-subsets expectation maximisation (AWOSEM) algorithm; it is easily applicable on a clinical gantry, introduces less noise than a geometrical model. Generated images do not require as many 3-dimensional (3D) Gaussian post-filtering operations. The present study sought to evaluate our reconstruction method under clinical conditions. **Material and Methods** All acquisitions were performed on a Biograph(TM) 6 PET/CT gantry (Siemens Medical Solutions). We compared our reconstruction method (AWOSEM_DR) with a standard clinical reconstruction method (AWOSEM_CL). To obtain similar noise levels in each technique, 3D Gaussian post-filters of 5.0 mm and 2.4 mm were applied to AWOSEM_CL and AWOSEM_DR reconstructions, respectively. Firstly, two parameters were extracted from images of a NEMA IEC body phantom with a contrast of 8:1: (i) the relative error (RE) with reference to the true contrasts between the spheres and the background and (ii) the noise (i.e. standard deviation) in both the background and the spheres. Secondly, maximum and average SUVs (SUVmax and SUVavg, respectively) and tumor volumes were calculated for 32 lesions (from 10 patients) with each method. **Results** The RE was systematically lower with AWOSEM_DR. The mean RE over the 6 spheres was 31% with AWOSEM_CL and fell to 20% with AWOSEM_DR. The two methods did not differ significantly in terms of the SUVavg measured in healthy livers. However, a Wilcoxon test revealed significant inter-method differences for SUVmax and SUVavg (both $p < 0.001$) and the lesion volume ($p < 0.005$) in cancer patients. A Bland-Altman analysis showed a shift of 1.4 ± 0.8 in the mean value of the difference for SUVmax (range: -0.1 to 3.7; 95% confidence interval (CI): -0.2 to 2.9) and 1.1 ± 0.8 for SUVavg (range: -0.4 to 3.4, 95% CI: -0.6 to 2.7). This comparison revealed poor agreement between the 2 reconstructions for SUV measurements. **Conclusion** We have demonstrated the impact of our easily applicable reconstruction method on quantization accuracy with phantom and clinical images. AWOSEM_DR introduces less noise into images and thus requires less post-filtering than a standard iterative reconstruction method used in the clinic. Our technique should also maintain good spatial resolution.

P019

Comparison Study of Detection Models for Nuclear Probes

A. Hartl, M. Schwaiger, S. I. Ziegler, N. Navab; Technische Universität München, München, GERMANY.

Aims: Nuclear probes have been established for intra-operative functional imaging. Recently a method to provide 3D imaging using these probes has been introduced (freehand SPECT), where measurements of the manually moved probe are acquired together with spatial information from an optical tracking system. A 3D reconstruction can be computed similar to conventional tomography using ad-hoc models of the detection physics of the probe to cope with the random acquisition geometry. Such models are presented and evaluated in this work. **Materials and Methods:** For this work a low energy gamma probe with a scintillating crystal as detector was used (Intra Medical Imaging, CA, USA). To simulate the detection physics of the probe different models were developed. Model 1 computes the amount of activity from a single point source that reaches the detector with the solid angle subtended by the source and the front of the probe. In addition the angle between source and detector which influences the sensitivity of the probe towards this source is estimated by an approximated factor. In Model 2 not only rays that pass through the front of the probe are considered but also those that pass through the shielding around the detector. In order to compute the mean probability of detection for the rays from a point source the mean length these rays take through the shielding and the detector are computed. Model 3 is a simple look up table which was obtained by taking measurements of a point source of Tc99m (act: 7kBq) from an exhaustive set of angles and distances. **Results:** Three sets of five sources of Tc99m (2x 5-8kBq; 1x 5-8MBq) with a size of 5x5mm each were placed in different configurations on a plate in an area of 50x50mm. The probe and the plate were fixed on a positioning table which moved the probe over the area of the sources with a step size of 1mm. At each position a measurement of 1s with the probe was acquired. These experiments were then simulated by using the three models and their results were compared with the real measurements of the gamma probe by means of normalized cross correlation. NCC values between 77% and 95% were achieved. **Conclusion:** The presented models simulate the acquisition physics very close to reality. Although they do not differ very much in their results the more realistic models turn out to be slightly better.

The results of the comparison of the acquisition models with the measurements of a real gamma probe.

NCC with ground truth	mean	std. dev.	min-max
Model 1	88%	6%	77-95%
Model 2	89%	5.5%	81-95%
Model 3	90%	4.9%	83-94%

P05 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Physics & Instrumentation & Data Analysis: Software & algorithms/modelling

P020

Investigation of gamma coincidence effect in I-124 TOF PET

H. Lin, Y. Tai, C. Lin, K. Chuang; National Tsing Hua University, Hsinchu, TAIWAN.

Aim Time-of-flight (TOF) positron emission tomography (PET) has the potential to improve signal-to-noise ratio. For non-pure positron emitters, the cascade gamma rays lead to the complexity of coincidence detections. Thus in an analysis of the TOF gain with non-pure positron emitter for PET, it is useful to consider the separate effects of true, scatter, random and gamma coincidence. For this purpose, we present a simulation study of I-124 positron emitter to investigate the relative amount of scattered, random and gamma coincidences in TOF PET. **Materials & Methods** A Siemens Biograph 6 PET scanner is modeled with SimSET-GATE Monte Carlo software for this study. In order to evaluate SNR, a modified NEC for I-124 TOF PET is introduced. Acquisitions of F-18 and I-124 cylinder sources with different sizes were performed to compare the TOF gains. Each frame corresponded to a different activity is simulated to investigate the contributions from cascade gamma as well. Results For the phantom studies, the preliminary results showed the TOF distribution for gamma coincidence tends to be flat, while the gamma distribution of the sinogram changed subtly with the source location. The expected gains increased with the gamma fractions. The NEC of I-124 is 2 to 4 times worse than F-18 mainly due to the limited positron decay fraction. **Conclusion** The contribution of gamma coincidence is noticeable in 3D TOF PET. Our results suggested that conventional background correction for the gamma coincidence may be not enough in TOF PET. An advanced gamma correction method is explored in our future studies.

P021

A simulation study using the derivative of the volume-threshold function to estimate the intratumoral heterogeneity in PET images

N. Kubo¹, H. Aida²; ¹Hokkaido University, Sapporo, JAPAN, ²Ebetsu City Hospital, Ebetsu, JAPAN.

Aim: ¹⁸F-FDG PET images often contain highly heterogeneous spatial distributions of tumors. It has been reported that the intratumoral heterogeneity can be used to predict the response to therapy and the risk of recurrence. The derivative (dV/dT) of the volume-threshold function has been used to estimate the intratumoral heterogeneity. It is hypothesized that the intratumoral dV/dT decreases as the heterogeneity increases. We performed a simulation study to examine the effect of the intratumoral heterogeneity on dV/dT. **Materials & Methods:** Visual C++ was used for the simulation. We simulated 48-mm-diameter tumors and used a maximum of 4 kBq/pixel in a single slice. In the first simulation, the tumor model was assumed to have one defect and the defect diameter was varied from 1 to 20 mm. Tumors with large defects were considered to be highly heterogeneous. In the second simulation, the tumor model was assumed to have multiple defects with diameters of 5 mm; the number of defects was varied from zero to six. Tumors with many defects were considered to be highly heterogeneous. The images of tumors were blurred by the point-spread function (spatial resolution of 9.2 mm (full-width at half-maximum)). The intratumoral heterogeneity was obtained for each tumor by taking the derivative (dV/dT) of the volume-threshold function using thresholds in the range 40 to 80%. **Results:** Except with a defect diameter ≤ 4 mm, dV/dT decreased as the defect diameter increased. Thus, dV/dT did not reflect the intratumoral heterogeneity with very small defects due to the limited spatial resolution. dV/dT decreased as the number of defects increased, with the exception when the number of defects increased from five to six. One reason for this exception might be that six defects fused into a singular annular defect due to the limited spatial resolution. Therefore, the heterogeneity appeared lower than it actually was when there were six defects. **Conclusion:** The derivative (dV/dT) of the volume-threshold function can predict the intratumoral heterogeneity in PET images with sufficient accuracy if dV/dT is not influenced by the limited spatial resolution.

P023

Validation of new MRI- and operator-independent algorithm for robust and reliable quantification of DAT-PE2I SPECT images

P. S. Jensen, M. Ziebell, G. Skouboe, U. Khalid, G. Thomsen, G. M. Knudsen, C. Svarer; Neurobiology Research Unit, Copenhagen University Hospital, Copenhagen, DENMARK.

Aim: Dopamine transporter (DAT) imaging with the SPECT radioligand [123I]PE2I is used in patients with parkinsonism where diagnosis is not straight forward. Without MRI guidance, regions of interest (ROIs) are typically manually delineated directly on high-count striatal slices in the reconstructed [123I]PE2I SPECT image. However, as recently demonstrated in [Ziebell et al., 2010, JNM], the precision of such manual non-MRI guided ROI delineation is operator dependent. Ziebell et al. found an intraoperator variability in estimated BPND from manually

delineated caudate, putamen, and striatal ROIs equal to (mean±SD) 10.2 ± 9.2 %, 9.7 ± 5.4 %, and 7.0 ± 4.1 %. This demonstrates sub-optimal reproducibility of the manual technique. In this study, a robust semi-automatic MRI- and operator-independent method for quantifying [123I]PE2I SPECT images is developed and evaluated. **Materials & Methods:** In our method, striatal ROIs are delineated semi-automatically in the patient's reconstructed [123I]PE2I image and DAT BPND estimates are calculated. First, the image undergoes an automatic normalization to a SPECT template with anatomically correct ROIs using the average of two 12-parameter affine transformations estimated based on AIR and FLIRT routines. Then, the user has the possibility to manually fine-tune the exact position of the ROIs at the aligned image in template space, in order to correct for abnormalities (e.g. hydrocephalus) that the automatic normalization procedure cannot account for. **Results:** We evaluated our method using two independent test operators inexperienced in delineating ROIs at [123I]PE2I SPECT images. Images from 5 normals, 5 borderlines, and 5 PD patients, each of which had been quantified by an experienced physician using manual ROI delineation directly at the SPECT image, were used. The two resulting sets of semi-automatically obtained BPND estimates were then compared to each other to assess interoperator variability, and each of set was also compared to the corresponding set of manually obtained BPND estimates to assess reliability of the method.

ROI-specific correlation coefficients (r) from linear regression analyses on the three possible combinations of the manually and semi-automatically obtained BP_{ND} estimates when pooling all fifteen patients

	Putamen	Caudate	Striatum
Operator 1 vs. Operator 2	0.988	0.966	0.999
Operator 1 vs. Manual	0.949	0.899	0.954
Operator 2 vs. Manual	0.939	0.902	0.955

Conclusion: Our results show that the two operators obtain highly reproducible BPND estimates in both putamen (r = 0.988), caudate (r = 0.966), and striatum (r = 0.999), when using our semi-automatic method to quantify [123I]PE2I SPECT images. Further, it is demonstrated that all semi-automatically obtained BPND estimates correlate strongly (r > 0.899) with their corresponding manually obtained BPND values. These results show that we have developed a method which is highly operator-independent and comparable to delineator-dependent methods which are useful in the everyday clinic quantifying [123I]PE2I SPECT or other DAT-SPECT images.

P024

Comparative methods for PET image segmentation in pharyngolaryngeal squamous cell carcinoma using surgical specimen as reference

C. Lina Fuentes¹, J. A. Lee², R. A. Dierckx³, H. Zaidi¹; ¹Geneva University Hospital, Geneva, SWITZERLAND, ²Université catholique de Louvain, Brussels, BELGIUM, ³University Medical Center Groningen, Groningen, NETHERLANDS.

Aim: Several methods have been proposed for segmentation of ¹⁸F-fluorodesoxyglucose (FDG) uptake in positron emission tomography (PET). This study compares the performance of various FDG-PET segmentation methods in Pharyngolaryngeal Squamous Cell Carcinoma where the surgical specimen served as reference. **Materials & Methods:** Seven manual, semi-automated and fully automated PET image segmentation techniques were evaluated including: 1) manual delineation, 2) Fixed thresholding of 40% of the maximum SUV (Th_40) 3) Signal-to-Background Ratio (SBR)-based adaptive thresholding, 4) Region growing (RG), and three variants of a fully automated fuzzy clustering-based segmentation technique, namely 5) FCM, 6) FCM-S, and 7) FCM-SW. Segmentation results were then compared to the 3D (Gross Tumour Volume) GTV defined by histology on PET images of seven patients with T3-T4 laryngeal squamous cell carcinoma who underwent a total laryngectomy. The macroscopic tumour specimen was collected "en bloc", frozen and cut into 1.7- to 2-mm thick slices then digitized and used as reference. The algorithms were also evaluated using simulated data of the NCAT phantom incorporating heterogeneous lesions modeled from clinical head and neck PET/CT studies. **Results:** The GTVs estimated using the various segmentation methods as compared to surgical specimen used as reference are summarized in Table 1. Overall, SBR overestimates the average tumour volume (23.6 cc, p<0.02). The same applies to Th_40 and manual delineation techniques. Automated techniques including region growing, FCM and FCM-S underestimate the mean volume (12.4 cc, p=0.51; 10.3 cc, p<0.05 and 10.4 cc, p<0.04, respectively). FCM-SW provides a more accurate estimate of the tumour volumes (14.6 cc, p=0.842). The results obtained using simulated studies seem to indicate an underestimation of the tumour volumes when using Th_40, RG, and SBR techniques. **Conclusion:** The GTVs delineated using the automated FCM technique incorporating spatial information and modeling of heterogeneity of uptake (FCM-SW) was the most accurate segmentation technique and approximates closely the 3D GTV defined on the surgical specimen.

P025

Computational simulation of tumor lesions: A tool for evaluating heterogeneous uptake of FDG in PET images

A. R. Ventura¹, C. M. F. Gomes¹, A. Rodrigues², F. J. Caramelo¹; ¹Institute of Biophysics/Biomathematics - IBILI - FMUC, Coimbra, PORTUGAL, ²Institute for Nuclear Sciences Applied to Health - ICNAS - Coimbra University, Coimbra, PORTUGAL.

Aim: The principal goal of the present work is to develop a simple software algorithm to simulate heterogeneous tumors in PET-FDG images. This is part of a larger project where we intend to automatically classify the tumoral heterogeneity presented in PET-FDG images as a predictor of patient outcome. Actually, SUV (Standardized Uptake Value) is the most frequent parameter extracted from PET images both in diagnosis and staging of tumors. Intratumoral heterogeneity results on coexistence of multiple cell subpopulations with distinct biologic behaviors that affect the disease progression. Therefore, the quantitative analysis of the spatial distribution of FDG may reflect metabolic tumor heterogeneity and thus be used as a new predictive parameter. The developed algorithm will be used to test and validate the final tumoral heterogeneity classifier, which is the main objective of the entire project. The correct validation of this routine will foster a more accurate implementation of the heterogeneity classifier. **Methods:** We developed a

software routine in Matlab® to add lesions in real PET images. The user can control several parameters such as location, orientation, number of foci, radius and radius variation, maximum and minimum of intensity. Tumor simulation is obtained by generating several circles in consecutive slices of PET-FDG images. With an adequate combination of circles, with different radius and intensity, an ellipsoid with a specified orientation is defined. The process could be easily repeated throughout the image volume. We also performed a preliminary test for validating the algorithm. Two sets of images were defined: one consisting of 6 whole body PET scans with simulated tumors and the other comprehending 5 real whole body PET scans. We run a blind test where two clinicians were asked to analyze the images and classify them concerning the authenticity of the lesions and the heterogeneity (ranging from 0 to 5). The results were evaluated using a score defined by the sum of false positive and false negative divided by the total number of PET scans. Results: The routine is fully operational although a more friendly graphic user interface is being developed. The scores obtained were 3/11 and 5/11. Concerning heterogeneity results were inconclusive. Conclusion: Several aspects of the algorithm should be improved, such as tumor contour, contrast and foci relative position. Other aspects that essentially depend on the user can be optimized, namely the correct choice of the tumor radius, the intensity and the main tumor location.

P026

Peculiar Adjustments in Image Processing for an Evolution Decision Support System in Bone Scintigraphy

M. Costin¹, A. Ciobanu¹, C. Stefanescu², ¹Institute of Computer Science, Romanian Academy, Iasi, ROMANIA, ²U.M.F., Medicine Faculty, Iasi, ROMANIA.

Aim: In diagnosis and treatment survey, whole body bone scintigraphy image is normally accompanied by quite an important degree of variability in the acquisition process: different radiotracer radioactivity which depending either on the administered dose or on the acquisition moment, different patient body mass and amount of ingested liquid, slightly different position on the scinti-bed for the same person, are only some of the uncertainty factors that have to be approximated, not ignored. Therefore, as a support to the medical diagnosis, we propose a new method for numerical, objective processing on particular areas, in order to be able to better compare scintigrams belonging to the same patient, at different moments in the disease evolution. **Material and method.** Bringing in an objective manner two time delayed scintigrams to the same contrast and brightness might seem simple but it is a first important step in diminishing the degree of imprecision. Our method comprises more stages: 1) With a nuclear medicine physician supervised selection, two similar, equal, healthy bone areas are selected on two decayed images to be compared, and a mean difference method is applied on them, in order to obtain a significant index for the whole images. This constitutes a reference and a modified, enhanced, version of the image with had less gamma-energy emission is created. 2) Frontal images of the same patient, in the two different stages (using the enhanced version) are placed aside. Similar, anterior images of the same patient are placed on the same analyzing screen. 3) Images are separated into significant, symmetric, geometrical regions in order to be compared. 4) Step by step, each region is compared to the similar one, in a semi-supervised computing process. When necessary, due to unclear areas, a combined spatial enhancement method is used, on similar geometric areas selected on the image. **Results and conclusions.** Having the two time delayed images on the same frame, and applying (on brightness equalized images) a threshold that clearly indicate areas that appear or disappear from an exam to the other, is an objective, quantifying, tool to be used in a decision support for the medical diagnosis. This method gives the possibility to numerical estimate ab-normal zones that uptake more or less radiotracer, the normal or the pathologic areas in an more objective comparison. Data is collected in order to formalize rules for a future decision support system in medical bone-scintigram diagnosis.

P027

PET volume segmentation: influence of different reconstruction algorithms, volume sizes and SBRs

B. Knäusl¹, A. Hirtl², K. Kletter², H. Bergmann³, R. Dudczak², D. Georg⁴, ¹Department of Nuclear Medicine and Radiotherapy, Medical University, Vienna, AUSTRIA, ²Department of Nuclear Medicine, Medical University, Vienna, AUSTRIA, ³Center for Medical Physics and Biomedical Engineering, Medical University, Vienna, AUSTRIA, ⁴Department of Radiotherapy, Medical University, Vienna, AUSTRIA.

Aim: To assess the influence of reconstruction algorithms on automated PET based volume definition. For quantitative application of PET images, the detected activity in the threshold (TH) defined volume was investigated for different reconstruction algorithms as function of volume size and signal-to-background-ratio (SBR), especially for volumes smaller than 1ml. **Material and Methods:** The measurements with the NEMA IEC/2001 image body phantom (Biodes) were performed on a Siemens Biograph 64 PET-CT scanner (Siemens, Medical Systems) for five different SBRs (3.8, 4.9, 6.7, 9.4 and w/o active BG). The phantom consisted of a water-filled cylinder with built-in plastic spheres (0.27, 0.52, 1.15, 2.57, 5.58 and 11.49ml). For the TH-based volume segmentation the software Rover (ABX, Dresden) was used. The following algorithms available on the Siemens Syngo workstation were evaluated: Iterative TrueX (4 iterations, 21 subsets), Iterative OSEM (4 iter 21s) and back-projection (BP). **Results:** For sphere volumes (SV) larger than 2ml a constant TH (SD < 10%) was found for a given SBR and reconstruction algorithm. For the OSEM algorithm the TH could be calculated using the inverse function $TH = 37.3 + 47.6 * (1/SBR) (R^2 = 0.9)$ and decreased with increasing SBR for all sphere sizes. The threshold for small spheres with 0.27, 0.52 and 1.15 ml ranged from 33.4 to 20.9%, 36.7 to 30.0% and 44.2 to 37.4%, respectively. The TH for the TrueX algorithm was substantially lower (up to 30%) than for the OSEM algorithm for all sphere sizes. The maximum activity in the TH defined volume yielded the true activity for the OSEM algorithm when using a correction factor C, which was independent of the SBR. However, C depended on the sphere size and was constant for the largest 4 volumes with 1.2 ± 0.2 . For smaller volumes it increased due to the partial volume effect and could be calculated using the exponential function $C = 12.1 * \exp(-SV/0.2) + 1.2 (R^2 = 0.8)$. For the TrueX algorithm the maximum activity varied with different SBRs and did not represent the true activity. Changing the number of iterations (2, 4, 8) and subsets (4, 8, 14, 21), the variation of the maximum activity was negligible for the OSEM algorithm when using at least 4 iterations but was

pronounced for the TrueX algorithm, especially for small volume sizes and less than 8 iterations (maximum 60%). **Conclusion:** The threshold for PET based target segmentation increased with increasing sphere size for all algorithms. True activity values in phantoms could be extracted using experimentally determined correction factors. The TrueX algorithm has to be used carefully for quantitative comparison and multicenter studies. Using an automatic segmentation method requires phantom measurements for every specific PET scanner and reconstruction algorithm.

P028

Non-invasive estimation of input function for rapid CBF-CMRO2 measurement using PET with DARG

N. Kudomi¹, H. Watabe², T. Hayashi³, Y. Sasakawa¹, Y. Yamamoto¹, Y. Nishiyama¹, H. Iida³; ¹Kagawa University, Kagawa, JAPAN, ²Osaka University, Suita, JAPAN, ³National Cardiovascular Center, Suita, JAPAN.

Background and Aims: CBF and CMRO2 can be quantitatively measured using 15O-PET. Recently, we have developed a novel method which implements in short time PET protocol and formula for CBF and CMRO2 (DARG). One of problems, so far, is need of invasive arterial blood withdraw for input function. The aim of the present study was to develop a technique to obtain quantitative CBF and CMRO2 measurements by estimating the input function from dynamic PET images, non-invasively. **Methods:** Normal subjects (n=6) and patients with cerebrovascular disorder (n=6) were studied with DARG, in which two tracers of 15O2 and H215O are sequentially administered with 5 (normal) or 10 min (patients) intervals during a single PET scan. During the scan arterial blood was sampled and activity concentration was determined invasively to serve as reference measurements. The present technique consisted of the following two characteristics, i.e., using a model input function and simultaneously fitting multiple liver time-activity curves (TAC) from images. For parameters which consist the model function, one combination for which the residual sum of square between the tissue TACs and fitted curves from model input is minimized was determined, and then the input function was obtained from the determined parameters. The CBF and CMRO2 values were computed by the estimated and measured input functions. **Results:** The estimated input functions were well reproduced against the measured ones. In addition, the calculated CBF and CMRO2 values were not significantly different (P > 0.05 for both) between the methods and difference was 12% and 15%, respectively. **Conclusion:** The presented results demonstrate that the input function can be estimated directly from tissue TAC's extracted from dynamic PET imaging. This suggests the possibility to enable the noninvasive assessment of CBF and CMRO2.

P029

TPClib.Model: a package of quantification analysis for PET study data

C. Han, H. Merisaari, K. Liukko, S. Nesterov, V. Oikonen, M. Teräs; Turku PET Centre, Turku, FINLAND.

Aim: TPClib is a library for processing PET-related data developed at Turku PET Centre (Turku, Finland) using C# programming language. TPClib.Model is designated to develop a module under TPClib framework for quantification analysis of PET study data. TPClib is an open source library and is free for academic use. **Materials and methods:** This module is developed using C#-programming language with Microsoft VisualStudio 2008. Least square and four basic optimization algorithms, Random-direction, Nelder-Mead, Powell-Brent and ITGO (iterate TGO) are included for data fitting. Adams-Moulton and Runge-Kutta algorithms are coded for solving ordinary differential equations. Based on Adams-Moulton algorithm, four compartment model elements, i.e. 1, 2, 3 (in parallel and in series)-tissue compartmental models are created. Based on these four elements, most specific compartment models can be easily implemented in the future. Currently, heart-related models, such as O-15 water, Rb-82 rubidium and N-13 ammonia for perfusion studies, and additionally, the general 1, 2 and 3 (in parallel and in series) have been implemented. Furthermore, this module also contains basic calculation methods, such as Patlak, Logan and Kmno (monoexponential decay fitting). **Results:** All the models have been implemented in Carimas 2. Carimas 2 is a general PET data analysis package developed at Turku PET Centre (<http://www.turkupetcentre.net/carimasturku>). All the models have been verified based on simulation data and comparison with the modelling programs developed in Turku PET centre previously. TPClib has been verified on other platforms, such as Linux and Unix, using Mono. Validations for specific models implemented in Carimas2 based on true data were under processing. **Conclusion:** TPClib.Model is a useful library for quantification analysis of PET study data. Heart-related, certain widely used models and methods are available in the current version, and more models will be developed and implemented. It is free and downloadable for academic use. Its website is http://www.turkupetcentre.net/programs/tpc_csharp.html

P06 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Physics & Instrumentation & Data Analysis: Pre-clinical imaging

P030

Data-driven arterial input function in mice, comparison to arterial blood samples

D. Schulz¹, A. Tapfer², S. Reder¹, A. K. Buck¹, S. I. Ziegler¹, M. Schwaiger¹, R. A. Bundschuh¹; ¹Klinikum rechts der Isar der TU München, München, GERMANY, ²Department of Physics TU München, München, GERMANY.

Objectives: Retrieving the accurate time-tracer activity concentration curve of the blood (arterial input function) is mandatory for performing analysis of dynamic PET data. Especially in small rodents, gathering the input function remains an active area of research. While surgically catheterizing blood vessels of rodents is possible, it is labour intensive and time resolution is restricted due to the limited amount of overall blood and the procedure of blood withdrawal itself. Obtaining the input function from the PET images seems thus to be favourable, but suffers

from spill in of adjacent tissues. Particularly in mice and for 18F-FDG the spill in denies using the time-activity curve (TAC) from a region of interest (ROI) over the left ventricle (LV) because myocardial uptake and the input function interfere within the ROI. We propose non negative matrix factorization (NMF) as an image based algorithm for separating myocardial tracer concentration from the blood input function. The aim of this study was to evaluate the potential of NMF as an image based algorithm for retrieving the input function. **Method:** The femoral arteries of eight mice were surgically catheterized. With the injection of 18F-FDG, a 60 minute PET scan was started during which blood samples were manually drawn from the catheter. After completion a CT scan was conducted for attenuation and scatter correction. For Analysis NMF was performed in a ROI placed over the LV. The NMF algorithm shares similarities with principal component and factor analysis, the advantages over the later two being its non negativity constraint and being based on Poisson statistics. For normalization of the NMF extracted curve, the peak value of tracer activity in an early image of the LV and a late blood sample was used. The normalized NMF curve was visually compared to the TAC retrieved from the blood samples and Pearson correlation between the two curves was calculated. **Results:** TAC based on NMF and arterial blood samples were obtained in all 8 mice. Visually the NMF extracted curve and the blood TAC were in good accordance with each other. The Pearson correlation ranged from 0.21 to 0.92 with an average of 0.69. The values for each animal can be found in the Table. **Conclusion:** NMF seems to be a promising method for the extraction of the input function from PET images of small rodents without the need for arterial blood samples.

Animal 2 3 4 1 5 6 7 8

Pearson 0.49 0.21 0.68 0.90 0.62 0.82 0.92 0.87

P031

Development of iterative reconstruction algorithm incorporating transaxial distance-dependent resolution compensation for small animal PET

K. Matsumoto¹, Y. Wada², K. Murase³, T. Mukai¹, Y. Watanabe², ¹Kyoto College of Medical Science, Kyoto, JAPAN, ²RIKEN Center for Molecular Imaging Science, Kobe, JAPAN, ³Graduate School of Medicine, Osaka University, Osaka, JAPAN.

Objectives: Simultaneous PET measurement of the target-animal and the control-animal is effective for molecular imaging research. However, the spatial resolution of small animal PET is degraded at the edge of the field of view (FOV) due to parallax error as well as clinical PET scanner. On the other hand, iterative reconstruction techniques such as the ordered subsets-expectation maximization (OSEM) algorithm can easily incorporated various physical models of attenuation, scatter and resolution. The purpose of this study was to develop an iterative reconstruction algorithm incorporating compensation for parallax error in small animal PET. **Methods:** A small animal PET scanner, Siemens Healthcare Inc. microPET Focus 220 was used to evaluation of spatial resolution. Spatial resolution was measured with a point source of ¹⁸F in a glass capillary tube with a 0.14 mm inner diameter and a 0.6 mm outer diameter. The source was positioned at 0 mm, 5 mm, 10 mm 25 mm, 50 mm, 75 mm and 85 mm off center of the FOV. A new iterative reconstruction algorithm (NIRA) was including sinogram-based corrections and an experimental stationary model of resolution, has been designed. A NEMA NU 4-2008 image-quality phantom and healthy mouse injected with F-18 were scanned to evaluate the image quality. We also compared the image of filtered back projection and ordinary OSEM algorithm. **Results:** As for the point source image reconstructed with NIRA, the spatial resolution was constant without depending on the distance from the center (FWHM=0.8 mm). The mouse images reconstructed with NIRA demonstrate better delineation of the white- and the gray-matter in time-averaged images. **Conclusions:** In not only the usual high-resolution PET acquisition but also the simultaneous PET measurement, this algorithm including the parallax error compensation can improve quantitative accuracy by reducing the partial-volume effects.

P032

A Monte Carlo study of qualitative and quantitative accuracy of 89Zr small animal PET images

D. D'Ambrosio, F. Zagni, D. Pancaldi, S. Fanti, M. Marengo, S.Orsola-Malpighi Hospital, Bologna, ITALY.

Aim: Actually there is a big interest of radiotracer research in non-standard PET radionuclides such as ⁶⁴Cu, ⁸⁹Zr, ¹²⁴I and others as they allow to study new radiopharmaceutical probes. In our institution we recently produced the cited nuclides and, thus, we are interested in studying the qualitative and quantitative accuracy of PET images that they are able to produced. In particular, in this work attention was focused on ⁸⁹Zr PET images. The accuracy evaluation was performed using Monte Carlo simulation. **Materials and methods:** A Monte Carlo model of the NEMA NU4-2008 image quality phantom for small animal PET scanner was realized using GATE. Simulation of a ⁸⁹Zr and ¹⁸F image acquisition was performed using the GE Xplore Vista model created using GATE. More precisely, simulations using 100kBq/cc of ¹⁸F and about 450kBq/cc of ⁸⁹Zr in background and rods with different diameters were performed. A cylinder was filled with activity (cylinder/background equal to 5) while the other cylinder was left cold. Simulated acquisition time was equal to 800s. Different energy window (EW) acquisition were also simulated: 100-700keV, 250-700keV, 400-700keV. Both true and total counts data were, thus, reconstructed using a 2D-OSEM algorithm. Line profiles were traced across rods and cylinders to perform a qualitative analysis of the reconstructed image. Region of interests (ROI) were drawn on reconstructed data in order to evaluate the quantitative accuracy of the images. Noise was estimated as standard deviation of the central uniform region. Contrast of hot and cold cylinders were also calculated with respect to the background region and recovery coefficients were estimated from rods ROIs **Results:** In table 1 results obtained for 100-700keV EW are reported. Noise values measured using wider EWs were greater than values of 100-700 keV EW, for both the radionuclides. Also hot and cold cylinders contrast calculated for 250-700 and 400-700 keV EWs were greater than values measured in the narrower EW. **Conclusions:** Preliminary results from Monte Carlo simulation showed that ⁸⁹Zr images are similar to ¹⁸F images in terms of noise and hot and cold region contrast. This showed that the effect of 909keV single photon on image quality is almost negligible in small animals. Our results confirm that ⁸⁹Zr is one of the most promising radionuclides for preclinical PET imaging.

Table 1

	89Zr True (total) coincidences image	18F True (total) coincidences image
Noise	9.7% (9.4%)	7.9% (7.8%)
Hot region contrast	352.4% (323.8%)	362.5% (335.3%)
Cold region contrast	84.7% (79.9%)	85.7% (81.3%)

P07 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Physics & Instrumentation & Data Analysis: Patient dosimetry & protection

P033

Direct Urine Activity Measurement in Toilet for ¹⁷⁷Lu PRRT: Feasibility Study for Personal Dosimetry

B. Liu¹, P. Bode¹, W. A. P. Breeman², ¹TU Delft, Delft, NETHERLANDS, ²Erasmus MC, Rotterdam, NETHERLANDS.

Aim: The remaining patient activity post ¹⁷⁷Lu PRRT can be indirectly determined by quantifying excreted activity in urine. Our aim is to develop a patient friendly technique to measure urine activity in toilet directly in hospital. The key issues are the activity overflow and distribution in U tube of toilet. This paper presents optimizations and preliminary analysis of applied measurement methods, including probe positioning. **Method:** The excreted urine was collected for 5 patients in four intervals: 1, 4, 10 and 24 h after infusion. The urine activity was quantified with gamma counter. The gamma fluences of 208 keV at different positions around toilet for different distributions in U tube were calculated by MCNP5 code. The toilet was simplified as a porcelain shell and water inside with the truncated wedge geometry. For experiments, a CZT detector (15x15x7.5 mm³) was positioned 28 cm from toilet center at side and a LaBr₃ detector (Φ38x38 mm³) was 2.15 m at ceiling. ¹⁷⁷Lu-containing solutions with 37 MBq in 200-500 mL were added into toilet at a flow 16 mL/s mimicking urinating flow. Responses (cps/MBq) were determined by spectrum acquisitions with 1min interval. **Results:** The total urine volume within 24 h is 3150±206(SD) mL. The volume and activity per urination could vary in 225-513mL and 77-3700MBq respectively if urinating frequency is 7-11 times/day. Amongst supposed distributions, variations of calculated gamma fluences on side wall at height of the U tube center are less than 1% comparing to uniform distribution, and -22% to 10% at 2 m top on side wall. The deviation of responses measured amongst 4 volumes is ±1.2% (with a coverage factor k=2, unless otherwise stated) (CZT detector) and ±16% (LaBr₃ detector). If another CZT detector of 10x10x10 mm³ were used, the response could be 0.832±4.8% cps/MBq. The total measurement uncertainty of activity per urination will be ±6.9% if the statistical uncertainty of counts is ≤ ±5%. **Conclusion:** The impact of activity distribution in U tube can be minimized by positioning probe on side wall at height of the U tube center. And experimental results match with simulations very well. The affection of the activity overflow can not be identified in our preliminary experiments, especially for the CZT detector at side. The activity per urination could be measured with accuracy ≤10% without any modifications to current toilet and sewer system. The project is funded by NUTS-OHRA (project number: 0804-047).

P034

Individual effective half-life in Lu-177 Dota-Tate therapy

J. Fitschen¹, B. O. Knoop¹, W. H. Knapp², L. Geworski¹, ¹Department of Medical Physics and Radiation Protection, Hannover Medical School, Hannover, GERMANY, ²Department of Nuclear Medicine, Hannover Medical School, Hannover, GERMANY.

Aim: Lu-177 Dota-Tate is predominantly used for therapy of neuroendocrine tumours. As according to German legal requirements the integrated radiation dose emitted by the patient to his surroundings after discharge (48h p.i.) shall not exceed 1mSv per year, the individual determination of dose gains importance, especially if the therapy has to be repeated several times a year, which is true for nearly all patients. This radiation dose depends on dose rate as measured on the patient and effective half-life. The often used approximation by physical half-life is conservative but probably too stringent to fulfil the given dose limit. It is the purpose of this study to determine the individual effective half-lives for a larger patient collective. **Methods:** In 45 patients the dose rate has been measured at a distance of 2m (1m above ground) using a Szintomat 6134A (automess, Inc.). Data were taken at 20h, 24h, 29h, and 46h after application of 8000 MBq Lu-177 Dota-Tate (range 7000 - 8500 MBq). In the time range specified the measured dose rates can be well described by a monoexponential function and allow the calculation of individual effective half-life. The resulting integrated dose to the surrounding after patient discharge are determined and compared to the dose resulting from physical half-life and from the mean effective half-life resulting from all patients. **Results:** The mean effective half-life and its standard deviation was 55h ± 16h (range 30h - 100h). Using the maximal observed effective half-life of 100h results in a 38% reduction in estimated dose (still conservative) as compared to using the physical half-life of 161h. Using the mean value leads to a reduction in dose estimation of 66%, but is no longer strictly conservative (2 out of 45 patients deviated by 32% or 93%, respectively) for doses near the given dose limit. The variations in effective half-lives could not be attributed to factors as general condition, tumour entity, weight, age or gender. **Conclusions:** In the study presented the maximum observed effective half-life was 100h. Replacing the physical half-life of Lu-177 by this value results in a nearly 40% reduction in conservatively estimated dose to the surroundings induced by the patient and facilitates repeated therapies. According to the data currently available a further reduction in dose estimation by using the mean effective dose will not be strictly conservative.

P035

Additional doses to healthy tissues due to possible release of radionuclides in nuclear medicine therapies

M. Cremonesi¹, S. Papi², M. Ferrari¹, L. Bodei², F. Botta¹, A. Di Dia¹, L. Garaboldi², A. Rossi¹, G. Pedrolì¹, G. Paganelli²; ¹Medical Physics Division, European Institute of Oncology, Milano, ITALY, ²Nuclear Medicine Division, European Institute of Oncology, Milano, ITALY.

Rationale: During radionuclide therapies (RNT), the release of unconjugated radionuclides (UnRad) due to incomplete labelling, impurities, or in-vivo de-conjugation, cannot be excluded. Aim of this work was to estimate UnRad doses in several RNT and to identify applications requiring more caution. **Methods:** Considering the natural tropism of radionuclides (ICRP30), the number of decays in source organs (RADAR-www.doseinfo-radar.com) per unit of UnRad activity were assessed for ⁹⁰Y, ⁹⁰Sr, ¹⁷⁷Lu, ^{177m}Lu, ¹¹¹In, ¹⁸⁶Re, ¹⁸⁸Re, ¹⁵³Sm, ¹³¹I, and absorbed doses per UnRad unit activity (D/UnRad) estimated (OLINDA/EXM). The following RNT (and commonly administered activities) were considered: Peptide-Receptor-Radionuclide-Therapy (⁹⁰Y-PRRT-[3.7GBq], ¹⁷⁷Lu-PRRT-[5.55GBq], ¹¹¹In-PRRT-[7.4GBq]); bone palliation (¹⁸⁶Re-HEDP-[1.30GBq], ¹⁸⁸Re-HEDP-[4.4GBq]; ¹⁵³Sm-EDTMP-[2.96GBq]); Radio-Immuno-Therapy (¹³¹I-RIT[5.5GBq], Bexxar®[20GBq], ⁹⁰Y-RIT[5.5GBq], standard/myeloablative Zevalin [1.2GBq/5.5GBq]. A 5% de-conjugation fraction was considered as conservative-but plausible- hypothesis accounting for potential incomplete-labelling, impurity, and instability. Moreover, the dose impact from certified amounts of ^{177m}Lu and ⁹⁰Sr (^{177m}Lu/¹⁷⁷Lu=10⁻³, ⁹⁰Sr/⁹⁰Y=10⁻⁵) was investigated. **Results:** The table summarises essential results, reporting D/UnRad (mGy/MBq) and dose per administration (Gy/cycle). ^{177m}Lu and ⁹⁰Sr give negligible doses (<0.01Gy/cycle), while red-marrow doses due to ¹⁷⁷Lu or ⁹⁰Y UnRad (0.4Gy/cycle or 0.6Gy/cycle, respectively) are not irrelevant in ¹⁷⁷Lu-⁹⁰Y-PRRT (comparable to those from PRRT itself), especially considering that multiple cycles are needed. Instead, in ⁹⁰Y-RIT, UnRad impact less on red-marrow (e.g. 5-10-fold lower than that from standard/myeloablative Zevalin). In ¹³¹I-RIT, thyroid irradiation would be comparable/higher to an ablation therapy. No further risks are foreseen for other organs or RNT. **Conclusion:** Especially for RNT using bone-seeker radionuclides and high activities, additional doses to red-marrow should be individually taken into account. Even 5%UnRad, which might be considered allowable, may contribute to red-marrow impoverishment or to thyroid damage in ¹³¹I-RIT, leading to hypothyroidism. However, recommendations and stabilizing methods exist (e.g. quantitative radiolabelling/purification, DTPA addition before injection, effective thyroid blocking) and must be applied. This in order to eliminate all but the unavoidable variable (i.e. individual in-vivo stability), which should be estimated specifically for RNT and patient. In conclusion, the two major risk factors from UnRad (i.e.to red-marrow and thyroid)can be minimised following basic safety rules. This study remarks the importance of good clinical practice compliance.

D/FFR (mGy/MBq)

	⁹⁰ Y	¹⁷⁷ Lu	¹⁸⁶ Re	¹⁸⁸ Re	¹⁵³ Sm	¹³¹ I(30% uptake)
Red-marrow	3.24	1.47	0.21	0.09	0.52	0.07
Liver	3.92	0.23	0.41	0.17	2.60	0.01
Thyroid	0.07	0.01	48.3	20.9	0.004	475
Total-body	0.51	0.24	0.31	0.14	0.14	0.22

(Gy/cycle)	⁹⁰ Y-peptides	¹⁷⁷ Lu-peptides	¹⁸⁶ Re-HEDP	¹⁸⁸ Re-HEDP	¹⁵³ Sm-EDTMP	¹³¹ I-MoAbs	Bexxar
Red-marrow	0.6	0.4			0.08	0.02	0.07
Thyroid			3.1	4.6		~130	~450

P036

Conversion of Dose-rate in Retained Activity for Discharging Patients Treated with ¹³¹I. an Experimental Model.

N. Urbano, M. Rinaldi, G. Rinaldi, A. Scopece, S. Modoni; Medicina Nucleare, Azienda Ospedaliero-Universitaria "Ospedali Riuniti", Foggia, ITALY.

Aim. The largest of ¹³¹I activity allowed in Italy for outpatients is 600 MBq. In order to apply this regulation to discharge hospitalized patients treated with larger activities, we need to convert their dose-rates into retained activity, respectively. For this reason, we measured the effective dose-rate from patients administered with activities below 600MBq and set up a corresponding reference scale. **Materials and methods.** Group A: 103 patients (28M, 75F, age 17-84yrs) received ¹³¹Iodine (74-592 MBq) for a) hyperthyroidism (n=48); b) diagnostic whole-body-scan for thyroid cancer (n=55). Group B: 434 hospitalized patients (97M, 337F, age 16-81yrs) were treated with activities larger than 600 MBq (740-7400 MBq) for a) uni- multi-nodular toxic goiters (n=9); b) large non-toxic goiters (n=3); c) thyroid remnant ablation (n=342); d) thyroid cancer metastases (n=77); e) high thyroglobulin levels without known metastases (n=3). In both groups, dose-rate (μSv/hr) measurement was performed by Radalert50 dose-meter positioned on a level with stomach at 1 m distance immediately after ingestion of capsules (T₀) and 1 hour later (T₁) without voiding urinary bladder (group A), and 1hr and 48hrs after radioiodine administration (group B). For each patient Body-Mass-Index (BMI) and Body-Surface-Area (BSA) were calculated. In group A, T₀ and T₁ dose-rates were correlated with ¹³¹I activities administered. These data were used to realize the following linear regression model: dose-rate=0.063activity+0.1062, which was used to get the estimated retained activity in the patients of group B. Moreover, dose-rates (m±sd) were correlated to homogeneous groups of activities (74-81.4, 170-185, 207-296, 370, 444-592 MBq) too. **Results.** Significant correlation was observed between dose-rates at T₀ and T₁. T₁ dose-rates were more homogeneous and slightly lower than T₀ values because of body distribution of radioactivity either in the whole group of patients or in the subgroups (table below).

Group	T ₀ (μSv/hr)	T ₁ (μSv/hr)
All patients (n=103)	12.43±10.3	10.83±8.9
74-81.4 MBq (n=55)	5.41±0.9	4.83±0.5
170-185 MBq (n=22)	13.77±2.4	11.72±1.0
207-296 MBq (n=13)	18.15±2.2	15.20±1.4
370 MBq (n=5)	27.21±6.2	23.00±2.0
444-592 MBq (n=8)	38.79±9.0	35.14±5.9

No correlation was observed between BMI, or BSA, and dose-rates in the subgroups. In the group B, 48 hrs after radioiodine administration, 428/434 (98.6%) patients showed dose-rates lower than 37.8 μSv/hr corresponding to retained activity of 600 MBq. Only 6 patients needed an additional day of hospitalization to fall into limits for discharge. **Conclusions.** Our algorithm could be an useful tool to estimate the retained activity of ¹³¹Iodine in discharging patients after treatment.

P037

Yttrium-90 peptide therapy: Practical considerations for ensuring the radiation dose is given to the patient and not the staff

R. C. Fernandez, S. J. Allen, Y. F. Tan, J. R. Ballinger; Guy's & St Thomas' NHS Foundation Trust, London, UNITED KINGDOM.

Introduction Peptides labelled with beta-particle emitting radionuclides such as yttrium-90 (⁹⁰Y) are increasingly being used for treatment of somatostatin receptor-positive tumours. There are inherent complications in using ⁹⁰Y due to the physical characteristics of emitted radiation, with significant implications for both accurate measurement of activity and radiation protection. As there is comprehensive data on operator radiation exposure during ⁹⁰Y radiopharmaceutical preparation, our focus was on optimisation of radiation protection during ⁹⁰Y administration. This study shares our experience of recently commencing these therapies and summarises the important practical aspects when assaying ⁹⁰Y and the logistics during administration to minimise staff radiation dose. **Method** Measurement precision and consistency between 5 radionuclide calibrators (4 Capintec CRC-15R, 1 Amersham ARC-120) was performed using a standardised ⁹⁰YCl₃ solution calibrated to a national standard. To assess the effect of geometry on measurement accuracy, calibration factors were determined for various plastic syringe sizes anticipated for clinical use. The 20 ml syringe, selected for therapy administration to minimise operator finger dose, requires assay using non-standard geometry. Consequently, we investigated the effect of filling volume on measurement accuracy. For constant ⁹⁰Y activities, filling volume was varied over the expected clinical range and variation in calibrator response, relative to the calibrated geometry, measured. During all administrations, in-house built Perspex shielding was used for vials and infusion system. We assessed the need for additional personal shielding using electronic personal dosimeters (Mirion Technologies, USA), which were worn by operators either side of 0.2 mm lead-equivalent X-ray aprons for the first 10 patient administrations. **Results** All calibrators measured ⁹⁰Y accurately, within measurement uncertainty, when compared to the national standard. Measurements were consistent between calibrators (maximum difference 1.54%). Activity corrected for mass/decay/background varied by <30% for the range of plastic syringes investigated. For the 20 ml syringe, filling volume over range 0.5-10 ml had minimal effect on calibrator relative response (standard deviation 0.55%, maximum 1.62%). During therapy administration (mean administered activity 2416 MBq), mean operator whole body depth/surface dose outside the X-ray apron were 0.05/1.03mSv respectively. Use of the apron is recommended as it afforded mean depth/surface dose sparing of 97.1%/98.7% respectively. **Conclusion** There are important logistical/practical considerations prior to commencing ⁹⁰Y peptide therapy. Calibration traceability and consistent geometry are essential for ensuring delivery of the correct therapeutic dose. Appropriate shielding (both personal and surrounding infusion equipment) together with suitable monitoring devices and staff training, ensure occupational radiation exposure is kept at acceptable levels.

P038

Dosimetric audit of radiopharmaceutical medicine administration for nuclear pediatrics

J. Delage¹, A. Salles¹, I. Gardin², P. Bohn², J. Basuyau¹, P. Vera²; ¹Department of Pharmacy, Henri Becquerel Center, ROUEN, FRANCE, ²Department of Nuclear Medicine, Henri Becquerel Center, ROUEN, FRANCE.

Aim: In order to optimize the patients' exposition to ionising radiation, Diagnostic Reference Levels (DRLs) concept was introduced in publication 73 of the International Commission on Radiological Protection (ICRP). DRLs are dosimetric indicators to quality of practices, intended to identify situations requiring a corrective action. In practice, the national data's analysis is effective for adults since 2006. However, for children, yet particularly sensitive to the effects of ionising radiations, the relevant data are neither collected specifically nor analyzed. Therefore, we have carried out an audit of the activities administered to children in our unit. **Materials&Methodes:** The study was undertaken on a retrospective basis for a total of 250 children (Average Age 5,4 years, from 1 month to 15 years) having received a radiopharmaceutical drug for the purpose of one of the 6 following examinations: renal function exploration with ^{99m}Tc-DMSA (n=66) or ^{99m}Tc-MAG3 (n=30), bone scintigraphy with ^{99m}Tc-HDP (n=64), PET exam with ^{18F}-FDG (n=48), neural crest tumors scintigraphy with ^{123I}-MIBG (n=30), thyroid scintigraphy ^{99m}Tc (n=21). Activities administered on the basis of weight were compared to the product licence of the radiopharmaceutical drug and to EANM's (European Association of Nuclear Medicine) recommendations, with Student's Test. **Results:** For examinations with ^{99m}Tc-HDP, ^{99m}Tc-MAG3, or ^{18F}-FDG and for thyroid explorations with ^{99m}Tc, administered activities proved to comply with the product's licence (absence of statistically significant difference) but higher than the EANM's recommendation (p<0.0001). For explorations of the renal function with ^{99m}Tc-DMSA, administered activities proved to be lower than the activities recommended by the product's licence (p=0,04) but higher than EANM's recommendation (p=4,8.10-4). Administered activities of ^{123I}-MIBG were 1,5 times lower than the product licence (p=0,013) but not significantly different from the EANM's recommendations.

To optimize the patient's exposure to ionising radiations, our results will be studied by a working group, composed of nuclear medicine doctors, medical physicists and radiopharmacists. Practices will be analyzed from a technical perspective (performances of the cameras), a clinical perspective an organisational perspective (taking care of children in an adult unit) and specifically to the radiopharmaceutical drug's characteristics (adjustment of the volume activities to the administration of small activities...). Conclusion: The radiopharmacist as any professional participating in medical acts, which exposed the patient to ionising radiation is involved in radioprotection on the patient. The assessment of practices in this field leads to an optimisation of quality and security in the context of administration of radiopharmaceutical drugs which prove to be necessary.

P039

Radiation Absorbed Dose of Tehran population from Diagnostic Thyroid Nuclear Medicine Examinations

F. Tabeie, I. Neshandar Asli, M. Motazedian; Shaheed Beheshti university of medical sciences, Tehran, IRAN, ISLAMIC REPUBLIC OF.

Aim: Among diagnostic nuclear medicine examinations, the thyroid procedures have a long history in diagnosis and treatment of thyroid disease. The aim of this study is to provide an updated nationwide report on thyroid nuclear medicine procedures in Tehran to calculate the collective effective dose to the Tehran population to be compared with the previously published data. **Materials & methods:** Comprehensive data including annual frequency of thyroid diagnostic nuclear medicine procedures, type and amount of administered radiopharmaceuticals, age and sex distribution of patients were obtained from 34 nuclear medicine departments out of 40 active departments in Tehran from April 2003 to March 2004. The collective effective dose was calculated based on frequency of each examination in five age groups including 1, 5, 10, 15 and adult and the corresponding mean administered activities, the effective dose per unit administered activity for each radiopharmaceutical and age groups reference to ICRP 53 and ICRP 80. **Results:** The relative frequency of thyroid examinations was 26.7% and the contribution of thyroid examinations from collective effective dose was 8.83%. The mean effective dose per patient was 1.87 mSv which corresponds to 11.2 µSv per caput. About 1.34% of annual thyroid nuclear medicine examinations were performed on patients younger than 15 years and the corresponding collective effective dose was 3.495 human-Sv that contributes 0.48% of collective effective dose for all thyroid patients annually. The mean effective dose per pediatric patient was calculated to be 2.02 mSv. **Conclusion:** The relative frequency of thyroid examinations have changed from 82% in 1989 to 30% in 2004, which shows considerable decrease (2.7 folds). The decrease in thyroid procedures could be mainly due to national salt iodization program first introduced in 1994 which has had a major role in decreasing the goiter incidence and also implementation of other diagnostic modalities for evaluation of thyroid disease. The contribution of ¹³¹I from population dose has reduced from 71% in 1989 to 11% in 2004, which indicates a decrease of ¹³¹I use for diagnostic purposes.

P040

Current practices in radioiodine I-131 therapy for Differentiated Thyroid Carcinoma (DTC) in Greece: Some practical and radiation protection considerations based on measurements of dose rates and I-131 retention of patients at discharge.

A. P. Samartzis, P. Mavrokefalos, M. Molfetas, I. Datsaris, C. Alevizaki; Evangelismos General Hospital of Athens, Athens, GREECE.

Aim: To assess radiation hazard and evaluate some radiation protection parameters during I-131 treatment of patients for DTC in a large tertiary Hospital. **MATERIALS-METHODS:** A total of 2260 adult patients received I-131 therapy for DTC during the decade 1999 to 2009. These were hospitalized in the dedicated ward for 2 to 3 days. I-131 sodium iodide capsules were given in activities ranging from 1480 MBq (40 mCi) to 11100 MBq (300 mCi), depending on tumor staging and extent, size of thyroid remnant and thyroid uptake of tracer radioiodine. About 2 hours before discharge from the hospital, external exposure rates were measured using a calibrated ionization survey meter, with measurements taken at 1 meter from the patient's upright body axis (stomach to thyroid). Vertical movement of the survey instrument was utilized to obtain the maximum reading each time. Statistical analysis was performed using the SPSS package. **RESULTS:** The total number of patients treated per year showed a slight but statistically significant tendency for increase over the decade ($r=0.87$ $p<0.002$). No significant changes with time were found in either activities administered or I-131 retention at discharge ($p>0.6$). Distribution of activities administered was markedly skewed to the right [median and modal 2590 MBq, mean {3533.5 MBq +/- 1642.8 MBq (SD)}]. Distribution for values of I-131 retention was similarly skewed [median 177.6 MBq, modal 173.9 MBq, mean {220.15 MBq +/- 181.3 MBq (SD)} with 95% of values lower than 555 MBq (15 mCi)]. In 28 cases only a higher retention [740 MBq (20 mCi) to 1295 MBq (35 mCi)] was observed. A very short effective radioiodine half-life was found in the latter cases, when it could be measured. **CONCLUSIONS:** The probable explanation and significance of these findings will be discussed. In conclusion during I-131 therapy for DTC, 2-3 days hospitalization seems to cover radiation protection requirements except for very few special cases.

P041

Collective effective dose from radiopharmaceuticals for Nuclear Medicine diagnostic procedures in patients in 2009

B. Lopez Lorenzo; Hospital Universitari Vall d'Hebron, Barcelona, SPAIN.

Aim Medical use of ionizing radiation has grown very fast over the last decades. This growth should be linked to a thorough evaluation of the population radiation exposure. As Nuclear Medicine procedures may have a large contribution, our aim is to calculate the effective dose per patient and the annual collective effective dose as an indicator of the potential induced health effects. **Materials and Methods** We calculated the effective dose and collective effective dose from radiopharmaceuticals for patients that underwent diagnostic procedures in Nuclear Medicine Service in our hospital (Hospital Universitari Vall d'Hebron) during 2009. The number of patients for every type of examination was obtained from the Radiopharmacy Unit database.

Effective doses for nuclear medicine studies were obtained from International Commission on Radiological Protection Publication 80 (ICRP-80). **Results**

2009	No. Patients	% patients	Collective Effective Dose (person-Sv)	CEDE%	Per capita Effective Dose (mSv)
Brain	748	7,28	6,79	10,41	0,08
Thyroid	593	5,77	1,87	2,86	0,03
Lung	645	6,28	3,25	4,98	0,02
Cardiac	2521	24,53	23,21	35,57	0,01
GI	199	1,94	0,05	0,07	0,04
Renal	487	4,74	0,50	0,77	0,01
Bone	3919	38,14	20,64	31,63	0,00
Infection	255	2,48	0,88	1,34	0,01
Tumor	855	8,32	7,93	12,15	0,19
Miscellaneous	54	0,53	0,14	0,21	0,07
TOTAL	10.276	100,00	65,25	100,00	0,03*

* Average annual effective dose per capita. Results obtained showed that cardiac and bone related explorations are the main sources of radiation that contribute to the collective effective dose as they represent the great number of patients. Nevertheless, the group of explorations with higher effective dose per capita is the tumour related. This is because of the radionuclides used for these diagnostic procedures (In-111, Ga-67 or I-123). **Conclusion** In order to provide a systematic assessment of radiation from practice in Nuclear Medicine services, we propose to evaluate the collective effective dose every year. The increasing number of explorations involving PET or hybrid CT, like SPECT or PET-CT make necessary in future studies, to include the effective dose from these procedures, as it represents an important additional radiation exposure for patients. It is necessary to promote a rational and sustainable development of medical procedures involving ionizing radiation to always maintain an acceptable benefit/risk ratio.

P08 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Physics & Instrumentation & Data Analysis: Staff dosimetry

P042

Radiation protection in nuclear medicine therapeutic procedures

C. Fabri, F. Del Dottore, L. Tassinari, S. Pagan, M. Rustignoli, P. Motta, M. Casi, M. Bartolomei, G. Sarti; Bufalini Hospital, Cesena, ITALY.

Aim: In nuclear medicine therapeutic procedures, unsealed β-γ emitting sources are used (15 GBq ⁹⁰Y each session). Inside the manipulation cell and during the patient administration, the electrons radiation field is inhomogeneous thus the skin exposure is very high and the exposure of the extremities is nonuniform. The object of this study was to assess an appropriate personal dosimeter that is able to respond to the β field in order to measure the maximum skin dose. **Materials & Methods:** Particular individual monitoring system was adopted: single TLD (GR200A), wrapped in polyethylene film and placed on an adhesive tape are positioned on tip of the fingers; 6-10 dosimeters are assigned to each operator per sessions. This study included the results of the characterization of GR200A in mixed beta-photon radiation fields. The energy-angle response was studied for X ray spectra and ⁹⁰Cr/Y and ²⁰⁴Tl. A unique mean calibration factor relative to beta-photon radiation was calculated in order to assess Hp(0.07). The combined uncertainty was calculated following the Guide to the Expression of Uncertainty in Measurement and Radiation Protection n.160. The method was developed by a statistical package in MATLAB software. **Results:** We verified the good performance requirements of this dosimetric method to International Standard (IEC 62387-1 007). The standard combined uncertainty evaluation by Monte Carlo method in ⁹⁰Y procedures monitoring was within 11%; the coverage interval (95%) varied from 0.93 to 1.24. The readings for a single manipulation were ranging from 0.2 to 30-40 mSv depending whether or not the automatic fractionation system and the shielding / spacing devices (plexiglass/lead materials) were used. Owing to the strongly inhomogeneous dose distribution, the ratio between the highest and the lowest value on the fingers, for a single manipulation and operator, is significantly greater than 1 and up to 30-40. In the year 2009 (40 therapy sessions) survey measurements resulted: median Hp(0.07)=0.27 mSv (range: 0.1-36.4) for radiochemist/physician dedicated to the manipulation in the hot cell the; median Hp(0.07)=0.39 mSv (range: 0.1-21.7) for the physician who delivered the therapy. In the year 2010, in a new investigation, the individual extremities doses are being estimated to reveal the critical steps separately during: labelling, quality assurance procedures, transfer from a mother vial solution, fractionation and administration. **Conclusion:** The method revealed the critical steps for further optimisation of practices and it ensures the respect of dose limits.

P043

Determination of the staff's I-131 incorporation on a radioiodine therapy ward. Is incorporation monitoring required for routine practice?

C. Happel, W. T. Kranert, J. Gessler, I. Selkinski, P. N. Truong, B. Sauter, M. Middendorp, F. Grünwald; Hospital of the Johann-Wolfgang Goethe University, Frankfurt / Main, GERMANY.

Aim: Aim of the study is to determine the annual I-131 incorporation of staff (different professions) on a radioiodine therapy ward and the resulting annual effective and organ (thyroid) dose, respectively, caused by incorporation. The necessity of incorporation monitoring is discussed in comparison to the cut-off values according to the German incorporation guideline^[1]. **Methods:** I-131 activity concentration in urine samples (collection for 24 h) of the responsible

physician, technical, nursing and cleaning staff were examined fortnightly over a period of one year by the magisterial designated Bavarian state office of environment. During this period 677 GBq I-131 were handled and administered to patients, mainly in form of I-131 capsules. Preparation was done in a flue. Following the German guide line^[1], a regular incorporation monitoring is necessary in cases of an effective whole body dose above 1 mSv/a. Below 1 mSv/a an incorporation monitoring by a radiation protection authority is not required. Results: For the physicians and technical staff most measurements were below detection limit, 6 Bq/a and 24 Bq/a respectively, corresponding to an effective whole body dose of 0.002 mSv/a and 0.01 mSv/a. 493 Bq/a for the nursing and 4.6 102 Bq/a for the cleaning staff were recorded resulting in effective doses of 0.28 mSv/a and 0.06 mSv/a, respectively. Conclusions: At present the cut-off value of 1 mSv/a is not exceeded by the investigated professional groups. Regarding the employees who spend most of their working time nearby the patient (nursing and cleaning staff) an incorporation monitoring might be required depending on how much activity is administered per year. Physicians and physicists do not require an incorporation monitoring due to their short attendance in the patient room. Approximately, an incorporated activity (percentage of the incorporated activity related to the administered activity in the observed period of time) of 3×10^{-10} for the physicians, 2×10^{-9} for the technical staff, 4×10^{-9} for the nursing- and 8×10^{-9} for the cleaning staff can be assumed. References: [1] Guideline of physical radiation protection for determination of body dose; Part 2: Determination of body dose caused by internal radiation exposure (incorporation monitoring)(§§ 40, 41 and 42 StrlSchV); 12.01.2007

P044

An investigation for effects of nursing level in various performance status of patients on dose of radiation exposure of F-18 FDG-PET.

K. Watanabe¹, Y. Kusano¹, A. Okizaki², T. Aburano², J. Sato¹, K. Shiba¹, J. Ueda¹; ¹Asahikawa Medical College Hospital, Asahikawa, JAPAN, ²Asahikawa Medical College, Asahikawa, JAPAN.

Aim Generally speaking, F-18 fluorodeoxyglucose (F-18-FDG) positron emission tomography (PET) is useful to evaluate malignant tumor or inflammations. Doctor or nursing staff are unable to avoid the radiation exposure when the radiotracer injection. The time, distance and shielding from radioactivity affect an amount of radiation exposure (ARE). We hypothesized that the ARE to the medical staff who performed an injection of radiotracer may depend on patient's situation. We investigated the relationship between the ARE, which was to the medical staff during the injection of 18F-FDG and treatment for the patients, performance status of patients and treatment to patients. **Materials & Methods** Measurements of the ARE to our three medical staffs were carried out with individual electronic dosimeters in 958 F-18-FDG injections. We defined good performance status patients (good PS, n=889) as patients who could walk by themselves, moderate performance status patients (moderate PS, n=50) as patients who needed wheelchairs, and poor performance status patients (poor PS, n=20) as patients who were permanently bedridden and needed stretchers for transportation. Furthermore, moderate PS and poor PS were categorized into 3 groups, like the nursing criteria recommendations of, Kyoto University. These 3 groups were composed of patients who were able to move by themselves (grade 1), who could change their position by themselves (grade 2), and who were completely bedridden (grade 3). First, the ARE from good PS, moderate PS and poor PS were compared. Second, the ARE with oral and actual instruction to good PS were also evaluated. Third, the ARE from grade 1, 2 and 3 patients were investigated. To test the differences of ARE, the two-tailed Student t-test or the Welch modified t-test was used depending on the equality of variances which calculated by using Leven's test. A p value less than 0.05 was considered statistically significant. Results The results were summarized in the tables. The average of ARE from good PS was significantly lower compared with moderate PS and poor PS (Table1, $p < 0.0001$ and $p < 0.0005$, respectively). The average of ARE with oral instruction was significantly lower than it with actual instruction (Table2, $p < 0.0001$). The average of ARE from grade 3 patients was higher than grade 2 (Table 3, $p < 0.05$). Conclusion To minimize ARE to medical staffs, the patients who were completely bedridden have to be carefully examined.

Table1: The ARE of Good PS, Moderate PS and Poor PS

	Good PS	Moderate PS	Poor PS
Average	1.337*	6.220**	8.150
SD	0.841	4.239	6.761

(* $p < 0.0001$; ** $p < 0.0005$, compared with poor PS)

Table2: The ARE with oral and actual instruction

	Oral instruction	Actual instruction
Average	0.222*	1.116
SD	0.447	0.856

(* $p < 0.0001$;))

Table3: The ARE of grade 1, 2 and 3 patients

	Grade 1	Grade 2	Grade 3
Average	5.625	5.259*	8.963
SD	2.604	3.145	6.881

(* $p < 0.05$, compared with grade 3)

P045

Radiation Protection for Accompanying Person and Radiation Workers in PET/CT

M. Demir¹, B. Demir², H. Sayman¹, S. Sager¹, A. Ahmed¹, I. Uslu¹; ¹Istanbul University, Dept of Nucl Med., Istanbul, TURKEY, ²Istanbul University, Science Faculty, Istanbul, TURKEY.

Aim: The aim of this study is: (1) to quantify the excretion of ¹⁸F-Fluorodeoxyglucose in the urine for the patients undergo PET/CT imaging, (2) to measure the total radiation doses for the radiation workers and for the accompanying person to the patients; and (3) guide line for dose minimization to minimize dose for the accompanying person and radiation workers. **Method:** Forty Five patients were injected intravenously with 15 mCi (555 MBq) ¹⁸F-Fluorodeoxyglucose. Urines of patients were taken at 30, 60, 90, 120, 240, 360 minutes after injection and activity of these urines were determined: in vitro from urine sample. Dose rates at different distances from parents were measured using a Geiger Muller detector and total radiation dose from patients to accompanying person of the patients were measured with electronic personnel dosimeter. **Results:** While activity concentration of ¹⁸F-Fluorodeoxyglucose in urine at 30 minute after injection or after collection of sample was 90.2 MBq/ml activity concentration was decreased to 39.2 MBq/ml at 120 minute. According to our results, 19.2 % of ¹⁸F-Fluorodeoxyglucose was excreted out of the body with urine in 120 min after injection. At 120 min after injection, dose rates at 0.1 m, 0.25 m, 0.50 m, 1.0 m and 2.0 m were determined as 345 μ Sv/h, 220 μ Sv/h, 140 μ Sv/h, 50 μ Sv/h and 15 μ Sv/h, respectively. The whole body total radiation dose after 120 min were measured as 3.92 mSv at 0 m, 2.11 mSv at 0.25 m and 1.08 mSv at 0.5 m. **Conclusion:** Within the first two hours after injection, (19.3 %) of ¹⁸F-Fluorodeoxyglucose radioactivity injected to the body was excreted out of the patients body by way of urinating. The amount of activity retained in the patient's body yield an external dose of about 1,08 mSv within a distance of 0.5 m from the patient's body. Hence, the person living with patients should take necessary precautions from the point of radiation protection within these two hours, and there is no need any protection precautions after that time.

P046

Radiation Exposure Assessment of Unclassified People Who Come into Contact with Patients Undergoing Nuclear Medicine 99mTc Investigations

G. Nardella, N. Urbano, M. R. Cintoli, L. Pinto, S. Modoni; Azienda Ospedaliero-Universitaria Ospedali Riuniti, Foggia, ITALY.

Patients administered with radiopharmaceuticals become radioactive sources representing potential trouble especially to unclassified members of hospital staff (accompanying nurses, health assistants, physicians in other departments), patient's relatives and members of public. **Aim.** To estimate, at departure from nuclear medicine unit, the real dose rates of the patients who underwent different scans. **Materials and methods.** 105 patients (47 M, 58F, age 25-83 yrs) were administered with 99mTc-MDP (activity range 500-670 MBq), 5 patients (4M, 1F, age 56-76 yrs) with 99mTc-MAA (activity range 150-195 MBq), 14 patients (8M, 6F, age 50-83 yrs) with 99mTc-HMPAO (activity range 600-700 MBq), 12 patients (10M, 2F, age 34-77 yrs) with 99mTc-DTPA (activity range 70-178 MBq), 10 patients (5M, 5F, age 40-64 yrs) with 99mTc-nanocolloids (activity range 35-75 MBq) for sentinel node scintigraphy, 15 patients (5M, 10F, age 23-80 yrs) with 99mTcO₂Na (activity range 63-100 MBq) for thyroid scintigraphy. The dose rates (μ Sv·h⁻¹) were measured by KATA DGM1500 Turva dose-meter positioned on a level with stomach at 1 m distance immediately after administration (T₀) and, respectively, 3 hours later (T₃), when the patients presumably left the department. **Results.** The highest dose rates were observed in bone scans (T₀: 8.03±3.9 μ Sv·h⁻¹, range 1.9-22.0; T₃: 3.2±1.4 μ Sv·h⁻¹, range 1.0-7.5), followed by lung perfusion scan (T₀: 7.26±0.1 μ Sv·h⁻¹, range 7.2-7.5; T₃: 2.36±0.3 μ Sv·h⁻¹, range 2.0-2.9) and brain SPET (T₀: 5.18±2.1 μ Sv·h⁻¹, range 3.0-9.0; T₃: 2.99±1.1 μ Sv·h⁻¹, range 2.0-5.0). Lower dose rates were recorded in kidney DTPA (T₀: 1.54±0.5 μ Sv·h⁻¹, range 1.90-2.5; T₃: 1.1±0.4 μ Sv·h⁻¹, range 0.7-1.9), sentinel node scintigraphy (T₀: 1.18±0.4 μ Sv·h⁻¹, range 1.0-1.9; T₃: 0.84±0.36 μ Sv·h⁻¹, range 0.1-1.5) and thyroid scan (T₀: 0.89±0.2 μ Sv·h⁻¹, range 0.7-1.4; T₃: 0.69±0.3 μ Sv·h⁻¹, range 0.3-1.2). **Conclusions.** Apart from the administered activities, the kinetics of different radiopharmaceuticals played a major role in determining T₃ dose rates. Thus, even presuming a close and lasting proximity, the radiation exposure risk for unclassified people who assist the patients submitted to a nuclear medicine investigation is widely below the limits outlined in the national legislation.

P047

Radiation protection design and procedures in a renewed Radionuclide Therapy Department

F. Fioroni, E. Grassi, M. Sarti, A. Versari, D. Salvo, G. Borasi, M. Iori; S. Maria Nuova Hospital, Reggio Emilia, ITALY.

Purpose: Radioiodine (iodine-131) therapy has been used successfully in thyroid therapy for more than 50 years. Moreover, the rapid and widespread growth in the use of nuclear medicine therapy of disease has required the introduction of new isotopes in clinical practice (i.e. yttrium-90, lutetium-177, radium-223). These new isotopes, beta and alpha emitters, require other precautions than gamma emitters, especially during preparation and administration. The extension of our metabolic therapy department, that included the design of two new protective rooms and other new spaces, has requested the evaluation of shielding requirements and procedures for different therapy treatments. A further aim was to review practical radiation safety concerns associated with hospitalized patients receiving radionuclide therapies, in order to minimize potential exposure and contamination problems. **Material:** Calculated shielding requirements for room facilities were performed considering iodine-131 attenuation coefficients, following NCRP 147 recommendations. The most critical wall was built using a composition 1 cm thick lead and 10 cm thick heavy concrete. Because the iodine-131 photons are penetrating, it was necessary to consider uncontrolled areas above and below the metabolic therapy facility as well as those adjacent on the same level, open to the general public. The use of radioactive nuclide beta and alpha emitters for cancer therapy are performed in the same department. These activities required the introduction of new radioactive handling solutions, proper shielding and devices, specific dosimeters. **Results:** Radiation protection surveys performed in adjoining areas, after the building of the new rooms, showed the complete observance of the project dose limits. The monitoring of the staff in charge of radiopharmaceuticals preparation, administration and assistance respects the threshold limits reported by ICRP and European Directive EURATOM 96/29, for exposed workers (maximum whole-body effective dose < 20mSv/year; maximum skin equivalent dose < 500mSv/year). Last three years have shown a decrease of the mean fingertip doses for radiochemists responsible for labelling processes (a 50% reduction from 2007 to 2009). The same trend in terms of fingertip doses was also for nuclear medicine physicians, involved in patient administration (a 70% reduction from 2007 to 2009). **Conclusion:** The introduction of isotopes with different physical properties in radionuclide therapy demands the investigation of

changing safety assessment. To keep radiation exposure as low as reasonably achievable, staff handling radiopharmaceuticals must maintain good laboratory practice and patient management needs the compliance of safety procedures and improvement of devices.

P048

Evaluation of wrist and finger dose of dedicated medical workers operating in PET/CT departments

K. Dalianis, F. Vlachou, V. Filippi, L. Gogou, D. Kechagias, K. Gogos, A. Tsaroucha, I. Andreou, V. Prassopoulos; D.T.C.A. Hygeia Department of PET/CT, Athens, GREECE.

Purpose: Positron emission tomography is growing rapidly in Greece, four sites are operating at this time and a few more are going to operate soon. Our Hospital was the first PET/CT facility to operate in Greece. The use of 18F FDG for clinical studies increases workers radiation dose exposure because of the higher γ radiation energy of this isotope than other conventional γ radiation emitting isotopes. The aims of this study were to estimate the effective dose to wrist and fingers for the staff that is responsible for dose segmentation and dose injection. Method: Radiation dose measurements were performed for multi dose vial of 18F FDG concerning the segmentation of the doses and the administration of the radiopharmaceutical. To estimate the effective dose all members of the staff, two medical physicists and two nurses had TLD badges worn at the right wrist and finger TLD badges at the middle finger. Results: In the period of January 2009 to December 2009 a total of 1152 PET/CT studies. The administered activity for all scans except brain scans is between 370-410 MBq (10-11 mCi). The accurate activity is normalized to body surface area of the patients. For brain scans the dose activity is approximately 220 MBq (6 mCi). The wrist and finger doses received by all 4 members of the PET/CT staff were the following: Nurse 1 received 14.2 mSv as a wrist dose and 145 mSv as a finger dose and Nurse 2 received 13.6 mSv wrist dose and 168 mSv finger dose respectively. Medical Physicist 1 received 22.7 mSv wrist dose and 341 mSv finger dose and Medical Physicist received 21.2 mSv and 325 mSv respectively. Conclusion: The personnel dose results are significantly lower than the recommended annual dose by International Commission for Radiological Protection. The higher value of gamma dose for PET/CT workers by comparison with the staff operating conventional Nuclear Medicine procedures is attributable to the higher specific gamma constant of 18F, as well as the longer exposure time required for accurate positioning.

P049

Evaluation of Personnel Radiation Dosimetry during Myocardial Perfusion Scintigraphy for Cardiology Staff

A. Skopljak-Beganovic, N. Beslic, E. Kucukalic-Selimovic, A. Beganovic, B. Turkic; Clinical Centre of Sarajevo University, Sarajevo, BOSNIA AND HERZEGOVINA.

The aim of this study was to assess radiation doses to noninvasive cardiology staff during myocardial perfusion scintigraphy. Noninvasive cardiology staff members do not belong to the group of occupationally exposed workers and evaluation of radiation doses was important issue in the aspect of radiation protection. It was necessary to investigate staff doses received during treadmill exercise and try to measure and minimize external exposure from patient. Radiation dose assessment was performed with electronic personal dosimeters (ED) and dose rate was measured with ionization chamber. Myocardial perfusion scintigraphies are performed one or two times per week, with two to five patients each time. The radiopharmaceutical used for myocardial imaging was Tc-99m MIBI in activity range 260-333 MBq for stress studies and 777-999 MBq for rest studies. All treadmill exercise studies are performed in Cardiology department in a presence of nurse and cardiologist and a team from nuclear medicine. The nurse and cardiologist were equipped with electronic dosimeter over the chest. The nuclear medicine technologist and nuclear medicine physician attending examination carried TLD-s and ED-s. Physicist made dose rate measurements at 1 m distance from the patient. The whole body radiation doses were evaluated during 2 months period. In that period 14 measurements were made and 51 patients performed treadmill exercise as a part of stress study. The mean \pm SD total effective dose per patient received by nurse during treadmill exercise was 0,986 \pm 0,129 μ Sv, measured with ED. Dose received by cardiologist was 0,242 \pm 0,80 μ Sv per patient. Dose rate 1 m from injected patient was 0,007 \pm 0,003 mSv/h. Extrapolation of these numbers to an annual dose revealed that the annual extrapolated values of dose received by nurse and cardiologist from the exposure during treadmill exercise in stress study are 300 μ Sv/a and 75 μ Sv/a, respectively. The dose received by noninvasive cardiology staff is a result a time spent and a distance from the patient after injection of Tc-99m MIBI. They do not handle or inject radiopharmaceuticals. These results showed that radiation doses received by non invasive cardiology staff were low and under the authorized limits for workers classified to work in a radioactivity-controlled area.

P050

Radiochemical and Alpha Spectrometry Analysis of Uranium Isotopes in the Civilians of Gaza.

A. Durakovic¹, T. Weyman²; ¹Uranium Medical Research Centre, Washington, DC, UNITED STATES, ²Uranium Medical Research Centre, Toronto, ON, CANADA.

Purpose: The presence of the isotopes with enriched uranium signature from the guided weapons used in the recent military conflicts in Lebanon (2006) and Gaza (2009) has been reported (C. Busby; ECRR No2 Brussels 2010). The aim of our study was to analyze a possible contamination of the civilian population of Gaza Strip. Materials and Methods: The team of the Uranium Medical Research Center (UMRC) collected the urine samples of civilians in Gaza Strip exposed to the dust following Operation Cast Lead (December 2008 - January 2009). Twelve subjects from Jabaliya, Beit Lahia, Rafah, and Gaza City, selected on the basis of their history of exposure and the standard profile symptoms, had their 24 hour samples of urine analyzed for the uranium isotopes at the Laboratories of the Harwell Science and Innovation Centre, England, by the method described in HS/GWI/2055. The urine samples were digested for three hours after addition of nitric acid, calcium chloride carrier and a yield tracer. The uranium was co-precipitated on a Calcium/Magnesium phosphate precipitate which was filtered and ashed in a

muffle furnace. The residue was dissolved in hydrochloric acid, aluminum nitrate and hydrolysed to orthophosphates, passed through anion exchange column as a chloride. The column was washed with hydrochloric and nitric acid, uranium eluted with nitric acid and evaporated to dry. The residue was dissolved in sulphuric acid, the pH adjusted and the uranium electrodeposited onto a stainless steel discs for alpha spectrometry. Results: The results were expressed in Bq/L⁻¹. The minimum reporting levels are 2mBq/24 hours. The measured peaks for U-234, U-235, and U-238 were 4.776, 4.395, and 4.196 MeV respectively. The analysis was carried out with reagent blank, spiked with U-232 tracer solution. U-236 (4.494 MeV) could not be accurately measured by this method because of the proximity of U-234 and U-235 peaks. Our results indicate the ranges of <1 - <7 for U-234, U-235, and U-238 (mBq/L⁻¹), with mass-metric equivalents of U-234=437*10³ ng/L. U-235=12.6ng/L. U-238 =81.1ng/L as an estimated value. Conclusions:Neither depleted uranium nor man-made uranium isotopes were detectable in the urine samples of Gaza civilians following the recent military conflict of 2008/2009. This method provides no alternative to detection accuracy of inductively coupled plasma mass spectrometry (ICP-MS).

P051

The Assessment of the Radiation Protection Quality and the Effective Dose of the Nuclear Medicine Workers, a Single Centre Nine-Year Retrospective Study.

J. Dolezal, J. Vizda, E. Urbanova, P. Kafka, J. Kulir, M. Matysova; Department of Nuclear Medicine, Teaching Hospital, Hradec Kralovce, CZECH REPUBLIC.

Aim: To assess a radiation exposure and a quality of radiation protection as to nuclear medicine staff at our department as a nine-year retrospective study. The therapeutic radionuclides as a ¹³¹I, ¹⁵³Sm, ¹⁸⁶Re, ³²P, ⁹⁰Y and diagnostic ones as a ^{99m}Tc, ²⁰¹Tl, ⁶⁷Ga, ¹¹¹In were used. **Material and Method:** The effective dose was evaluated in the period of 2000-2008 for nuclear medicine physicians (n = 7), technologists (n = 12) and radiopharmacists (n = 2). A personnel film dosimeter and a thermoluminescent ring dosimeter for measurement (1-month periods) of personal dose equivalent Hp(10) and Hp(0,07) were used. Dosimeters were worn obligatory within the frame of nation-wide service of the personal dosimetry. The total administered activity all radionuclides during these nine years at our department was 26 712 GBq (^{99m}Tc 22 102 GBq, ¹³¹I 3 743 GBq, others 867 GBq). The administered activity of ^{99m}Tc is similar, but the administered activity of ¹³¹I in 2008 increased by 244%, as compared with the year 2000. **Results:** The mean and one standard deviation (SD) of the personal annual effective dose (mSv) for nuclear medicine physicians was 1.9 \pm 0.5, 1.9 \pm 0.6, 1.8 \pm 0.8, 1.2 \pm 0.8, 1.4 \pm 0.8, 1.3 \pm 0.6, 0.8 \pm 0.4, 1.2 \pm 0.7, 1.1 \pm 0.5 and for nuclear medicine technologists was 2.3 \pm 1.4, 1.9 \pm 0.8, 1.7 \pm 1.4, 1.0 \pm 1.0, 1.1 \pm 1.2, 0.9 \pm 0.4, 0.7 \pm 0.2, 1.0 \pm 0.5 and 0.9 \pm 0.5 in 2001, 2002, 2003, 2004, 2005, 2006, 2007 and 2008 respectively. The mean (n = 2, estimate of SD makes little sense) of the personal annual effective dose (mSv) for radiopharmacists was 9.0, 3.2, 1.8, 0.6, 1.3, 0.6, 0.3, 0.8 and 0.5. Although the administered activity of ¹³¹I increased the average effective dose per year decreased during nine years. **Conclusion:** In all three professional groups of nuclear medicine workers a decreasing radiation exposure was found although the administered activity of ¹³¹I increased during years 2000-2008. Our observations suggest successful radiation protection measures at our department.

P052

Various Devices of [¹⁸F]-FDG Dispensing

A. Sperandeo¹, A. Cistaro², D. Busetta¹, N. Paligoric¹, R. Mangiapane¹, U. Ficola¹; ¹La Maddalena, Palermo, ITALY, ²Irmet, Torino, ITALY.

Introduction. Our nuclear medicine department has begun the PET activity in 2002. Injectable doses were prepared manually and directly from the main vial, so operators were getting high absorbed doses. Our department was also supplying FDG daily to another hospital; Operators were preparing vials containing a large amount of activity (25 GBq). Operators nearly reached the limit on absorbed doses. That's why we had the urgency of an automatic dispensing system. The first one that was bought was the DDSA (TEMA Sinergie) in 2003. This device was able to make vials (for external supply) and syringes (for individual doses). Two years later we switched to another dispenser, RP300 (MASPRESS). This dispenser was able to make vials and syringes using another technology which caused less machine failures. Due to our needs, an upgrade was installed in our site shortly after. **Aim.** Optimization of dispensing procedures of ¹⁸F-FDG to decrease absorbed doses by operators. **Materials and methods.** We used 3 different dispensers: DDSA (TEMA Sinergie), RP 300 (MASPRESS) and an upgraded version of it. We had problems using the DDSA due to multiple failures on peristaltic pump, that was the core of this model. Another problem was represented by concentration of main vial. DDSA system was intended to work with low activity concentration in the main vial (800 MBq/ml). Our productions were a lot more concentrated (due to the external FDG supply), and we were forced to split the main vial in several smaller fractions. On RP300 model we tested some parameters such as accuracy of dispensed volume, reproducibility of it and eventual machine failures. The main problems were: related to lack of automatic dilution option for syringes and vials; There was just 1 gamma counter in our cell, forcing us to constantly switch main vial with the syringes to check the dispensed activity. We requested an upgraded version with some new features: Automatic dilution option with NaCl 0,9% and an additional gamma counter to check constantly vial activity and dispensed activity. **Results and discussion.** Using the first two models (DDSA and the first RP300), we had not a significant decreasing of operator's absorbed doses. Due to the a listed problems, a lot of interventions were needed, exposing operators to unnecessary extra doses. Thanks to the new features implemented in the upgraded version of RP300, operators are much less exposed to unnecessary doses and absorbed doses are significantly lower.

P09 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Physics & Instrumentation & Data Analysis: Management of quality & risk

P053

Importance of qualification and monitoring of PET/CT in multicentre trials: The SAKK 56/07 trial experience

F. A. Camus; Institut de Radiophysique, Lausanne, SWITZERLAND.

Aim In the Swiss Group for Cancer Research (SAKK) 56/07 multicenter trial on dasatinib first-line treatment in gastrointestinal stromal tumors, our PET Core Lab is responsible for the qualification and monitoring of the participating sites. Each site must meet entry criteria before trial participation and enrolling patients, and these criteria must be met periodically. Material and Methods Each participating centre has to submit PET/CT acquisitions from a water-filled uniform phantom containing 5.5 kBq/mL of ¹⁸F-DG and scanned according to their standard oncologic protocol. The mean standardized uptake values (SUVmean) are measured in the reconstructed image along 38 centered axial slices. The expected SUVmean should be 1.00 g/mL in any slice with an acceptable range from 0.90 to 1.10 g/mL. Then, monitoring was performed every 3 months, or earlier if PET/CT maintenance occurred. Results The variation of SUVmean for uniform phantom images among the 7 participating PET/CT scanners was characterized during 3-8 sessions (39 sessions or 1482 SUVmean measurements in total). Among these measurements, 84 (5.7%) were outside the accepted limits. And out of these wrong values, 28.6% were out of range on 1st measurement, indicating that SUV calibration is crucial before enrolling a center. For instance, the first session from Center #1 showed that 24/38 measurements (63%) were out-of-range (max SUVmean = 1.148); after corrective calibration, values returned within acceptable range (max SUVmean = 1.019). Moreover, periodic monitoring of SUV calibration is essential: The last session (8th) from Center #1 showed unexpectedly 71% of out of range values (max SUVmean = 1.126). Center #3 showed acceptable SUV values at the 1st session, but 2 (33%) of the following sessions showed out-of-range values. Center #5 had within range SUVmean over time, but monitoring showed a slow drift of the SUVmean towards lower values, which could be corrected before values were out of range by preventive maintenance. These examples highlight the need of periodic monitoring during the whole trial duration, and not only prior to centre enrollment. Conclusion SUV accuracy needs to be verified in each centre before any trial activity, and regular SUV accuracy monitoring using a standardized phantom is desirable in any clinical trial using PET/CT for quantitative assessment of therapeutic response.

P054

Stability of off-set parameters in PET/CT systems

L. Geworski¹, B. O. Knoop¹, E. Fitz¹, C. Karwath¹, M. Plotkin²; ¹Department of Medical Physics and Radiation Protection, Hannover Medical School, Hannover, GERMANY, ²Clinic for Nuclear Medicine, Charite, Berlin, GERMANY.

Aim: PET/CT hybrid systems are the method of choice in performing PET examinations. The adjustment of gantries and patient bed (off-set) of both modalities will influence image fusion and the quality of absorption correction at regions of changing attenuation coefficients. While routine control of the basic modalities PET and CT are described by appropriate regulations, corresponding instructions with regard to the interface connecting both are still missing. The aim of this study was to examine the accuracy and stability of gantry adjustment as basis for routine control. Materials and methods: On a Biograph 16 (Siemens, Inc.) the off-set measurements were performed following manufacturer's recommended method, but notably more often. These measurements were performed over an observation period of 10 months, supplemented by measurements with additional load to the patient bed (up to 135 kg), and different vertical bed positions (100, 177, and 206 mm). Therefore, 165 emission and CT-based transmission data were acquired in total. Results: The average off-set [mm] in x-direction was 1.38 +/- 0.04, and in y-direction -1.22 +/- 0.05, respectively. The distance between CT and PET gantry (z-direction) was 867.00 +/- 0.15 mm. With additional load, these values differed by less than 0.1 mm. The average off-sets [mm], for the different vertical bed positions (100, 177, and 206 mm) in x-direction were 1.97 +/- 0.09, 1.38 +/- 0.04, 1.21 +/- 0.05, in y-direction -1.57 +/- 0.06, -1.22 +/- 0.05, and 1.02 +/- 0.14, respectively. The trend in mean off-set parameters perceptible as a function of bed height can be attributed to a slight rotation the PET and CT coordinate systems to each other in the x-y plane, which is apparently compensated for during image reconstruction. The mean off-set in the z-direction was found to be independent on bed height. Conclusion: The deviation between PET and CT coordinate systems averaged less than 2 mm and can be stored as correction factors, as justified by the small standard deviations found. This also holds true for several mechanical gantry disconnections due to maintenance included in the observation period. So, for the construction principle tested routine controls have not to be extended beyond manufacturer's recommendation (twice/year).

P055

Hierarchic risk management in nuclear medicine

J. R. de Jong, J. Medema, A. K. van Zanten, H. H. Boersma, A. H. Brouwers, P. H. Elsinga, A. W. J. M. Glaudemans, J. Pruijm, R. A. J. O. Dierckx; University Hospital Center Groningen, Groningen, NETHERLANDS.

AIM: Current trends show governments pushing for a centralized structured methodology for risk management as well as hospitals utilizing industrial experience to develop their own methods. We present the 'Groningen interpretation': our current progress in establishing a solid risk management system for our nuclear medicine department on the basis of established methods. METHODS: The backbone of our risk management system is the risk assessment & evaluation (RAE). It serves as a master checklist and inventory that takes the primary processes, as already defined for the ISO 9001, as input and tracks whether the presence of e.g. risk analysis and work instructions is covered. This approach is highly compatible with the IAEA 'Quality Management Audits in Nuclear Medicine Practices'. The risk analysis of processes is performed through a hierarchic task analysis (HTA). Processes are analyzed by subdividing them into sub-tasks. A risk

assessment method, such as SAFER/HFMEA or, when quantitative risk analysis is possible, the Fine-Kinney model is subsequently applied in order to evaluate the sub-task and formulate corrective action when required. RESULTS: An HTA has been performed for processes such as radionuclide production, diagnostics using PET/SPECT, radionuclide therapy and radiopharmaceuticals production. In the majority of cases, the risk assessment method confirmed the soundness of our procedures. However, in some cases analysis yields the conclusion that corrective action is required. In other cases it was found that sub-tasks that are the most critical and that show the highest risks, were in fact different from our initial thoughts on for which sub-tasks this would be the case. For e.g. radionuclide therapy we found that i) certain documentation was missing ii) transportation of radionuclides and waste required additional precautions iii) radiation dose-rate measurements before release of patients was required also in the case of polyclinic treatment. CONCLUSION: Setting up a risk management system is a very effective way to screen for weak spots in the procedures that belong to processes. Moreover, it yields insights and information for both managers and workers on which aspects of processes involve the most risk and how to counter these effectively. Finally, it produces a verifiable set of documents and analyses with which external demands on safety and risk from both government and industry can effectively and demonstratively be met.

P056

An overview of quality control of nuclear instrumentation used in the Czech Republic

Z. Paskova¹, J. Zimak², D. Valachova², P. Maca³, J. Sabol⁴; ¹State Office for Nuclear Safety, Prague, CZECH REPUBLIC, ²Motol University Hospital, Prague, CZECH REPUBLIC, ³Hospital Na Homolce, Prague, CZECH REPUBLIC, ⁴Charles University in Prague - 2nd Faculty of Medicine, Prague, CZECH REPUBLIC.

Radiation exposures of patients undergoing nuclear medicine examinations and therapy depend also on the quality of instrumentation used. The quality control system being introduced at nuclear medicine facilities, which is required by the current legislature of the Czech Republic, includes among other things, regular inspection of all essential instruments utilized for the measurement of ionizing radiation, based on which valuable information required for the diagnosis or treatment is obtained. In 1999, the State Office for Nuclear Safety (SONS) issued its recommendations on the quality assurance system of instruments at nuclear medicine facilities. The paper presents an overview of the recommended inspections of the relevant instruments such as dose calibrators, single-detector systems for measurements in vitro and in vivo, multi-detector systems for measurements in vitro, imaging devices, and radiation protection instrumentation. The scope and frequency of these inspections carried out at nuclear medicine facilities is given in the SONS document "Programme on Quality Assurance", which has been adopted at these facilities. Quality control of imaging systems prescribed by the SONS is consistent with the present recommendations of the EANM, however, they have been expanded to include the quality control of new techniques namely SPECT/CT, PET and PET/CT.

P057

Ten years of experience with quality management in the nuclear medicine department

J. Medema¹, M. N. Lub-de Hooge¹, A. H. Brouwers¹, A. Dekker¹, H. J. van Veen², R. A. J. O. Dierckx¹, A. K. van Zanten¹; ¹University Medical Center of Groningen, Groningen, NETHERLANDS, ²ZIN these, ZIN, Groningen, NETHERLANDS.

AIM Although Quality Assurance is an important issue in Nuclear Medicine, the department of Nuclear Medicine and Molecular Imaging in Groningen is one of only a few centers that has qualified for ISO 9001 certification for the third time in a row. The department uses ISO 9001 and European Foundation of Quality Management (EFQM) guidelines as tools to create the necessary conditions for systematic quality management. The goal is to become an excellent, EFQM-qualified organization. METHODS The development of the quality management system starts with the identification of critical processes and their mutual relationship. In order to be able to manage the outcome of a process, it is necessary to describe the requirements which have to be met. Uniformity in language is started with the publication of a Quality manual. To link the conceptual model to the real business, the role of process owner is implemented. This role embodies the process control by monitoring the performance. EFQM offers the framework for an integral quality approach with a customer-oriented and risk management focus and stimulates the use of self-assessment and review instruments. RESULTS

Year	Key issues	State of maturity	Result
2000	-	Process orientation	ISO 9001 certification Quality manual Strict document control procedures Use of process performance indicators
2004	ISO 9001	Process orientation	Determining quality objects Intern process audit Yearly review of all processes Zero measurement and EFQM self assessment Second ISO 9001 recertification / focus on patient
2005	EFQM	System orientation	Patient satisfaction survey
2007	approach	Customer focus	Referrers survey Cluster audits (department) Site accreditation by the EANM Contractresearch (manufacturing license radiopharmaceuticals) Third EFQM self assessment Third ISO 9001 recertification Risk management / PRISMA analyses Update GMP facility NM Chain audits (hospital)
2008	GCP	Chain orientation	
-	GMP	A link in the chain of	
2010	Good Safety Practice	excellent healthcare	

2010
- TQM Center of excellence
2015

State of the art center
GMP radiopharmacy facility
Dutch National Quality Award
European Quality Award (EFQM)

CONCLUSION The ISO system provides for many things a reminder to perform an action and is considered a catalyst to go for TQM. What started as a pioneer project is now integrated in all processes in our department. ISO is also an effective tool to implement standards as GMP, GCP, GLP and (patient) Safety Systems. To achieve a Total Quality Management framework the combination of ISO 9001 and the EFQM-approach has proven to be useful so far.

P058 Risks Analysis in Nuclear Medicine

I. Quelven¹, C. Rouet¹, N. Ficat², J. Monteil²; ¹Service de Médecine Nucléaire-Radiopharmacie, CHU Dupuytren, Limoges, FRANCE, ²Service de Médecine Nucléaire, CHU Dupuytren, Limoges, FRANCE.

Aim Avoiding medical mistakes is a mandatory purpose of any patient care. In Nuclear Medicine, the dose the patient receives for diagnostic use is lower than the one he receives for Radiotherapy. However, radiation protection of patients should always be optimized according to the ALARA rules. Unnecessary patient exposure to ionizing radiation is the main failure risk, but not the only one. Indeed, diagnosis failure could induce delayed or non-optimal patients care. Studying the risks hierarchy should help to identify and to prioritize preventive actions. This kind of study has proved to be efficient in industry and now hospitals start to apply it. In France, failure risk study in Nuclear Medicine is required to the national hospital certification and is a law requirement for Radiotherapy. **Materials & methods** We first gathered a working group made of each professional profiles of Nuclear Medicine. We used the Failure Mode Effects and Criticality Analysis (FMECA) focused on the patient risks. For each step of clinical patient care in Nuclear Medicine, we reviewed failures mode, the associated risks and causes, and the preventive measures already set up. With a four steps scale, we evaluated both damage severity and estimated frequency of occurrence. We obtained a risk criticality index by multiplying these two quantifiers. **Results** Patient course was analyzed in seven processes: appointment planning, administrative admission, medical evaluation, radiopharmaceutical preparation, injection, image acquisition and interpretation. Our study identified two of them as risk processes: radiopharmaceutical preparation and administration. Even if the preventive measures already put into practice lower the risk frequency, they fail at reducing damage severity. The image acquisition step is less critical since we can most of the time repeat the data acquisition without new injection. In each process, patient identification appeared as a major failure risk and concerns all departments of the institute. Identity strap is therefore already used for all the hospitalized patients. However, most of Nuclear Medicine exams concern outpatients, which raise this failure risk. Finally, staff management is mainly important: stress and overwork may disturb professional attention. **Conclusion** Although FMECA is a subjective method, this a priori approach analyzes the whole process and lists the failure modes independently from their occurrence. Failure risk study could also be estimated by a retrospective analysis of adverse events declarations. However, this method frequently underestimates failure by non-systematic declaration. We should now apply the measures that would prevent the critical failures we identified.

P10 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Molecular & Multimodality Imaging: PET/CT - Methods and pitfalls

P059

Clinical PET/CT operations for oncology imaging are not standardized: Results from an ongoing international, web-based survey

T. Beyer¹, L. Freudenberg², F. Walter³, J. Czernin³; ¹cmi-experts, Zürich, SWITZERLAND, ²ZRN Grevenbroich, Grevenbroich, GERMANY, ³UCLA, Los Angeles, CA, UNITED STATES.

OBJECTIVES To compare clinical PET/CT operations worldwide. To review PET/CT protocol parameters for oncology patients. To support discussions regarding the use and standardization of clinical PET/CT imaging. **MATERIALS AND METHODS** An internet-based survey of PET/CT users was initiated in 11/2009: http://www.surveymonkey.com/s.aspx?sm=RSVLhZIS_2fHR6Eeh7oWo0g_3d_3d. Users were asked 50 questions related to (A) PET/CT centre and installation (eg, location, #systems, staffing) and (B) variations in FDG oncology imaging protocols. This survey is ongoing and intermediate results are presented here. **RESULTS** (A) Responses collected so far originated from centres in the US (66%), Europe (22%) and APAC (12%), with most responding sites being public (65%). PET/CT were installed in Nuclear Medicine (74%) and Radiology (26%) departments whereby 56% of the sites operating a PET/CT have PET-only experience for 10 y, or more. Over 50% of all sites operate 2 PET/CT systems, or more. PET/CT imaging is employed for torso/whole-body oncology (95%), local examinations (55%), RTP (45%), cardiac (61%) and neurology (81%). (B) Average fasting prior to FDG-PET/CT was 7 (4-12) h. All sites measured blood glucose levels while using different cut-offs (50%: 200 mg/dL). Weight-based activity injection is performed at 38% sites. Mean FDG activity injected is 360 (200-555) MBq for 3D-PET. Mean uptake time is 64 (20-90) min. Split protocols involving patient repositioning are employed at 52% sites. Only 39% use patient positioning aids. 19% sites employ IV contrast in ≥75% patients. 44% sites employ oral contrast in ≥75% patients. Most sites (89%) measure SUV_{max} values. 18% of the sites report PET and CT from PET/CT separately. Non-FDG PET tracers are used in <3% of all patients. **CONCLUSION** An ongoing international survey among clinical PET/CT users reveals significant variations in standard FDG-PET/CT protocol parameters. This illustrates the need for continuous training efforts and standardization to further integrate PET and CT experience for optimized PET/CT imaging in oncology. **ACKNOWLEDGEMENT** We thank the Academy of Molecular Imaging for their ongoing support of this survey.

P060

Systematic reviews of PET in oncology: A map of the evidence

F. Scheibler, R. Grossefinger, I. Janssen, S. Sauerland, M. Schroerer-Guenther; Institute for Quality and Efficiency in Health Care, Cologne, GERMANY.

Aim The aim of our study was to identify systematic reviews (SRs) of PET in oncology, with a focus on diagnostic accuracy. We wanted to determine, for various indications, whether high quality SRs exist, need to be done or need to be updated. **Methods** We did a systematic literature search for SRs and Clinical Practice Guidelines or HTA reports based on SRs. The publications that we found covered 7 types of cancer (adenocarcinoma of the pancreas, melanoma, thyroid cancer, oesophageal cancer, ovarian cancer, breast cancer, and bone and soft tissue tumours) and 23 indications. Quality assessment was carried out using the index developed by Oxman and Guyatt. Inclusion criteria, methods of analysis, results and dates of last search update were extracted. **Results** We were able to identify 18 SRs of sufficient quality covering 17 indications (with several reviews covering two or more). No SR was identified for the other 6 indications. Only 4 of these were based on searches more recent than 24 months and only 2 more recent than 12 months. In 8 indications only one SR of medium quality could be found, in 2 we found only one SR of high quality. **Discussion** The results indicate that there is a greater need for up-to-date systematic reviews in some areas of PET research in oncology than in others. For example, imaging of bone and soft tissue carcinomas or breast cancer seem to be promising fields to gain relevant information by conducting new SRs. **Conclusions** More systematic reviews with more narrowly focused research questions need to be carried out in the field of PET. Considering the great need for high quality evidence in this field, it seems to be crucial that further research should focus on areas in which no good quality evidence currently exists.

P061 FDG PET

M. Hanako; Medical, Amagasaki, JAPAN.

Background Assessment of tumor response is an important component of anticancer therapy clinical trials. **Objectives** This retrospective study investigated the interobserver reproducibility of SUV of 18F-FDG PET as well as CT size measurements, and the changes observed in those measurements, in tumors prior to and after treatment. **Methods** In total, 52 tumors obtained from 25 patients (6 male, 19 female; mean age 51 years) were assessed using 18F-FDG PET/CT imaging. For each tumor, maximum SUVs as well as CT size measurements were evaluated independently on pretreatment and posttreatment scans with the help of 8 different readers, 4 assessing 18F-FDG PET and 4 assessing CT scans, by routine nonautomated clinical methods. Percentage changes in CT size and maximum SUV between pretreatment and posttreatment scans were estimated. Interobserver reproducibility of CT size, maximum SUV and changes observed in these values were analyzed using estimates of variance and intraclass correlation coefficients (ICC).

P062

SUV normalization to 1 hour post-injection in ¹⁸F-FDG-PET Imaging

E. F. G. Laffon¹, H. de Clermont², R. Marthan³; ¹Hôpital Haut-Lévêque, Pessac, FRANCE, ²Hôpital Pellegrin, Bordeaux, FRANCE, ³Université Bordeaux 2, Bordeaux, FRANCE.

Purpose: To overcome the need for a strict time delay between ¹⁸F-FDG injection and PET data acquisition in clinical practice. **Methods:** A previous model analysis has shown that, assuming irreversible uptake, when the SUV (Standard Uptake Value) is not corrected for the ¹⁸F physical decay, its value (SUV_{uncorr}) is nearly constant (with a reasonable ±2% relative-measurement-uncertainty) in each individual patient, if there is a time delay between tracer injection and PET acquisition, which falls in the range 60-110 min. In order to validate the model, ¹⁸F-FDG PET imaging was performed in 10 patients, each with 1 or more lung cancer lesions (n=15). **Results:** For a 60-110-min time delay between ¹⁸F-FDG injection and acquisition, a graphical comparison between the model analysis results and uncorrected patient data showed a significant agreement (p<0.02). Therefore a very simple normalization, producing a decay-corrected SUV obtained 1 hour after tracer injection (SUV_N), can be proposed: SUV_N = 1.46 * SUV_{uncorr}, where the factor 1.46 arises from decay correction at 1 hour. **Conclusions:** The proposed method has proven effective in overcoming the need for a strict ¹⁸F-FDG injection-acquisition time delay. Under the assumption of irreversible trapping, it is suggested that it could be applied to other ¹⁸F-FDG studies of neoplasms, and further that its principle could be applied to other PET tracers.

P063

Delayed ¹⁸F-FDG/PET-CT scan, impact in the correct evaluation of lung lesions

M. P. Talavera Rubio¹, A. M. Garcia Vicente¹, A. Palomar Muñoz¹, A. A. León Martín², J. M. Cordero García¹, V. M. Poblete García¹, M. E. Bellón Guardia¹, B. González García¹, I. Cepedello Boiso¹, J. P. Pilkington Woll¹, A. Núñez García¹, A. M. Soriano Castrejón¹; ¹Nuclear Medicine Department, University General Hospital., Ciudad Real, SPAIN, ²Investigation Unit, University General Hospital., Ciudad Real, SPAIN.

Aim: To assess the value of dual time point ¹⁸F-FDG/PET-CT imaging in the correct evaluation of lung lesions. **Material and methods:** We studied retrospectively 67 lung lesions (45 studies; 43 patients: age 26-96; 13 females). There was tumoral background in fifty-three lesions, principally lung cancer, (5 Unknown Origin Tumor, 2 staging, 22 post-treatment, 24 suspicious of recurrence) and being the remaining fourteen submitted for benign/malignant characterization of pulmonary lesion. All patients underwent ¹⁸F-FDG/PET-CT: a first study at 60 min and a second study centered in thorax, 2-3 hours after intravenous injection of 370 MBq of ¹⁸F-FDG. The images were evaluated qualitatively and semiquantitatively. The SUV_{max} of the lesions was measured

for both studies and the percentage change was calculated. In the early and delayed study, a lesion was classified as malignant if the SUV max was higher than 2.5. Attending to the percentage change, we classified a malignant lesion if there was an increase of SUV max between both studies and benign if the SUV max was equal or less. The results were statistically analyzed using ROC curve. The final diagnosis was obtained by histological assessment (19) and clinic follow up (range 10–36 months) and/or diagnostic techniques (48). **Results:** The best statistical parameters were obtained when considering the percentage change.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Early study	42%	41%	31%	53%	42%
Delayed study	65%	34%	39%	61%	46%
% change	92%	34%	47%	86%	57%

Attending to the percentage change 16 lesions were considered as benign by ^{18}F -FDG/PET-CT, 14 of them corresponded to infectious disease, being the remaining 2 false negative, corresponding to post-treatment control both of them (2 and 6 months after the therapy). All the 51 lesions considered malignant by ^{18}F -FDG/PET-CT showed a percent change higher than 10%. 27/51 were finally clinical benign lesions [The purpose of the study was differential diagnostic in 11, 1 UOT and 15 post-treatment (11 of them, the time after the end of therapy was lesser than five months)]. **Conclusion:** This study shows that the percentage change is the best tool of the dual time point ^{18}F -FDG/PET-CT thoracic images. It has been a useful method in the evaluation of lung lesions, mainly in patients with tumoral background and the interval after therapy of at least six months.

P064

Usefulness of dual phase 18 FDG PET/CT in differentiation of pulmonary nodule

J. Kunikowska¹, L. Opoka², M. Dabrowska³, M. Kobylecka¹, J. Maczewska¹, K. Fronczewska-Wieniawska¹, L. Krolicki¹, A. Drobniak⁴, ¹Medical University of Warsaw, Warsaw, POLAND, ²Institute of Tuberculosis and Pulmonary Disease, Warsaw, POLAND, ³Department of Internal disease, Pulmonology and Allergy, Medical University of Warsaw, Warsaw, POLAND, ⁴Students' Scientific Association, Medical University of Warsaw, Warsaw, POLAND.

The accurate diagnosis of any solitary pulmonary nodule (SPN) is crucial not only for early detection of malignancy, but also to avoid unnecessary thoracotomies for benign lesion. Positron emission tomography (PET) with ^{18}F -fluorodeoxyglucose (18FDG) has become an important tool in evaluation of SPN. **METHODS:** We examined 150 patients, underwent 18FDG PET/CT for evaluation of pulmonary nodule. For semiquantitative analysis, maximum SUV (SUV max) was measured in all nodule. PET/CT imaging was performed on PET/CT scanner Biograph 64, 60 minutes post injection 300–370 MBq 18FDG. True X software was used for reconstructions. In 39 cases dual phase PET/CT was performed (app.120 minutes post injection of 18FDG) **RESULTS:** In 80/150 patients an increased uptake of 18FDG was found. In 70/150 nodules an accumulation of 18FDG was similar to background. A final diagnosis of nodule was obtained either by pathological examination or radiological follow-up for more than 1 year in 74/150 patients (33 with accumulation similar to background and 41 with increased uptake of 18FDG). Benign character of nodules was confirmed in all 33/33 pts (SUV max <1.2) and in 6/41 cases with higher accumulation of FDG. In the higher accumulation 18 FDG dual phase examination was performed, median SUV max 60 was 2.8 (range 1.3–5.6), in all cases uptake increase in delayed phase SUV max 120 was 4.65 (range 1.6–11). In 35/41 patients with malignant nodules the diagnosis was confirmed by histopathological examination - median SUV max 11.7; SUV max range 2.1–39.2. The difference between SUV max 60 pi in benign and malignant nodule is statistically significant ($p < 0.05$). Dual phase examination was performed in 33/35 malignant cases with increasing uptake of 18 FDG. The malignant nodule presented significant (about 62%) rising of uptake median SUV max 60–11.7 (range 2.1–39.2) and SUV max 120–18.9 (range 2.7–45.7) ($p = 0.0001$) Basis on our data sensitivity of 18 FDG PET/CT was 100% and specificity 85%. **CONCLUSION:** Dual phase 18 FDG PET/CT is an useful techniques in determination the nature of pulmonary nodules. The malignant pulmonary nodules have more higher uptake of 18 FDG, than benign one, which usually accumulate 18 FDG like the background. In malignant nodules a significant increase of 18 FDG uptake in delayed phase was observed.

P065

Tampon position causes artefactual FDG-uptake in vaginal tampons due to urinary contamination

I. A. Burger, D. A. Scheiner, D. W. Crook, T. F. Hany, G. K. von Schulthess; University Hospital Zurich, Zurich, SWITZERLAND.

Objective: To determine the etiology of FDG-uptake in vaginal tampons (VT), a known artifact in premenopausal women evaluated by PET/CT. FDG-uptake may be caused by menstrual blood, direct urinary contamination or capillary effect of the cotton string. **Materials and Methods:** This IRB approved study consisted of retrospective and prospective parts. We prospectively included 24 women (20–48 years old) with known or suspected malignancy after obtaining written informed consent. All of these patients were referred for staging or follow up of malignancy and were provided with a commercial VT (Ob® Johnson&Johnson, NJ, USA) to be used during the entire examination. Ten of these VT were modified by replacing the cotton string with a non-absorbent nylon string (Dermalon 3-0, Tyco Healthcare, USA). Between the uptake phase and imaging, all patients were asked to void. PET/CT images were analysed to determine the localization and the standard uptake value (SUV) of the VT. VT were further analysed for creatinine concentration and blood traces. The retrospective analysis included 685 women examined between 2008 and 2009 regarding the presence / uptake and localisation of a VT. **Results:** In the prospective study, 7 out of 24 (29%) women had an increased FDG-uptake in the VT (518 ± 308 kBq). Six women with high FDG-activity had a normal VT, one woman a modified VT. The creatinine concentration was significantly increased in all 7 FDG-active VT (base: 728 ± 871 μmol/l, middle: 469 ± 595 μmol/l, top: 216 ± 149 μmol/l), but not in the FDG-negative VT. Four of 24 women had blood traces but no FDG-uptake. All FDG positive VT were localized significantly below the pubococcygeal (PC) line (14.6 ± 11.4 mm), whereas most of the inactive VT were above the PC-line ($p = 0.009$, t-Test). In the retrospective part, 38 women used a VT, of

those 17 (45%) demonstrated an increased FDG-activity. Localization of the FDG-avid VT were significantly below the PC-line (12 ± 11.9 mm) compared to not active VT (1 ± 6.9 mm above the PC-line, $p < 0.001$, t-Test). **Conclusion:** FDG-uptake in VT is caused by urine contamination, probably due to localization below the PC-line and therefore contact to the voiding pathway and not to a capillary effect of the string or menstrual blood.

P066

^{18}F -FDG PET/CT with retrograde filling of the urinary bladder: impact in the detection of gynaecological and bladder cancer

A. Garcia Vicente, A. Nunez Garcia, J. Pilkington Woll, B. Gonzalez Garcia, A. Palomar Munoz, M. Bellon Guardia, M. Talavera Rubio, J. Cordero Garcia, V. Poblete Garcia, I. Cepedello Boiso, A. Soriano Castrejon; HOSPITAL, Ciudad real, SPAIN.

Aim: To assess the value of PET/CT pelvic imaging with retrograde bladder irrigation (RBI) in order to clarify urothelial and gynaecological pathology in metabolic image and evaluate the diagnostic impact. **Material & Methods:** 62 studies belonging to 52 patients (27 female and 25 male), average age of 64 (41–84), with background of urothelial (35) and gynaecological (27) neoplasm, were assessed with PET/CT. 16 underwent previously surgical procedures and/or radio/chemotherapy. All patients were suspicious of pelvic pathology in previous diagnostic CT. All patients underwent standard PET/CT protocol, 60 min after the intravenous injection of 370 MBq of ^{18}F -FDG. The images were reviewed; if any difficulty in the evaluation was detected, a second PET/CT acquisition with filled bladder was obtained. The inclusion criteria was indeterminate or equivocal foci in pelvis or radiological alterations in bladder wall. Both series of images were assessed by two experienced observers. A lesion was classified as malignant if it showed a SUV greater than 2.5 or in case of lesions smaller than 1 cm, any uptake greater than background activity that kept or increased in delayed pelvic imaging. Pathologic locations in pelvic organs (included bladder), were assessed as the additional value of filled bladder image with respect to standard PET/CT. The pathologic lesions were histologically or clinically evaluated with a minimal follow up of 12 months. **Results:** About final diagnosis, malignancy was confirmed in 37 cases: 16 in bladder, 17 in other pelvis organs and 4 in extrapelvic locations. 34 cases were evaluated histologically and 28 by clinical follow up. 41/62 studies were pathologic in PET/CT. 35 showed abnormalities in pelvis, 4 of them were false positive. In 19 cases was detected pathologic ^{18}F -FDG uptake in bladder wall, 16 were true positive by histopathologic examination. With respect to standard acquisition, RBI helped to confirm/rule out bladder and gynaecological disease in 42 and 13 cases respectively. The annexed table shows the final statistic results.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Bladder	100%	93%	85%	100%	95%
Pelvis	93%	86%	88%	92%	90%

Conclusion: Retrograde filling reduced the interference with physiological urinary accumulation of ^{18}F -FDG PET/CT, helping in the diagnosis of pelvic lesions, especially in bladder, where none false negative was documented. In ^{18}F -FDG PET/CT studies, retrograde filling of the urinary bladder is a recommendable procedure to assess bladder wall lesions and malignancies in pelvic locations.

P067

Nonmalignant lesions detectable with PET/CT

M. Ono¹, K. Kobayashi¹, Y. Miyatake¹, T. Katoh¹, W. Ko¹, T. Ushimi¹, T. Kojima¹, S. Yasuda²; ¹Yotsuya Medical Cube, Tokyo, JAPAN, ²Tokai University School of Medicine, Kanagawa, JAPAN.

Aim: Clinically important benign lesions are occasionally found during PET/CT study. This study was conducted to determine the types and frequency of clinically meaningful nonmalignant lesions detectable with PET/CT. **Subjects and Methods:** Subjects were 2937 asymptomatic individuals (1790 men, 1147 women, 53.7±12.3 years old) who underwent PET/CT studies at our institution as part of a cancer screening program from August 2005 to December 2009. PET/CT was performed 60 min after injection of 145 to 260 MBq FDG (Discovery ST, GE Healthcare). PET/CT images were visually evaluated and prospectively recorded by two physicians (MO, SY). The PET findings were compared with final diagnoses obtained by other imaging modalities, laboratory studies, and clinical follow-up. **Results:** A total of 411 lesions were detected in 382 (13.0%) of the 2937 subjects. Of the 411 lesions, 202 lesions (49.1%) were PET positive, and 209 lesions (50.9%) were PET negative and detected on CT images. The lesions were classified into the following three sites. 1) Head & neck: 175 lesions were found, including chronic thyroiditis (120), maxillary sinusitis (27), and benign thyroid tumor (17). Among these there were pituitary adenoma (3) and Graves' disease (2). 2) Thorax: 25 lesions were found, including atypical mycobacteriosis of the lung (7), sarcoidosis (4), and emphysema (4). Among these there were pulmonary tuberculosis (1) and thymoma (1). 3) Abdomen: 226 lesions were noted, including cholecystolithiasis (116), urinary tract stone (40), adrenal tumor (19), colorectal polyp (7), and abdominal aneurysm (7). Among these there were autoimmune pancreatitis (1) and retroperitoneal neurogenic tumor (1). **Conclusion:** Clinically meaningful nonmalignant lesions were discovered at a rate of 13.0% in our subjects. A wide variety of clinically important benign lesions can be incidentally found at a substantial rate and is an added advantage of PET/CT.

P068

False Positive (^{18}F)-FDG PET-CT Findings after H1N1 Vaccination

I. A. Burger, T. F. Hany, L. Husmann, N. G. Schaefer; University Hospital Zurich, Zurich, SWITZERLAND.

Purpose To analyze the effect of H1N1 vaccination in patients undergoing FDG-PET/CT for staging or follow up of malignant disease. **Methods** Medical history off all patients scheduled for FDG-PET/CT during the national vaccination campaign against H1N1 was evaluated for a recent vaccination against H1N1. The site of injection and the time between FDG-PET/CT and the date of vaccination (ΔTime) was determined. FDG-uptake, using SUVmax, was measured ipsi- and contralateral in the deltoid muscles and the axillary lymph nodes. The difference of SUVmax

(dSUV) in the deltoid muscle or axillary lymph nodes was used to determine a positive reaction to the vaccination, defined as a dSUV > 0.5 mg/ml. With a receiver operator characteristic (ROC) curve, the cut off dTime for still visible reaction in axillary lymph nodes was determined. Short axes of the axillary lymph nodes were measured and correlated with dSUV. **Results** Out of 269 patients, 58 had a vaccination against the H1N1 within the last 4 weeks. The dTime ranged from 1 to 30 days (mean 14.5 ± 8.7 days). Seventeen patients had positive lymph nodes with a dSUV > 0.5 mg/ml (mean 1.43 ± 1.06 mg/ml; dTime < 15 days). In 41 patients, no significant uptake was visible (dSUV -0.03 ± 0.23 mg/ml), for 18 of them dTime was < 15 days. Positive axillary lymph nodes were larger with 9.3 ± 1.7 mm vs. 5.1 ± 1.8 mm for non active nodes. The area under the ROC curve revealed a strong relation between time delay (dTime) and activity in the ipsilateral lymphnodes (0.9 ± 0.43 / CI 95% 0.816 - 0.983). The period with the highest probability for axillary reaction was between 2 and 13 days. Three patients with recent vaccination (1-3 days) had increased dSUV in the deltoid muscle without activity in the ipsilateral lymph nodes. Two patients (dTime = 14 days) had increased activity in the axillary lymph nodes, without corresponding activity in the deltoid muscle. After a follow up time of 3 months, no patient received local treatment or had proven disease in the ipsilateral lymph nodes. **Conclusion** Vaccination for H1N1 can cause false positive FDG-PET/CT findings. The time interval between vaccination and FDG-PET/CT correlates with dSUV, in 48% of patients with a vaccination less than 15 days ago a visible reaction occurs. Increased FDG-activity in the ipsilateral deltoid muscle is a key finding for accurate interpretation of increased FDG-activity in axillary lymph nodes.

P069

The effect of influenza vaccination on FDG-PET/CT imaging

N. Shirone¹, **T. Shinkai**², **F. Uto**¹, **H. Yoshimura**¹, **H. Tamai**¹, **T. Imai**³, **T. Yamane**⁴, **M. Inoue**², **S. Kitano**², **K. Kichikawa**², **M. Hasegawa**², ¹Takai Hospital, Tenri, JAPAN, ²Nara Medical University, Kashihara, JAPAN, ³Saiseikai Nara Hospital, Nara, JAPAN, ⁴Institute of Biomedical Research and Innovation, Kobe, JAPAN.

Aim: It has been reported that FDG uptake is not specific for malignancy and increased uptake occurs in benign conditions with increased glycolysis such as infection, inflammation, and granulomatous disease. A vaccination may cause temporal inflammation at lymph nodes. We investigated whether influenza vaccination has any influence on FDG-PET/CT imaging. **Materials & methods:** This study included 172 healthy adults (71 females, 101 males; mean age: 57.7 ± 10.7 years) who underwent FDG-PET/CT for cancer screening at our hospital from November 2008 to March 2009. Questions about their history of vaccination were asked. 3MBq/kg body weight ¹⁸F-FDG was administered one hour before acquisition using a PET/CT scanner (discovery LS, GE). In the case of having recent vaccination history, injection was given from the opposite side of the vaccinated site. **Results:** Eighty-three of 172 had vaccinated against influenza of those season before PET/CT exam. Five out of 83 were vaccinated within a week. As to the 4 out of 5 who underwent vaccination within a week, unexpected accumulations were visualized at the axilla and medial upper arm on the same side of the vaccination. Low dose CT revealed small size (<10mm) lymph nodes at that site. The range of SUVmax was 2.3 to 6.9. There was no abnormal uptake related to vaccination among all of the other 78 persons who had vaccinated before more than one week. **Conclusion:** Influenza vaccination within a week of the FDG-PET/CT examination may frequently cause ipsilateral axillary LN accumulations. Questions about vaccinated history are necessary to avoid misleading by false positive findings.

P070

Determinants of 18F-FDG uptake in brown adipose tissue

L. Pace¹, **E. Nicolai**², **D. D'Amico**², **F. Ibello**², **A. Della Morte**², **B. Salvatore**², **L. Micol Pizzuti**¹, **M. Salvatore**¹, **A. Soricelli**³, ¹Università degli Studi di Napoli Federico II, Napoli, ITALY, ²Fondazione SDN-IRCCS, Napoli, ITALY, ³Università degli Studi di Napoli Parthenope, Napoli, ITALY.

18F-FDG uptake in brown adipose tissue varies in function of age, sex and outdoor temperature. The aim of this study was to assess independent predictors of FDG uptake in brown adipose tissue in patients undergoing repeated PET/CT scans. **Methods:** 848 (mean age 50.9 ± 16 years, 415 female) patients in whom PET/CT scan was repeated (mean interval 5 ± 1.5 months) without any change in therapy between the 2 studies constituted the study group. 18F-FDG uptake was considered to be present when the uptake in characteristic areas of brown fat localization, having the CT density of adipose tissue (>250 to 50 Hounsfield units), was greater than background soft-tissue activity. Both distribution and SUVmax were registered. Data on age, gender, height, weight, medications used, diagnosis, coffee intake (> espressos/day), physical activity (in the 24 hours before the scan) and smoking history were collected for each patient. **Results:** 18F-FDG uptake in brown adipose tissue was present in 8.6% patients at first scan. Independent predictors of presence of uptake were age (younger), gender (female), body mass index (lower) and maximum outdoor temperature (lower). Age was the only independent predictor of body distribution of 18F-FDG uptake in brown adipose tissue, while SUVmax was related to both age and outdoor temperature. Independent determinants of persistence of 18F-FDG uptake in brown adipose tissue at second PET/CT were outdoor temperature at time of 2nd scan and extension of metabolically active brown adipose tissue at 1st scan. **Conclusions:** Metabolically active brown adipose tissue is present in adult humans, with a women predominance. Age, body mass index and outdoor temperature are significant determinants of its evidence at PET/CT repeated scans. Moreover, extension of brown adipose tissue and outdoor temperature are the strongest determinant of persistence of brown adipose tissue evidence on 18F-FDG PET/CT in repeated scan.

P071

Diffuse physiologic FDG uptake in the esophagus

M. Takechi¹, **S. Yasuda**¹, **J. Kasanuki**², **T. Ushimi**², **W. Ko**², **T. Kato**², **K. Kobayashi**², **Y. Miyatake**², **M. Ono**², **S. Ozawa**¹, **Y. Kondo**¹, **K. Ogoshi**¹, **H. Makuuchi**¹; ¹Tokai University School of Medicine, Kanagawa, JAPAN, ²Yotsuya Medical Cube, Tokyo, JAPAN.

Aim: Physiologic FDG uptake is well documented in the intestine but not in the esophagus. In a previous study, we found that localized physiologic FDG uptake in the esophagus was infrequent

(2.8%) and most often related to the presence of hiatal hernia. We also encountered cases with diffuse esophageal FDG uptake. The aim of the present study was to determine the frequency and causes of the diffuse esophageal FDG uptake. **Methods:** Subjects were 732 asymptomatic individuals (497 men, 253 women; mean age, 53 years) who underwent PET/CT study at our institution between November 2008 and December 2009 as part of a cancer screening program. Endoscopy was performed one day prior to PET/CT. Sixty minutes after injection of 200 MBq FDG, PET/CT (Discovery ST, GE Healthcare, WI) was performed. The PET/CT images were visually evaluated retrospectively, and diffuse longitudinal FDG uptake along the entire esophagus equal to or higher than that in the mediastinum was considered a positive PET finding. For each subject with diffuse esophageal FDG uptake, the PET and endoscopic findings were compared. **Results:** Diffuse FDG uptake along the entire esophagus was observed in 21 subjects (2.9%). Endoscopy revealed 23 specific disorders in 12 of the 21 subjects (57.1%): reflux esophagitis (LA grade A) (5 cases), Barrett's esophagus (4 cases), glycogenic acanthosis (3 cases), and papilloma (2 cases). None of these disorders, however, were considered to be causes of the diffuse esophageal FDG uptake. **Conclusions:** Diffuse FDG uptake along the entire esophagus was observed at a rate of 2.9% in our subjects, and the findings were considered to be physiologic uptake.

P072

Imaging features of ocular adnexal lymphoma: FDG-PET versus MR imaging.

K. Hayasaka¹, **M. Koyama**¹, **T. Yamashita**¹, **T. Nihashi**², ¹Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, JAPAN, ²Nagoya Graduate School of Medicine, Nagoya, JAPAN.

Purpose: To define the characteristics of ocular adnexal lymphoma (OAL) on FDG-PET and MR images. **Materials and methods:** We evaluated 42 patients who had been examined by FDG-PET and MR imaging at diagnosis and who had biopsy-proven malignant lymphoma at 48 sites. All information was obtained from a retrospective review of their medical records as well as FDG-PET and MRI findings. **Results:** Forty two patients (mean age, 66.8 years; range 33-91 years; 25 females and 17 males) were studied. The major histopathological subtypes were mucosa-associated lymphoid tissue (MALT; n = 30) and non-MALT (n = 12: follicular lymphoma (FL), n = 5; diffuse large B-cell lymphoma (DLBCL), n = 7). Magnetic resonance imaging of 47 sites revealed 31 isointense, 5 hypointense and 5 hyperintense areas on T1-weighted images, 26 hyperintense and 4 isointense areas on T2-weighted images and 41 areas of moderate enhancement with gadolinium injection. Ten patients with systemic lymphoma involvement were upstaged, since FDG-PET is more sensitive than MRI. The SUVmax of FDG was < 1.5 at two MALT sites, 1.5 ~ 2.5 at 16 MALT and one DLBCL site, and > 2.5 at 29 sites. Sensitivity was lower for MALT (50.0%) than for non-MALT (92%). Fifty-four patients had stage I (overall sensitivity, 70.4%: patients with MALT, 64%), 17 had stage II (overall sensitivity, 80% and 50% for patients with MALT), and seven had stage IV (100% sensitivity) disease. Twenty two patients were followed up using FDG-PET, which detected relapse in three of them. Other findings comprised high LDH and high serum interleukin 2 receptor values in 3 and 25 of the 42 patients respectively. **Conclusion:** Magnetic resonance imaging is essential for evaluating OAL in terms of location, size and degree of infiltration. We identified FDG avidity in 60% of OAL, but in 50% of MALT, non-MALT in 92%. Nevertheless, these results suggested that FDG-PET is a useful tool with which to stage, restage after therapy, or monitor the course of OAL.

P073

Incidental findings on enhanced full dose 18F-FDG PET/CT in cancer patients.

R. Jover-Diaz¹, **L. Gorospe-Sarasúa**¹, **A. Vicente-Bártulos**¹, **J. García-Poza**¹, **D. Lourido-García**¹, **M. Orduña-Díez**¹, **M. Pozo**², **R. Núñez-Miller**¹, **J. Alfonso Alfonso**¹; ¹Instituto Tecnológico de Servicios Sanitarios, MADRID, SPAIN, ²Instituto Pluridisciplinar-Univ. Complutense, MADRID, SPAIN.

OBJECTIVE: The purpose of this study was to report the prevalence of incidental findings (cancer and non-cancer related) on both the PET and the CT components of contrast-enhanced full dose PET/CT in patients with cancer. **PATIENTS AND METHODS:** Images from all contrast-enhanced full dose PET/CT studies performed at our institution on patients with cancer (non-small cell lung cancer, 16%; head and neck cancer, 16%; breast cancer, 15%; gastrointestinal tract cancer, 12%; tumor of unknown origin, 10%; gynecologic cancer, 10%; lymphoma, 2%; other types of cancer, 19%) were retrospectively reviewed. Two hundred fifty patients (158 men; 92 woman, mean age 58 years; age range: 22-84) underwent contrast-enhanced full-dose PET/CT studies (initial staging and restaging) on a GE ST PET/CT unit. All studies were reviewed by experienced nuclear medicine physicians and radiologists, who documented all unexpected abnormalities present on both the PET and the contrast-enhanced full dose CT components. **RESULTS:** 1.- Previously unsuspected second primary malignancies were found (lung, 1; head and neck, 1; prostate, 1; bladder, 1; renal, 1; colorectal, 5; uterus, 1) in 11 patients (4.2%). 2.- Detection of incidental hypermetabolic thyroid nodules in 3 patients (1.5%). 3.- Unsuspected thromboembolic disease in less than 5% of the patients (deep venous thrombosis; pulmonary embolism; tumour thrombus) and other vascular disorders (superior vena cava syndrome; brain and aortic aneurysms) 4.- Detection of unsuspected metastases in 2% of the patients (brain, 2; renal, 2; heart, 1; bone and adrenal, 1) 5.- Detection of colonic polyps in less than 1% of the patients. **CONCLUSION:** Incidental findings (both cancer and non-cancer related) were detected in 11.2% of cancer patients. Many of these findings can be clinically important, and some of them may influence clinical management. Therefore, all incidental findings detected on contrast-enhanced full dose PET/CT studies should be included in the final report.

P11 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Molecular & Multimodality Imaging: SPECT/CT - Clinical applications

P074

A GATE simulation study of a Fan-Beam Collimator for SPECT Mammography

R. Capote, P. Almeida; University of Lisbon, Faculty of Sciences, Physics Department and Institute of Biophysics and Biomedical Engineering, Lisboa, PORTUGAL.

The development of dedicated imaging systems with high sensitivity and spatial resolution are crucial for early breast cancer diagnosis. This work presents the Monte Carlo evaluation of a new collimation geometry for a dual planar scanner SPECT mammography unit, able to track small lesions near the chest wall with both high resolution and sensitivity. In SPECT imaging the choice of a collimator represents a trade-off between three parameters required to properly visualize the target object or organ: the size of the Field of View, the sensitivity and spatial resolution. Taking into account these parameters several collimation geometries had been studied to perform high resolution SPECT mammography. We have designed and tested a fan beam collimator adapted to the geometry of a variable angle dual-headed APD-based system, using GATE. The collimator has tapered holes focused toward the breast that increase in size with distance from the collimator surface. This permits capturing a magnified projection of the imaged object, allowing a maximum surface usage of the crystal to capture imaging data. Collimator holes are aligned with the APD detector elements. In order to image the chest wall and the axillary lymph nodes, the field of view of the collimator includes the entire breast and also these two regions. The values for sensitivity and spatial resolution were calculated for several collimator hole lengths. A realistic description of the detector geometry, radiation environment, physics and instrumentation factors was adopted, allowing obtaining realistic imaging data with the help of a numerical phantom of the breast.

P075

Added Value of Low-dose SPECT/CT Imaging in Evaluation of Indeterminate Bone Lesions

G. Cobzac, A. Brumboiu, S. Manole, L. Muresan, A. Chirila, G. Andries; Clinical County Hospital Cluj, Cluj-Napoca, ROMANIA.

Purpose: To evaluate the role of low-dose SPECT/CT in diagnosis of bone metastases in patients with known cancer and indeterminate bone lesions on ^{99m}Tc -HDP planar whole-body scan. **Material and Method:** 53 consecutive patients (17 men, 36 women) with known malignant tumor and at least 1 area of abnormal uptake on bone scintigraphy were enrolled in the study. SPECT/CT was performed in all 53 patients with a hybrid system (Symbia T2 - Siemens) using a standard protocol. SPECT images were corrected for attenuation and fused with correspondent CT images in three perpendicular planes. All images were interpreted independently by two nuclear medicine physicians and one radiologist. The diagnostic confirmation is based on biopsy in 4 patients and radiological follow-up in the rest of patients. **Results:** 87 lesions were identified on planar bone scintigraphy. SPECT/CT fusion images showed 39 bone metastases, 40 skeletal benign lesions, 6 equivocal and 2 pleural metastases. In addition, SPECT/CT showed other 38 bone lesions with normal or faint abnormally radioactive uptake, 23 of them being metastases, 11 benign and 4 unspecific bone lesions. In 6 patients, SPECT/CT depicted extraosseous metastases. Finally, were identified 127 bone lesions, 66 of them being bone metastases and 61 benign lesions. The sensitivity of planar whole-body bone scan for all 66 bone metastases was 57,6%. SPECT/CT sensitivity, specificity and accuracy were 93,9%, 90,1% and 92,1%. **Conclusion:** Low-dose SPECT/CT has a great sensitivity, specificity and accuracy in diagnosis of bone metastases in patients with known cancer, as a result of precise anatomical localization and morphological details of the scintigraphic detected bone lesions. Furthermore, bone lesions with normal uptake and extraosseous lesions revealed on CT images in some patients complete the oncological evaluation.

P076

SPECT-CT contribution to conventional bone scintigraphy in the diagnosis of foot and ankle pain

C. J. Caicedo, C. Vigil, I. Dominguez-Prado, M. García-Velloso, P. Garrastachu, M. Rodríguez-Fraile, M. González-Forero, C. Villas, M. Alfonso, J. Richter; Clínica Universidad de Navarra, Pamplona, SPAIN.

AIM: Disorders of the foot and ankle are common. Given the complex anatomy and function of these joints, they present a clinical challenge and significant difficulties in evaluating by means of imaging techniques. The aim of this study was to assess the contribution of the SPECT-CT to conventional bone scintigraphy in a group of patients with foot or ankle pain. **MATERIAL AND METHODS:** Sixty-one patients, 39 women and 22 men (medium age: 46y [3 - 81]) were explored in an hybrid system (SYMBIA TruePoint SPECT-CT SIEMENSTM). The protocol included: planar images in different projections (AP/PA/Lateral) and a fast SPECT with low dose CT acquisition. A three-phase bone scintigraphy was performed in 53 patients. Moreover a foot or ankle MRI was performed in 17 patients at the same time. Conventional scintigraphic studies (planar and dynamic) were evaluated and compared with SPECT-CT results. An agreement between SPECT-CT and MRI findings was also contrasted. **RESULTS:** Final diagnosis was established as inflammatory joint disease (n = 33), osteonecrosis (n = 10), fracture (n = 8), osteochondritis (n = 3), plantar fasciitis (n = 2), orthopedic screw loosening (n = 2), soft tissue pathology (n = 1), complex regional pain syndrome (n = 1). No pathological findings were observed in one patient. Three-phase bone scintigraphy played an important role in the cases of soft tissue pathology and complex regional pain syndrome. In 18 patients (29%), conventional scintigraphy contributed to complete a final diagnosis of the process (inflammatory joint disease in all cases). SPECT-CT gave superior diagnostic information in 40 patients (66%), (15 inflammatory joint disease, 10 osteonecrosis, 8 fracture, 3 osteochondritis, 2 plantar fasciitis and 2 orthopedic screw loosening). In the 17 patients with SPECT-CT and MRI, an agreement between both techniques was found in 11 patients

(65%), although the concordance in location of the pathological findings was detected in 13 cases (76%). **CONCLUSION:** The SPECT-CT is an important tool for the diagnosis of foot and ankle pain, contributing to precise the location of focal findings observed in planar images. This method played a special role in the diagnostic of polyarticular disease, osteonecrosis and osteochondritis. According to these preliminary results, MRI and SPECT-CT findings have a high concordance.

P077

Assessment of Registration Accuracy of Multislice SPECT/CT in Patients with Hand and Wrist Pain

C. Xie¹, L. Livieratos², H. Mohan², G. Gnanasegaran²; ¹Division of Imaging Sciences, The Rayne Institute, 4th Floor, Lambeth Wing, St Thomas' Hospital, London, UNITED KINGDOM, ²Department of Nuclear Medicine, Guy's and St Thomas' Hospital NHS Foundation Trust, London, UNITED KINGDOM.

Aim: Multislice single photon emission computed tomography (SPECT) and computed tomography (CT) is an effective co-registration technique that provides direct functional and anatomical correlation to localise and characterise lesions in the hand and wrist. However, misalignment between the two studies may position the elevated area of uptake onto a neighbouring region instead of the actual lesion, which may lead to a misdiagnosis. The aim of the study was to evaluate the hardware-based registration accuracy of multislice SPECT/CT of the hand and wrist, and determine the effect of the misalignment errors on the diagnostic accuracy. The relationship between misalignment with gender and age were also investigated. **Materials & methods:** 55 patients (32 women, 23 men, age range 22-74) who had multislice SPECT/CT of the hand and wrist between July 2008 to January 2010 were included in this study. Two experienced reviewers independently evaluated the fused images for any misalignments with six degrees of freedom: translation and rotation in the X, Y and Z directions. The results were tested against a rigid automated fusion tool (Syntegra). Misalignment of more than one pixel (4.66 mm) was considered a significant misalignment error. **Results:** More than half of the patients had moved during SPECT scanning (Reviewer 1: 29 patients; Reviewer 2: 30 patients). Eleven of these patients exhibited significant misalignments (>1 pixel), and they all originated in the Y direction translation (up/down). After misalignment correction, five patients had demonstrated a change in location of the elevated area of uptake that could have led to a misdiagnosis. Chi-square tests showed no significant association between gender and misalignment ($\chi^2 = 0.33$, $p = 0.57$), or between age and misalignment ($\chi^2 = 1.87$, $p = 0.392$). The Kappa Measurement of Agreement showed statistically significant ($p < 0.05$) agreement between the reviewers. The non-parametric Wilcoxon test indicated a statistically insignificant ($p > 0.05$) difference between the reviewers and Syntegra in measuring the significant misalignments. **Conclusion:** Multislice SPECT/CT imaging of the hand and wrist is clinically useful and accurate for localizing pathology. Hand movement during the SPECT scan was common, but movements leading to significant misalignments and subsequent misdiagnosis were infrequent. Given the subjective nature of observer-based studies the agreement in this case was satisfactory. There was no correlation between misalignments with gender or age. Future studies will investigate the use of hand and wrist immobilisation devices, and reductions of scan time to minimise patient motion.

P078

Pictorial review of multi-slice SPECT/CT in imaging the painful wrist: Moving from Better to Best

P. E. Jackson, F. Hassan, L. Livieratos, G. Gnanasegaran; Guy's & St Thomas' Hospital, London, UNITED KINGDOM.

Introduction: The anatomy of the hand and wrist is complex. The diagnosis and management of hand and wrist injuries and other pathology can be challenging. Wrist/hand pain is often difficult to accurately diagnose and localise clinically. Radionuclide bone scan is reported to be sensitive in detecting and diagnosing wrist injuries however, the specificity is relatively poor. Furthermore, accurate localisation of the bone scan abnormality is often difficult. Multi-slice SPECT/CT offers the advantage of distinguishing individual carpal bones and the small joints, unlike conventional bone scans which traditionally do not have sufficient spatial resolution. The additional anatomical information often demonstrates relevant incidental findings, anatomical variants, and characteristic structural pathologies. **Aim & Methods:** We present a series of clinical cases where SPECT/CT was found to be useful in the diagnosis and management of hand/wrist pain. The pictorial exhibit will include (1) principle and technique, (2) advantages and limitations of radiological and radionuclide techniques, (3) clinical examples; (a) fractures of carpal bones, (b) non-union and avascular necrosis, (c) infection, (d) abutments, (e) cystic changes and (f) degenerative disease (osteoarthritis, rheumatoid arthritis, scapholunate advanced collapse etc), (4) misalignments and artefacts, and (5) post-operative changes. **Results & Conclusion:** Early and accurate diagnosis of the painful hand/wrist may lead to effective management and prevention of further complications. SPECT/CT of hand/wrist is useful in localisation and characterisation of pathology, and improves diagnostic confidence.

P079

Can SPECT/CT be Helpful in Diagnosis of Avascular Necrosis of the Femoral Head of Adults?

L. Zadrazil, P. Libus; Hospital Havlickov Brod, Havlickov Brod, CZECH REPUBLIC.

Introduction: Bone scintigraphy (BS) is a very sensitive method of detecting avascular necrosis (AVN) of the femoral head. We have tested the contribution of SPECT/CT examination to specify abnormal findings in the hip joint on BS. **Patients and methods:** We present a collection of 19 patients, consisting of 22 hip's SPECT/CT examinations made within 26 months. These patients underwent a SPECT/CT examination after the whole body BS. Three-phase scintigraphy of pelvis was provided in 13 of all cases as well. Our collection consists of 13 males and 6 females of the average age of 47 years; the youngest is 22 and the oldest 59. If possible, we correlated the results with previous and next BS and radiological findings to achieve their diagnostic interpretation for the purposes of this study as precise as possible. **Results:** AVN of the femoral head was confirmed in 10 cases (45% of all examinations) at 7 patients (37% of all patients). 3 patients of them (42%) suffered from the recurrence of AVN at the opposite side. We found no

morphological changes on CT at 5 cases (50%), common changes on CT at 2 cases (20%) and no typical changes on CT or SPECT at 3 cases (30%) in this group. The other group includes 12 (55%) of all cases at 12 (63%) of all patients. We detected degenerative, posttraumatic or malignant affections there. CT mostly (10 cases, 83%) specified them. Other pathological changes in skeleton were presented in 5 cases (42%). Conclusion: Using CT to SPECT, you can evaluate secondary morphological changes resulting from AVN and distinguish other diseases affecting hip joint. We often saw a normal femoral head at AVN. When hip joint was affected with non-AVN changes, we found other changes in skeleton outside the hip joint on BS or CT in many cases.

P080

A comparison of planar scintigraphy and SPECT/CT in lung aerosol studies: measurements of regional deposition

L. Tossici-Bolt¹, J. S. Fleming¹, I. Katz², J. Conway³, G. Caillibotte², C. Majoral², D. Perchet², M. Pichelin², B. Muellinger⁴, G. Apiou-Sbirlea⁵, T. Martonen⁶, P. Kroneberg⁴, ¹Southampton University Hospitals NHS Trust, Southampton, UNITED KINGDOM, ²Air Liquide R&D/CRCO, Les Loges-en-Josas, FRANCE, ³University of Southampton, Southampton, UNITED KINGDOM, ⁴Activaero GmbH, Gemünden, GERMANY, ⁵University Paris Est, Créteil, FRANCE, ⁶Univ. of North Carolina, Chapel Hill, NC, USA.

Aim: Gamma camera imaging is extensively used to assess the deposition of inhaled aerosols in the lungs, providing valuable information in the development of drug delivery devices via the inhaled route. Conventional planar imaging is still the most widely used modality but, while satisfactory for measuring the total activity delivered to the lungs, it provides limited information on its regional distribution. In this study, single photon emission computed tomography (SPECT) was used to describe deposition in three dimensions (3D) and combined with x-ray computed tomography (CT) to relate this to lung anatomy. Its performance was compared to planar scintigraphy. **Methods:** Ten SPECT/CT studies were performed in healthy volunteers following carefully controlled inhalation of radioaerosol from a nebuliser, using a variety of inhalation regimes. Planar images were also acquired, before and after the SPECT/CT and 24 hours later. The spatial distribution of the inhaled aerosol was assessed using a "central to peripheral ratio" (C/P) normalised to lung volume (derived from CT). The C/P analysis was performed on both lungs on SPECT/CT images but only on the right lung on planar images, due to overlap of the stomach on the left lung. Planar and SPECT C/P results were correlated to the "24 hours clearance", the percentage of aerosol cleared from the lungs as determined from the initial and 24 hour planar images. This is considered to be a measure of aerosol deposited in the conducting airways. The SPECT/CT images were also used to calculate the deposition by airway generation for each lung, based on a conceptual airway model. From this, the conducting airways deposition fraction (CADF) was calculated and compared to the 24 h clearance. Results Analysis of regional distribution was possible for both lungs in 3D but not in 2D. For the right lung, the 3D C/P ratio correlated more closely with 24 h clearance than the 2D ratio (coefficient of variation, COV, 9% compared to 15% p<0.05). The mean CADF from SPECT for both lungs was not significantly different from 24 h clearance (COV 18%), confirming that in healthy lungs the clearance from the conducting airway is complete by 24 h. **Conclusions** Combined SPECT/CT enabled improved analysis of aerosol deposition compared to planar imaging. 3D radionuclide imaging combined with anatomical information from CT and computer analysis is recommended for applications requiring regional information on deposition.

P081

Successful localization of bronchial carcinoid causing ectopic Cushing's syndrome by SPECT/CT fusion imaging

E. Schmidt¹, E. Mezosi², Z. Tarjanyi², T. F. Molnar³, Z. Szabo¹, S. Szekeres¹, K. Rutz², O. Nemes², K. Zambo¹, ¹University of Pecs, Dept. of Nuclear Medicine, Pecs, HUNGARY, ²University of Pecs, 1st Department of Internal Medicine, Pecs, HUNGARY, ³University of Pecs, Department of Surgery, Pecs, HUNGARY.

Aim: Ectopic bronchial ACTH secretion causing hypercortisism is a very rare disease and difficult to diagnose and treat. The localization of ACTH source has crucial importance. Up to 80% of ectopic ACTH-producing tumors have somatostatin receptors, therefore ¹¹¹In-Octreotide scintigraphy seems to be a useful method in the diagnosis of this disease. **Material and method:** Four patients (2 men, 2 women, mean age 39 years) were investigated with severe Cushing's syndrome in the last five years in our departments. Small and high dose Dexamethason test, Sandostatint test, inferior petrosal sinus sampling, sella MRI, chest and abdominal CT, ¹¹¹In-Octreotide SPECT/CT scan and PET/CT were used for the diagnose. Results: An average 2.3 years period was elapsed from the first clinical signs to the successful treatment. The Dexamethason test, the inferior petrosal sinus sampling and the sella MRI were ambiguous in the differential diagnosis of the hypophyseal and peripheral disease. The most helpful method was the ¹¹¹In-Octreotide SPECT/CT scintigraphy which was successful in the correct localization of a 8 mm size tumor in the lung. The tumor was removed during chest surgery. The histological diagnosis was typical bronchial carcinoid tumor with intense ACTH positivity. **Conclusion:** These cases indicates that ¹¹¹In-octreotide scintigraphy could be successfully used to identify and localize ectopic ACTH-producing bronchial carcinoids and has a crucial role in the appropriate therapy.

P082

^{99m}Tc-tetrofosmin SPECT/CT in solitary pulmonary nodule (SPN) evaluation

A. Spanu¹, F. Chessa¹, D. Sanna¹, P. Marongiu¹, B. Piras¹, P. Pirina², S. Nuvoli¹, G. Madeddu¹, ¹Department of Nuclear Medicine - University of Sassari, Sassari, ITALY, ²Department of Respiratory Diseases - University of Sassari, Sassari, ITALY.

Aim: SPN is a frequent finding on clinical practice, especially during chest computed tomography (CT). However, the differentiation of malignant from benign SPN by CT has proved limited, especially for non calcified SPN. The aim of the present study was to investigate whether ^{99m}Tc-tetrofosmin SPECT/CT may play a role in SPN evaluation and to correlate the scintigraphic results with those of diagnostic CT. **Methods:** A consecutive series of 55 patients (50-84 yrs) with a non

calcified SPN (0.9-3 cm) at diagnostic chest CT were prospectively studied. At CT, 21/55 SPN were classified as probably malignant, 13/55 as probably benign and 21/55 as indeterminate. Within 1 week of CT, all patients underwent SPECT/CT of the chest using a rectangular dual head gamma camera integrated with a X-ray tube for low dose CT. SPECT images were corrected for attenuation and scattering, reconstructed with iterative method and fused with CT. SPECT/CT images were analysed qualitatively and considered positive if an increased radiotracer uptake was present in the SPN ascertained at CT. Definitive diagnosis was obtained in all cases after scintigraphy: 35/55 SPN resulted malignant (primary lung carcinomas in 26 cases, metastases in 7 cases and local recurrences in 2 cases), whereas 20/55 were benign. **Results:** SPECT/CT was true positive in 31/35 malignant SPN (sensitivity: 88.6%), including 13 SPN (4 adenocarcinomas, 2 bronchioalveolar carcinomas, 2 carcinoids, 3 metastases and 2 recurrences) indeterminate at CT (range size: 1-2.8 cm). SPECT/CT was false negative in the remaining 4/35 cases, 3 of whom with an adenocarcinoma each (size: 0.9-1.5 cm), indeterminate at CT, and 1 with a metastasis (size: 1.2 cm) positive at CT. SPECT/CT was true negative in 17/20 benign SPN (specificity: 85%), including 6 SPN (2 idiopathic fibrosis, 2 chronic alveolitis, 1 antracosis, 1 hamartoma) indeterminate at CT (range size: 1-2 cm). SPECT/CT was false positive, concordantly with CT, in the remaining 3/20 cases, 2 of whom with aspecific inflammation and 1 with a Wegner's granuloma (range size: 1-2.5 cm). Globally, SPECT/CT gave an additional value than CT in 19/55 cases (34.5%). SPECT/CT overall accuracy was 89%. **Conclusions:** ^{99m}Tc-tetrofosmin SPECT/CT proved highly accurate in differentiating malignant from benign SPN and played an important complementary role to diagnostic CT, especially when it was indeterminate. A larger clinical application of this procedure is thus suggested in the management of patients with SPN, even more when PET scanners are not available.

P083

Usefulness of SPECT-CT in detection of sentinel node in melanoma patients. Our experience.

A. M. Moreci¹, S. Ialuna¹, V. Margulio², G. Lo Baido², D. Sajevo², C. Rimi³, G. Caruso¹, S. Carluccio¹, A.O. O.R. Villa Sofia-Cervello Operative Unit of Nuclear Medicine Villa Sofia Hospital, Palermo Italy, Palermo, ITALY, ²A.O. O.R. Villa Sofia-Cervello Operative Unit of Plastic Surgery, Villa Sofia Hospital, Palermo Italy, Palermo, ITALY, ³Operative Unit of Pathological Anatomy, Villa Sofia Hospital, Palermo, Italy, Palermo, ITALY, ⁴Medical Biotechnology Department and Legal Medicine, section of Radiologic Science University of Palermo, Palermo Italy, Palermo, ITALY.

Introduction: The sentinel node biopsy has changed the treatment of melanoma, so it is the most important innovation in the last decade. The value of this methodology was identified with reference to both node staging and prognosis, is increasingly improved with successful treatment. In particular sentinel node biopsy has been applied to other diseases neoplastic pathologies affecting breast cancer, oral cavity and genitals. The correct application of this technique, although extremely simple to conceive, requires careful observation of procedural delay and a well integrated and effective operational team of nuclear physicians, surgeons and pathologists. **Aim:** evaluate usefulness of SPECT-CT tomographic acquisitions in detection of sentinel node in melanoma patients. **Patients and Methods:** the performing procedure includes a pre-operating lymphoscintigraphy (dynamic, static and SPECT-CT tomographic images were acquired with a free-geometry dual-head gamma camera with CT gantry, General Electric Infinia Hawkeye®); a proper biopsy, that avail itself of the aid of a vital dye-stuff, a gamma-radiation detecting probe (scintiprobe MR 100®, POL.HI.TECH) and an excision histological study. Between 2005 and 2009 were subject to search intraoperative radioguided SLN 60 melanoma patients with stage I and II according to the American Joint Committee on Cancer. All patients underwent biopsy and identification of LS after performing lymphoscintigraphy. Lymphoscintigraphy was performed using a first dynamic acquisition and subsequent static serial acquisitions. Since last four year, the test has been implemented including hybrid tomographic acquisition (SPET-CT) for 60 patients. **Results:** according to many authors, this imaging implementation does not meaningfully affect methodological reliability in values of 94-99%; in our opinion, indeed, it eases sentinel node detection and localization, in so reducing surgical times. **Discussion:** As a matter of fact, a preventive virtual TC-guided inspection of the site in examination gives the operator an extremely precise topographic image, guiding the development of a rationalized dissection operating strategy. The extent of this advantage is more important when it regards more complex anatomic localization (axillary cavity, neck), in overweight patients and in secondary sentinel node detections.

P084

Usefulness of ^{99m}Tc-labeled RBC scanning and SPECT-TC tomographic acquisitions in detection of duodenal bleeding.

S. Ialuna¹, S. Carluccio¹, G. Caruso², A. Moreci¹, ¹Operative Unit of Nuclear Medicine Villa Sofia Hospital, Palermo Italy, PALERMO, ITALY, ²Medical Biotechnology Department and Legal Medicine, section of Radiologic Science University of Palermo, Palermo Italy, PALERMO, ITALY.

Aim: evaluate usefulness of ^{99m}Tc-labeled RBC scanning for the evaluation of active high gastrointestinal bleeding, in particular, we report a case of patient with a ^{99m}Tc-labeled RBC scintigraphy positive for duodenal active bleeding. **Patient and methods:** a 81 years old female patient with clinical history of repeated digestive bleeding, admitted from the emergency department of our hospital for nausea, syncope and signs of anaemia. Laboratory examinations showed marked reduction of erythrocytes, haemoglobin and hematocrit. After hospitalization the patient had an episode of melena. A recent gastro-duodenoscopy performed three days before was negative for gastro-duodenal bleeding and for this reason was performed a video capsule endoscopy negative for obscure gastrointestinal bleeding. She underwent a blood transfusion and the next day was performed a ^{99m}Tc-labeled RBC scintigraphy to evaluate a possible upper gastrointestinal bleeding. The performing procedure includes dynamic, static and SPECT-TC acquisition (dynamic, static and SPECT-TC tomographic images were acquired with a free-geometry dual-head gamma camera with CT gantry, General Electric Infinia Hawkeye®) at 1-4 hours and at 24 hours. **Result:** ^{99m}Tc-labeled RBC scintigraphy and in particular topographic acquisition SPET-CT were positive and localized the site of bleeding at the distal duodenum. **Discussion:** ^{99m}Tc-labeled RBC scintigraphy and in particular tomographic acquisition SPET-CT are of great help in identifying sites of bleeding even when they are located in the duodenum.

P12 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Molecular & Multimodality Imaging: Miscellaneous**P085****Cost minimization analysis of PET/CT and c.e CT performed either in one single session or in two different sessions, in oncological patients.**

C. Crivellaro¹, M. Picchio², M. Mansueto³, A. Grimaldi¹, L. Guerra⁴, S. Marcelli¹, M. Arosio⁴, L. Gianolli², C. Messa⁵; ¹Molecular Bioimaging Center, University of Milano-Bicocca, Milan, ITALY, ²Nuclear Medicine Department, San Raffaele Scientific Institute, Milan, ITALY, ³Accounting and budget control office, Niguarda Ca' Granda Hospital, Milan, ITALY, ⁴Nuclear Medicine Department, San Gerardo Hospital, Monza, ITALY, ⁵Nuclear Medicine Department, San Gerardo Hospital, Monza; L.A.T.O., HSR-Giglio, Cefalù; Molecular Bioimaging Center, University of Milano-Bicocca; IBFM-CNR, Milan, ITALY.

Aim: To evaluate the economic impact of positron emission tomography / computed tomography (PET/CT) and contrast enhancement CT (c.e. CT) performed in one single session examination vs. PET/CT and c.e. CT studies carried out in two different settings, in cancer patients. **Material & Methods:** Between February 2007 and December 2008, 145 oncological patients who presented clinical indications for both PET/CT and c.e. CT for either staging (n=46/145) or re-staging (n=99/145), were enrolled in the study. Seventy-two/145 patients performed PET/CT and c.e. CT in one single session (group A) while 73/145 in two separate sessions (group B). A cost-minimization analysis was performed both for Hospital and for patient. Hospital economic data were collected from administrative sources and included 1) direct costs: staff cost (medical staff, technicians, secretaries), medical materials costs (PET tracer, iodinated contrast material, consumables) and equipment depreciation; 2) indirect costs: department utilities. Patient cost data were obtained by a specific survey provided to patients at the time of PET/CT examination and included: travel, food and accommodation costs, and lost of productivity. Hospital and patient costs of two groups were analysed and compared. **Results:** Economic data analysis showed that Hospital cost per examination was lower for group A than for group B (171€ less per examination). In particular, staff cost, materials cost, equipment depreciation and department utilities costs of group A resulted 38€, 3€, 86€, 44€ less, respectively, per test, than those of group B. Cost for patient of group A was 68€ less than the one of group B. In particular, due to the single approach to Hospital, patients of group A could economise travel costs (34€ less per patient) and accommodation costs (35€ less per patient). Conversely, food cost was almost identical in the two groups. Productivity lost resulted slightly lower for group A than group B (1 work-hour less per person). **Conclusion:** PET/CT and c.e. CT performed in one single session is cost-saving, reducing costs both for Hospital and for patients. These advantages are mainly due the execution of a single procedure instead of two, thus reducing staff cost, equipment depreciation and department utilities costs per test for the Hospital and travel and accommodation costs for patients.

P086**The application of ¹⁸F-FDG PET/CT in multiple primary cancer including lung cancer**

H. Zhang, J. Zhao, F. Hua, C. Zuo, Y. Guan; PET center, Huashan hospital, Shanghai, CHINA.

Aim: Retrospectively analyze clinical feature and imaging manifestation of multiple primary cancer (MPC) including lung cancer by ¹⁸F-FDG PET/CT. Summarize diagnosis procedure of MPC. **Materials & methods:** According to Warren and Gates 3 standards of MPC, we collected 45 patients in our PET center from Sep 2004 to Dec 2009. They were all confirmed as MPC by pathology of biopsy or surgery. All of them were scanned by Siemens Biograph 64(HD) PET/CT with ¹⁸F-FDG. The images were separately read by two experienced nuclear medical doctors. They determined nature of diseases and located them precisely by fused image. Patients with lung cancer as first primary cancer (FPC) were grouped in the First Primary Lung Cancer (FPLC). The rest were grouped in the Second Primary Lung Cancer (SPLC). The data was statistically analyzed by Excel and SPSS15.0. **Result:** The incidence of MPC was 1.55%. The most common second primary cancer (SPC) was lung cancer in FPLC, followed by pancreas cancer. The most common FPC was breast cancer in SPLC, followed by colorectal cancer and gastric cancer. The most common pathology of multiple lung cancer was adenocarcinoma. The male to female ratio was 1.25:1 in MPC. There was no significant difference of gender in FPLC and SPLC ($\chi^2=0.54, P>0.05$). Age of FPC was 55.8 years old on average. Age of SPC was 62.1 years old on average. Both of them got to the top in 60~70-year-old group. There was no significant difference of age between FPC and SPC in both FPLC and SPLC ($t=1.985, 1.646, P>0.05$). The average interval in FPLC was 76.6m, and in SPLC was 29.7m. There was significant difference of interval between FPLC and SPLC ($t=1.818, P=0.041<0.05$). 45 patients all took 71 PET/CT scans. 19 SPC and 5 SMP were detected by PET/CT. 16 patients (84.21%) had single lesions. SUVmax of 15 second primary pulmonary nodule was 1.3~22.9. The average was 6.5. The 22 FDG uptake focus had 1.9 signs on average in CT image. **Conclusion:** The incidence of MPC is 1.55%. Patients above 60 years old (especially >75 years old) take high risk. The most common SPC was lung cancer. There are some imaging manifestation in MPC as in primary cancer. Suspected lesions with FDG uptake should have biopsy or surgery.

P087**F-18 FDG PET/CT in Peritoneal Metastases (PM)**

J. Yang¹, N. Gandikota¹, L. Rivera¹, C. Love¹, R. Libes², G. Rosen², H. M. Abdel-Dayem¹; ¹SVCMC-NY, New York, NY, UNITED STATES, ²St. Vincent's Comprehensive Cancer Center, New York, NY, UNITED STATES.

Objective: PM vary in number and size, can be asymptomatic and can originate from tumors either outside or within the abdomen and pelvis. Diagnosis of PM by CT does not have the advantage of assessment of metabolic activity. 18F FDG PET enhances the detection of PM,

especially when combined with CT. PET/CT helps to differentiate bowel activity from true positive metastatic lesions. The purpose of this retrospective undertaking is to review the PET/CT studies of patients who were diagnosed with PM between May 2007 and December 2009 at SVCMC in order to recognize sites of primary malignancies and examine the value of combining PET and CT. **Material and Methods:** 18 pts had 27 PET/CT studies (low dose CT). Only 5 pts had additional diagnostic CT scans within two months, two with contrast. Studies were read jointly by Nucl Med and Diag Rad physicians. **Results:** Sites of primary malignancy in the 18 pts were in this order: 11/18 had primary outside the pelvis (3 NSCLC, 2 breast, 1 pleural mesothelioma, 1 liposarcoma thigh, 1 malignant fibrous histiocytoma, 1 multiple myeloma, 1 osteosarcoma femur, 1 synovial sarcoma). 1/18 had adenocarcinoma of unknown primary. 7/18 had only one or two lesions. 11/18 had multiple lesions. Most lesions were seen in both PET and CT (in general, studies were not read separately to determine the accuracy of each modality). The SUV max from all cases ranged from 2.3 to 16.5. 6 had repeated studies to determine response to therapy with results as follows: 1/6 showed complete resolution, 3/6 showed progression, 1/6 showed stable disease and 1/6 showed a mixed response. The location of the lesions included para/perisplenic and para/perihepatic peritoneal surfaces, omentum, paracolic gutters, iliac fossa, serosal surfaces of colon and anterior abdominal wall among others. **Conclusion:** 1) PM can arise from tumors within or outside the abdominal/pelvic cavity; in our series, PM was more common in tumors originating outside the pelvis. 2) Because PM could be small and asymptomatic, they should be carefully looked for. 3) Combined PET and CT increase the confidence in recognizing lesions. 18F FDG PET/CT adds metabolic information to the anatomical abnormalities and facilitates their identification. 4) 18F FDG is also useful for the follow-up and evaluating treatment response of PM.

P088**Peripheral Nervous System Involvement: an Aggressive Manifestation of Non-Hodgkin's Lymphoma**

P. Peller, I. Stoian, G. Wiseman; Mayo Clinic, Rochester, MN, UNITED STATES.

Purpose: Non-Hodgkin's lymphoma (NHL) infiltration of the peripheral nervous system (PNS) is rare. Our objective was to retrospectively evaluate disease extent and outcome in NHL patients with FDG PET/CT detected PNS involvement. **Methods:** A retrospective analysis of a prospective database of patients presenting with neuropathy and a PET/CT scan for recurrent NHL from 9/01/05 to 9/01/09 was undertaken. Patients were included if the neurologic examination documented motor or sensory deficits, peripheral nerve involvement was identified on PET/CT and PNS infiltration confirmed by biopsy and/or resolved with lymphoma treatment. The location of PNS involvement, presence of CNS disease and nodal and extranodal NHL on PET/CT was correlated to the pathologic results and clinical outcome. **Results:** Of 7331 PET/CT scans performed for NHL, 40 patients (14 female, 26 male; mean age 56.8 ± 16.7) were found to have neuropathy. The major neurologic symptom was pain (55%) with weakness (40%) and numbness (10%) less common. Diffuse large B-cell NHL was the dominant histology (87.5%). PET /CT scans identified multiple nerve infiltration in 50% of patients with synchronous CNS, cranial nerve and cauda equina involvement in 25%, 12.5% and 12.5% respectively. The sciatic nerve was the single most commonly affected nerve (40%). Concomitant nodal disease was present in 37.5% and other sites of extranodal NHL seen in 47.5%. NHL in the spleen and lung were the most common extranodal sites. In the 34 patients with >2 year clinical follow-up, 21 patients (62.8%) attained complete remission with combination chemotherapy and 13 patients died of CNS lymphoma. **Conclusion:** PET/CT readily detects lymphomatous involvement of the PNS in NHL patients presenting for neuropathy. PET/CT identifies lymphoma in multiple peripheral nerves, cranial nerves and the CNS. One third of these NHL patients died of CNS lymphoma in the first two years.

P089**Prognostic value of dual-point FDG PET/CT in locally advanced oesophageal cancer treated by neo-adjuvant chemo-radiotherapy**

M. C. Marzola¹, A. Zanoni², G. Grassetto¹, E. Banti¹, L. Rampin¹, A. Massaro¹, F. Pasini¹, V. Ambrosini², S. Fanti³, G. De Manzoni², C. Cordiano², D. Rubello¹; ¹S. Maria della Misericordia Rovigo Hospital, Rovigo, ITALY, ²Clinical Surgery, Verona University, Verona, ITALY, ³Policlinico S. Orsola-Malpighi, Bologna, ITALY.

Purpose: In the present study we wanted to investigate the role of dual-point FDG PET/CT as predictor of histopathological response to neo-adjuvant chemo-radiotherapy in locally advanced oesophageal cancer. **Methods:** At present, 32 consecutive patients with locally advanced (cT2-4NxM0) oesophageal carcinoma (squamous cell = 14 cases, adenocarcinoma = 18 cases) were enrolled in the prospective study. All patients underwent preoperative concomitant neo-adjuvant chemo-radiotherapy and subsequent surgery in the period from January 2008 to March 2010. Histopathological regression was defined as "Good Response" (pT0N0 or minimal residual disease (MRD) ≤ 10 mm N0), "Bad Response" (huge residual cancer Nx) and "Response on T (pT0-MRD) with N+." A low 2.22 MBq/kg/bw dose of FDG was injected and whole body 3D acquisition started 1 hour later. FDG PET/CT was performed before the beginning (SUVmax1) and 5 week after the completion of chemo-radiotherapy (SUVmax2). Moreover, ΔSUV was calculated as the percentage of decrease between SUVmax1 and SUVmax2. **Results:** SUVmax2 was significantly correlated with histopathological response, especially excluding patients pT0/pMRD N+ (p<0.005): Good responders had a median SUVmax2 = 3.35 (CI 1.9-6.5), while Bad responders had a median SUVmax2 = 7.45 (CI 7.1-19.6). A SUVmax2 threshold value = 6.5 was identified to dichotomize Good and Bad responders. In the category pT0/pMRD N+ SUVmax2 values were similar to Good responders possibly because PET/CT failed to recognize some nodal metastasis located close to the primary tumour. No correlation between SUVmax1 and histopathological response was found while in patients showing a Good Response a trend toward a higher ΔSUV was observed. **Conclusion:** Our preliminary data indicate that FDG PET/CT SUVmax2 is significantly correlated to histopathological response to neo-adjuvant chemo-radiotherapy in patients with advanced oesophageal cancer. These results appear to be particularly important in identifying "Bad responders" patients in whom a change of subsequent therapeutic strategy should be done. Further investigation is required to better define the potential prognostic role of ΔSUV.

P090**Semi-Automated Analysis of Standard Uptake Values in Serial PET/CT Studies in Patients with Lung Cancer and Lymphoma**

J. Ly¹, L. Edenbrandt², S. Garpered¹, E. Jönsson¹, S. Valind¹; ¹Dept. of Clinical Sciences, Skåne University Hospital, Malmö, Sweden, Malmö, SWEDEN, ²Dept. of Molecular and Clinical Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden, Malmö, SWEDEN.

Objectives: Changes in maximum standard uptake values (SUV_{max}) in PET/CT follow-up studies in oncologic patients are often used to determine disease progression or regression. Manual measurement of these changes can be time consuming. A semi-automatic method for calculation of SUV_{max} in serial PET/CT studies was developed to address this issue. **Method:** The program first automatically aligns the serial PET/CT studies based on the CT images. Thereafter, the operator selects an abnormal uptake in the first PET study and the program automatically delineates the pathological site and calculates SUV_{max}. The corresponding pathological site in the follow-up study is thereafter automatically identified and the difference between the SUV_{max} in the two studies is calculated. The results of the semi-automated analysis were compared to that of a manual calculation of SUV_{max} using a Philips PET/CT workstation (Philips Extended Brilliance Workspace, PET/CT Application Suite v1.5K). Patients with lung cancer and lymphoma who had undergone two PET/CT studies between July 2008 and January 2010 were included. Pathological sites with sharp contrast to surrounding areas and with no formation of a large conglomerate mass were selected. 16 patients (69% men, age 56 ± 15 (mean ± SD)) with 26 lesions were included. Each patient had one to four pathological sites for manual and semi-automatic measurement. The difference of SUV_{max} for each uptake was calculated with both measurement methods and tested for correlation using Bland-Altman analysis. **Results:** The mean SUV_{max} measurement for all 52 (2 times 26) sites was 8.3 ± 4.2 (mean ± SD) for the automatic method and 7.7 ± 4.0 for the manual method, p<0.001, with R²=0.99. Bland-Altman's 95% limits of agreement were 1.45 - -2.51. The difference in SUV_{max} between first and second study was 3.18 ± 5.37 (mean ± SD) for the semi-automatic method and 2.9 ± 5.04 for the manual method, p<0.001, with R²=0.99. Bland-Altman's 95% limits of agreement were 2.54 - -1.98. Manual and semi-automatic method agreed in all cases whether SUV_{max} had increased or decreased between serial studies. **Conclusion:** Good agreement was shown in absolute SUV_{max} measurements and in the difference in SUV_{max} between studies. The program shows systematically higher SUV_{max} compared with the manual method. This may be due to different filter settings between the PET/CT manufacturer and the program. The findings show feasibility of using semi-automated calculation of SUV_{max} in serial studies and encourage further development of programs using this type of methods.

P091**The role of FDG-PET-CT (PET) in characterising large-vessel vasculitis (V)**

F. Giacomuzzi, O. Geatti, M. Povolato, D. Stanic, A. Cecotti; Az. Ospedaliero-Universitaria, Udine, ITALY.

Purpose: to investigate the role of PET in the diagnosis and management of V. **Methods:** 54 consecutive patients (pts) with biopsy-proven or suspected V were examined and 85 PET performed (54 baseline, 31 in follow-up); in 63/85 cases (74%), pts were in immunosuppressive therapy (IT). The severity of large-vessels FDG uptake was visually graded using a 4-point scale: 0 = no uptake; 1 uptake < liver; 2 uptake = liver; 3 uptake > liver. Grades 2 or 3 in the aorta and visible uptake in other arteries were interpreted as pathological. PET scores were compared with CRP, ESR, histological findings and radiological investigations (RI, angiography, MRI, CT angiography, Doppler US). **Results:** PET revealed pathological findings in 31 of 85 scans; 54 were grades 0-1, 14 grade 2 and 17 grades 3-4. Grades closely correlated with both CRP and ESR levels (grades 0-1: CRP 7.9 mg/l, ESR 18.9 mm/h; grade 2: CRP 22.0 mg/l, ESR 32.1 mm/h; grades 3-4: CRP 66.2 mg/l, ESR 73.3 mm/h respectively). All pts with biopsy-proven V (8/15) had a positive PET (5 pts: grade 3; 3 pts: grade 2). After IT we always found a reduced FDG uptake (SUV from 4.1 to 2.8) in parallel with inflammatory markers (CRP and ESR from 50.0 to 11.9 and from 67.4 to 21.2 respectively). In 6/7 pts who had a biopsy negative for V, PET was negative as well (grades 0-1) and serum inflammatory markers were normal or slightly increase; in the 7th pt with a biopsy negative for V, PET was positive (grade 3), serum inflammatory markers were elevated and after IT a marked decrease in FDG uptake (from grade 3 to 1) was observed, in parallel with clinical amelioration. Of 55/85 pts studied with both PET and RI, 32/55 were concordant (12 positive, 20 negative); 5/55 were positive on PET only and 18/55 were positive on RI only. Discrepancies were mostly due to PET positive at diagnosis, before starting therapy (4/5) or negative, mainly after starting or during IT (16/18). **Conclusions.** Our data suggest that PET: • has high sensitivity and becomes positive earlier than RI (activation of leucocytes precedes the development of morphological changes) • has good correlation with inflammatory serum markers and histological findings • is valuable in assessing response to IT, as FDG uptake changes quickly in response of successful therapy.

P092**Initial experience with Gallium-68 Octreotate PET/CT for assessing suitability of paediatric patients with refractory metastatic neuroblastoma for radiolabelled peptide therapy**

G. Kong, M. Hofman, P. Eu, O. Neels, R. Hicks; Peter MacCallum Cancer Centre, East Melbourne, AUSTRALIA.

Aim: Paediatric patients with metastatic neuroblastoma who have refractory disease or relapse following multimodality treatments including high activity I-131 MIBG therapy have limited therapeutic options. Development of newer tumour targeting therapies is essential. Immunohistochemistry studies have indicated that most neuroblastomas express somatostatin receptors of subclass 2 (SSR-2), allowing imaging with Gallium-68 Octreotate PET/CT (GaTate), and potential use of tumour targeting peptide receptor radionuclide therapy (PRRT). We reviewed all consecutive GaTate studies performed for paediatric patients with known or suspected neuroblastoma at our centre to assess SSR-2 expression and hence potential suitability for PRRT. **Methods:** GaTate studies (n=14) were performed in 9 patients (2-8 years old) from October 2008 to March 2010 with blinded scoring of disease sites and semi-quantitative uptake

analysis. Of these, 8 patients had residual neuroblastoma despite heavy pre-treatment (including I-131 MIBG in 7/8 pts); the remaining patient had staging GaTate for suspected neuroblastoma despite negative conventional imaging. Comparison was made with previous I-123 or post-treatment I-131 MIBG studies to assess identification of additional disease sites, the concordance and degree of SSR-2 expression at known disease sites, and impact in relation to potential suitability for PRRT. **Results:** GaTate imaging demonstrated high tumour-to-background ratio at known sites of disease with a median SUV_{max} of 6.7 (3.9-15.3) in the most intense site of uptake. Additional sites of disease was shown by GaTate in 5/14 studies (36%) with upstaging in 3 studies by identification of bone involvement (all subsequently confirmed) and more lesions in 2 studies. Concordant or additional sites of SSR-2 uptake higher than background liver was shown by GaTate in 71% (10/14 studies), hence allowing consideration for PRRT. Overall, GaTate findings suggested potential suitability for PRRT in a high proportion of patients (7/9 patients; 78%). **Conclusion:** GaTate PET/CT was positive in high proportion of patients with known residual neuroblastoma indicating a sufficient degree of somatostatin receptor expression to allow consideration of peptide receptor radionuclide therapy as a potential new tumour targeting treatment option. It also identified additional sites of disease when compared to MIBG imaging and may be a useful staging technique.

P093**Comparison of (68)Ga-DOTA, Tyr(3), Thr(8) -octreotide PET/CT and (99m)Tc-HYNIC, Tyr(3), Thr(8)-octreotide SPECT/CT in neuroendocrine tumors**

B. Gunes¹, M. Ocak², L. Kabasakal¹, A. Araman², C. Decristoforo³, O. Ekmekcioglu¹, R. Kaya¹, M. Halac¹, I. Uslu¹; ¹Istanbul University Cerrahpasa Medical Faculty Nuclear Medicine Department, Istanbul, TURKEY, ²Istanbul University Pharmacy Faculty Department of Pharmaceutical Technology, Istanbul, TURKEY, ³Medical University of Innsbruck Clinical Department of Nuclear Medicine, Innsbruck, AUSTRIA.

Introduction: A new field of interest is the application of ⁶⁸Ga-labelled DOTA-conjugated peptides for positron emission tomography (PET). Previous studies have claimed that radiolabelled somatostatin analogues with positron emitters provide more information in the detection of somatostatin receptor (SSTR) positive tumors and their metastases than those of SPECT radiopharmaceuticals. **Aim:** The aim of the present study was to compare the inhouse synthesized ⁶⁸Ga-1,4,7,10-tetraazacyclododecane-N,N',N''-N'''-tetraacetic acid, Tyr³, Thr⁸-octreotide (⁶⁸Ga-DOTA-TATE) (selective SSTR2 PET ligand) PET/CT with in house prepared ^{99m}Tc-HYNIC-Tyr³, Thr⁸-octreotide (^{99m}Tc-HYNIC-TATE) SPECT/CT in the detection of SSTR and their metastases. **Materials and Methods:** The patients had given written informed consent to participation in the study, which had been approved by the local ethics committee. Twenty one patients (15 female, 6 male) with a diagnosis of primary or recurrent NET (10 NET, 4 MEN I syndrome, 3 medullary thyroid carcinoma, 3 carcinoid tumor, 1 paraganglioma) were prospectively examined. The mean age of enrolled patients were 54.4 ± 11.8 yr (range, 23-73 yr). Before beginning recent long acting cold somatostatin analogue treatment, patients were injected intravenously 186.11 ± 41.07 MBq ⁶⁸Ga-DOTA-TATE (which was synthesized by using Fractionated Modular System with 30 mCi ⁶⁸Ga/⁶⁸Ge Generator, Eckert & Ziegler Eurotope, Berlin, Germany). 46.76 ± 18.17 minutes after injection PET/CT images were obtained. For SPECT/CT images a mean activity of 555 MBq ^{99m}Tc-HYNIC-TATE was given intravenously. Whole body and SPECT images were obtained 4 hours after injection. All data obtained from PET and SPECT/CT studies were fused with a specialized software. **Results:** The image quality of ⁶⁸Ga-DOTA-TATE was not different than that of F-18 FDG PET. Physiological uptakes were observed in hypophysis, salivary glands, thyroid and adrenal glands. The number of lesions detected by PET images were higher than that of ^{99m}Tc-HYNIC-TATE as expected. The reader confidence in lesion detection and lesion localization was also higher with ⁶⁸Ga DOTATATE PET studies. **Conclusion:** The results of the present study have suggested that ⁶⁸Ga-DOTA-TATE PET imaging is superior to ^{99m}Tc-HYNIC-TATE SPECT imaging in diagnosis and localization of somatostatin expressing tumors especially in detecting small tumors or tumors bearing only a low density of SSTRs. It also shows perfect imaging characteristics and high tumor to background ratios. **Acknowledgements:** This work was supported by Scientific Research Projects Coordination Unit of Istanbul University. Project number 3264

P094**Role of 18F-DOPA PET/CT in detecting metastatic deposits of malignant pheochromocytoma**

E. Banti¹, L. Rampin¹, M. C. Marzola¹, G. Grassetto¹, A. Mazza¹, A. Massaro¹, E. Milan¹, V. Ambrosini², S. Fanti², G. Opocher³, M. R. Pelizzolo⁴, D. Rubello¹; ¹S. Maria della Misericordia Rovigo Hospital, Rovigo, ITALY, ²Policlinico S. Orsola-Malpighi, Bologna, ITALY, ³Istituto Oncologico Veneto, Padova, ITALY, ⁴Surgical Pathology, Padova University, Padova, ITALY.

Purpose: The vast majority of pheochromocytomas (PHEO) are benign adrenal lesions. 18F-DOPA PET showed good sensitivity in detecting benign PHEO. Malignant PHEO is a very rare condition, and the potential role of 18F-DOPA PET on the management of this disease remains unclear. We report here our experience with 18F-DOPA PET/CT in a group of patients with malignant PHEO. **Methods:** In the period Sep 2008 to Jan 2010 we studied by 18F-DOPA PET/CT 68 patients affected by endocrine tumour: 6 of them were referred to investigate recurrent malignant PHEO after primary adrenal surgery suspected on the basis of increased catecholamine serum/urinary levels; 3 F, 3 M; mean age 52.3 ± 7.4 yrs; 3 had sporadic PHEO, 1 was MEN-2A related, 1 von Hippel-Lindau related. C.e.CT/MRI, 123I-MIBG (370 MBq) and 18F-DOPA PET/CT results were compared. PET/CT was acquired from the level of the skull to the upper legs, 60-90 min after the injection of 150-200 MBq of 18F-DOPA. Every tracer uptake different from a physiological distribution was considered as pathological finding. Two skilled nuclear medicine physicians interpreted the data; in case of discrepancy a final diagnosis was reached by consensus. As gold standard surgical findings and/or clinical and imaging follow up were taken. **Results:** recurrent disease in the operated on adrenal bed was detected in 3 patients both by 18F-DOPA PET/CT and 123I-MIBG (in 2 of them c.e.CT/MRI were also positive). A lesion in the contra-lateral adrenal gland was depicted in 2 patients by all imaging methods. Lymph node mts were visualized in 3 patients by 18F-DOPA PET/CT; in 2 of them 123I-MIBG was also positive whereas c.e.CT/MRI were negative. Liver metastatic deposits were detected in 3 patients by 18F-DOPA PET/CT, in 2

patients by 123I-MIBG, in 1 case by c.e.CT/MRI. Lung metastatic deposits were detected in 2 patients by 18F-DOPA PET/CT as well as by c.e.CT while 123I-MIBG was negative. As a whole, 18F-DOPA PET/CT visualized 22 tumor deposits, 123I-MIBG 17 deposits, and c.e.CT/MRI 10 deposits. The 5 metastatic deposits showed at 18F-DOPA PET/CT alone were small sized (< 10–15 mm in maximum diameter). Conclusion. The present data show that functional imaging (18F-DOPA/123I-MIBG) is superior than morphological imaging (c.e.CT/MRI) in detecting deposits of malignant PHEO. Un details, 18F-DOPA PET/CT showed similar data than 123I-MIBG in revealing recurrent malignant PHEO in the adrenal beds whereas 18F-DOPA PET/CT had higher sensitivity in visualizing small-sized metastatic deposits to nodes and distant sites.

P095

68Ga-DOATATE PET/CT in neuroendocrine tumors - our first clinical experiences

J. Kunikowska¹, L. Krolcicki¹, D. Pawlak², R. Mikołajczak³, M. Kobylecka¹; ¹Medical University of Warsaw, Warsaw, POLAND, ²IEA POLATOM,, Świerk, POLAND, ³IEA POLATOM, Świerk, POLAND.

Neuroendocrine tumors (NETs) have distinct biological and clinical characteristics, in particular a high density of somatostatin receptors at the cell membrane. This property allows use of radiolabeled somatostatin analogs for imaging of these tumors. PET/CT with 68Ga-DOTATATE open new possibilities in the diagnosis of patients with NET. The aim of this study was to evaluate the diagnostic usefulness of a new somatostatin analog, 68Ga-DOTATATE, for PET/CT in patients with diagnosis of neuroendocrine tumors. METHODS: 70 patients with known NET were examined (30 men, 40 women; age range, 18–86 y; mean 51.4 +/- 12.5 y). PET imaging was performed on PET/CT scanner Biograph 64, 60 minutes post injection of 120–185 MBq 68Ga-DOTATATE. RESULTS: PET/CT was performed for unknown primary tumour detection (n=20), staging (n=21), restaging after surgery (n=29). In 14 of 20 patients 68Ga-DOTATATE PET/CT localized the site of the primary: intestine(7), pancreas(4) small nodule in lung(3). CT alone (on retrospective analyses) confirmed the findings only in 4 of 20 patients (20%). In 6 (30%) cases primary tumors were not found. In staging and restaging PET showed more lesions than CT in 20/50 patients, and the same number in 30/50. Staging of disease: 68Ga-DOTATATE PET/CT revealed new lesions in 8/21 patients: intestine(1), liver(3), bone(2), pancreas(4), lymph nodes in abdominal cavity(2), peritoneum(1) In the cases of restaging patients after surgery, PET/CT examination shown new foci in 12 patients: liver(4), lymph nodes in abdominal cavity(3), peritoneum(2), pancreas(1), intestine(2). CONCLUSION: The 68Ga-DOTATATE PET/CT is very useful non-invasive techniques in diagnosis of patients with NET, can be successfully use for detection of unknown primary tumors, staging and restaging of disease and gives more clinically useful information than CT.

P096

Increased F-18 Fluorodeoxyglucose Accumulation in Right Ventricular Free Wall in Pulmonary Hypertension

D. R. Neumann¹, I. Dostanic-Larson², F. DiFilippo¹, R. C. Brunken¹, S. C. Erzurum²; ¹Cleveland Clinic Imaging Institute, Cleveland, OH, UNITED STATES, ²Cleveland Clinic Respiratory Institute, Cleveland, OH, UNITED STATES.

AIM: To determine whether [¹⁸F]fluorodeoxyglucose (FDG) accumulation by the right ventricle is increased in fasting patients with primary pulmonary hypertension. MATERIALS AND METHODS: Eight subjects with pulmonary arterial hypertension (six with idiopathic and two with secondary) and six normal control subjects were studied. After fasting at least 8 hours, each subject received ¹⁸F-FDG intravenously. PET/CT imaging of the chest was performed, from which standardized uptake values (SUV) of FDG of the right and the left ventricular free walls were obtained. The SUV values were corrected for partial volume effect based on echocardiographic wall thickness measurements. Echocardiographic studies also provided measurement of right ventricular systolic pressures. RESULTS: The average corrected right ventricular free wall SUV in the pulmonary hypertensive group (51.7 +/- 3.2) was significantly greater than that of the normal group (19.8 +/- 0.9, p<0.01). However, the average corrected left ventricular free wall SUV in the pulmonary hypertensive group (49.1 +/- 4.9) was similar to that of the normal group (30.3 +/- 2.5, p=0.15). The corrected right ventricular free wall SUVs in the pulmonary hypertensive group were linearly related to right ventricular systolic pressures (r=0.62, p=0.05). CONCLUSION: The right ventricular free wall FDG accumulation corrected for partial volume effect is significantly increased in fasting pulmonary hypertensive patients compared to normals. Furthermore, the degree of right ventricular FDG uptake correlates with right ventricular systolic pressures in pulmonary hypertension. This suggests a compensatory increase in right ventricular myocardial glucose consumption in pulmonary hypertension to accommodate the increase in right ventricular stroke work

P097

Impact of FXIII A1, FII, FV, FGB and PAI1 Polymorphisms on Myocardial Perfusion: Correlation with Myocardial Single Photon Emission Computed Tomographic Imaging

M. Satra¹, M. Samara¹, G. Wozniak¹, A. Kontos¹, V. Valotassiou¹, I. Tsougou¹, P. Kollia², P. Georgoulis¹; ¹University of Thessaly, Larissa, GREECE, ²University of Athens, Athens, GREECE.

Coronary artery disease (CAD) is a significant cause of morbidity and mortality today. The association between genetic markers and CAD is still poorly understood. In this study we evaluated the effect of five genetic variants, Factor V Leiden (FV: G1691A), factor II prothrombin (FII: G20210A), plasminogen activator inhibitor 1 (PAI-1: 4G/5G) Beta-Fibrinogen (FGB: -455 G>A) and Factor XIII (FXIII: V34L), on myocardial perfusion. We examined 523 patients using exercise-rest myocardial perfusion single photon emission computed tomography (SPECT), where the summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS) indexes, were calculated. In order to examine the independent prognostic ability of genotypes on SSS and SDS, multiple linear regression models were used. It was found that FV, FXIII, FGB and PAI-1 4G/5G genotypes were independent prognostic predictors of SSS and SDS with F13A1 revealing the strongest association; moreover FII genotypes were independent prognostic predictors of

SSS. In conclusion, our study provides the first evidence of an association between these polymorphisms with myocardial perfusion. Therefore, we suggest that the process of coronary artery disease may be modified by the FV, FII, PAI-1, FGB and FXIII genotypes.

P098

T-cell activation and age-related effects influence quantitative characteristics of Hashimoto's thyroiditis phenotype

I. Mihaljević¹, S. Tokić², M. Štefanić¹, L. Glavaš-Obrovac¹; ¹Clinical Institute of Nuclear Medicine and Radiation Protection, University Hospital Centre Osijek, School of Medicine, University of J.J. Strossmayer, Osijek, CROATIA, ²Clinical Institute of Nuclear Medicine and Radiation Protection, University Hospital Centre Osijek, Osijek, CROATIA.

Hashimoto's thyroiditis (HT) is the most frequent autoimmune thyroid disorder mediated by deregulated T-cell responses. Several gene candidates with immune regulatory functions have been implicated in HT etiology, including vitamin D receptor (VDR), cytotoxic T-lymphocyte antigen-4 (CTLA-4), CD28 and CD45 genes. Aim: To evaluate clinical implications of VDR, CTLA-4, CD28 and CD45 mRNA expression profiles in peripheral T-cells of HT patients. Materials and methods: 42 HT patients (mean age 46±14.8 years, 3 male) were diagnosed on the basis of positive thyroid peroxidase autoantibodies (TPOAb), characteristic echosonographic findings, cytopathological features consistent with HT in high quality, ultrasound-guided fine needle aspiration biopsies and/or biochemical hypothyroidism (median TSH 5.27 mU/L, interquartile range 3.11–13.8 mU/L). Pretreatment TPOAb-IgG (median TPOAb titer 285 IU/mL, interquartile range 77–1777 IU/mL) were measured by an enzyme-linked immunosorbent assay calibrated against WHO reference MRC 66/387. At baseline, thyroid gland volume was measured by ultrasonography. Untouched T-lymphocytes were negatively isolated from peripheral blood of HT patients using magnetic beads procedure. Following T-cell isolation, total RNA was extracted and gene expression studied by RT-PCR. ImageQuantTL program was used for relative quantification of RT-PCR bands. An internal control gene was GAPDH. Comparative analysis of gene expression data versus FT4, FT3, TSH, TPOAb levels and goiter volume measurements was performed by Spearman rank correlations. Results: VDR, CTLA-4, CD28 and five isoforms of CD45 mRNA (CD45RABC, CD45RAB, CD45RBC, CD45RB and CD45R0) were expressed in most of the HT patients (n=36). Statistically significant positive correlation was detected between expression of the CD45RAB isoform and FT3 serum levels at diagnosis (P=0.0066, Spearman's rho=0.51). Furthermore, CD45R0 isoform expression in peripheral T-lymphocytes was positively associated with age (P=0.027, rho=0.34). Conversely, a negative correlation was detected between CD45RABC mRNA expression and goiter volume (P=0.032, rho=-0.364). However, no significant association was found between total levels of VDR, CTLA-4 or CD28 mRNA expression and quantitative characteristics of HT phenotype. Conclusion: Unlike naive T-cells which preferentially express large CD45 isoforms (CD45RABC, CD45RAB and CD45RBC), activated and memory T lymphocytes express the shortest one, CD45R0, which lacks RA, RB and RC exons, respectively. Our results indirectly suggest that peripheral FT3 levels and HT disease severity are significantly influenced by differentiation process and activation status of T-cells. Furthermore, higher prevalence of T-cells expressing CD45R0 activation marker in older HT patients emphasizes influence of age on T-cell development and function.

P099

I-123/Tc-99m Sestamibi Subtraction SPECT/CT in Recurrent Postoperative Hyperparathyroidism

D. R. Neumann, G. Wu, M. Lieber; Cleveland Clinic Imaging Institute, Cleveland, OH, UNITED STATES.

AIM: To determine the diagnostic accuracy of ¹²³I/^{99m}Tc-sestamibi subtraction SPECT/CT for the localization of parathyroid lesions in patients with primary hyperparathyroidism who have undergone previous parathyroid surgery. MATERIALS AND METHODS: A total of 36 consecutive surgical patients with primary hyperparathyroidism were studied, all of whom had undergone parathyroid surgery previously. Each patient underwent ¹²³I/^{99m}Tc-sestamibi SPECT/CT prior to reoperation using a hybrid SPECT/CT instrument that combined a dual-detector SPECT camera with a 16-slice multidetector spiral CT scanner. Four hours after taking ¹²³I sodium iodide orally, each patient received ^{99m}Tc-sestamibi intravenously, followed immediately by a simultaneous, dual-isotope SPECT scan of the neck and upper chest. Then, without moving the patient, a non-contrast CT scan of the same body region was performed. Normalization and subtraction of the ¹²³I SPECT images from the ^{99m}Tc SPECT images were performed. The subtraction SPECT images were coregistered with the CT images for interpretation. Surgical and histopathologic findings from reoperation were used as the standard of comparison. RESULTS: Surgery was successful in all 36 patients, with removal of 43 parathyroid lesions (a solitary parathyroid adenoma in 30 patients, double parathyroid adenomas in 4 patients, 4 hyperplastic parathyroid glands in 1 patient, and a solitary parathyroid carcinoma in 1 patient). 23% (10/43) of the resected parathyroid lesions were in ectopic or heterotopic locations. Subtraction SPECT/CT correctly localized 32 of the 38 parathyroid adenomas (84% sensitivity), 2 of the 4 hyperplastic parathyroid glands (50% sensitivity), and the parathyroid carcinoma. Subtraction SPECT/CT was positive in two benign reactive lymph nodes; there were no other false-positive subtraction SPECT/CT findings in this series. CONCLUSION: ¹²³I/^{99m}Tc-sestamibi subtraction SPECT/CT is a very sensitive modality for the detection and localization of parathyroid lesions in patients with recurrent postoperative primary hyperparathyroidism.

P100

Medetomidine alone and in combination with ketamine causes changes in the regional cerebral blood flow measured with single photon emission computed tomography in cats

T. Waelbers¹, K. Peremans¹, S. Vermeire¹, K. Piron¹, K. Audenaert², A. Dobbelaer¹, V. Boer³, H. de Leeuw³, M. Vente³, I. Polis¹; ¹Ghent University, Merelbeke, BELGIUM, ²Ghent University, Ghent, BELGIUM, ³UMC, Utrecht, NETHERLANDS.

Aim Sedation or anaesthesia before intravenous tracer administration is frequently required in cats. Since anaesthetics have an effect on neuronal activity and on the circulatory system and

hence on regional cerebral blood flow (rCBF), one should evaluate their effect on ^{99m}Tc -ECD distribution studies. Medetomidine alone or in combination with ketamine is frequently used for intramuscular sedation or anaesthesia in cats. The aim of this study was to evaluate the effect of medetomidine and ketamine on rCBF measured with ^{99m}Tc -ECD. **Materials and methods** The rCBF was measured in 6 adult cats according to three protocols. For the first protocol the tracer (^{99m}Tc -ECD) was injected in the awake cat, 5 to 10 minutes prior to IM administration of medetomidine (100 $\mu\text{g}/\text{kg}$) (condition A). For the following protocols the tracer was injected 15 minutes after IM sedation with medetomidine (100 $\mu\text{g}/\text{kg}$) (condition M) or with the combination of medetomidine (100 $\mu\text{g}/\text{kg}$) and ketamine (5 mg/kg) (condition MK). Anaesthesia was induced and maintained with propofol. Data were acquired with a triple head gamma camera (Triad, Trionix), equipped with multipinhole collimators (HiSPECT, Bioscan; 6 holes, 3 mm \varnothing , resolution 2.4mm). During the acquisition, which started 15 minutes after induction of anaesthesia, intermittent positive pressure ventilation was applied in order to maintain end tidal carbon dioxide (EtCO_2) between 35 and 45 mmHg. Differences between protocols were evaluated for nineteen regions: bilateral frontal, temporal, parietal and occipital cortex, bilateral thalamus, amygdala, basal ganglia and hippocampus and for the bulbus olfactorius, cerebellum and cingulate gyrus. These regions were predefined on MRI data (7T, Achieva) fused with the μSPECT data. Semiquantification of the rCBF was performed by normalising the average regional counts to total counts. **Results** Registered counts were significantly higher in conditions M and MK compared to condition A ($P<0.05$). Tracer uptake in the M-condition was higher, albeit not significantly, in all brain regions compared to the MK-condition. Significant higher perfusion indices were present in condition A in the subcortical regions (thalamus, amygdala, basal ganglia and hippocampus) ($P<0.05$) compared to the two other conditions. **Conclusion** Medetomidine alone or in combination with ketamine, prior to injection of ^{99m}Tc -ECD, provokes not only a generally increased tracer uptake in all brain regions, but also regional blood flow alterations. Thus caution is needed when evaluating rCBF under medetomidine or medetomidine/ketamine sedation/anaesthesia. Further studies are needed to evaluate the effect of these rCBF alterations on neurotransmitter studies.

P13 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Radiopharmaceuticals & Radiochemistry & Dosimetry: Radiopharmaceuticals - General

P101

Tumor cells damage induced by the influence of ^{188}Re -tricarboxyl citrate and ^{188}Re -tricarboxyl octreotide

O. E. Klementieva, V. Korsunsky, A. Malysheva, A. Malysheva; A.I. Burnazian Federal Medical Biophysical Center, Moscow, RUSSIAN FEDERATION.

The labeling of biologically active molecules with $^{188/186}\text{Re}$ for radiopharmaceutical purposes is a field of intense research. The beta-emitting radioisotope ^{188}Re ($T_{1/2}$ 17 h, E_{max} 2.12 MeV) has been introduced in the field of nuclear medicine for radiotherapy applications aiming at the delivery of therapeutically significant radiation doses to malignant lesions without adversely affecting normal tissue. The aim of this work is the evaluation of tumor cells damage induced by ^{188}Re -tricarboxyl complexes attached to the tumor-specific ligands (citrate and octreotide). **Materials and Methods** [$^{188}\text{Re}(\text{CO}_3)_3^+$] was prepared from $\text{Na}^{188}\text{ReO}_4$ solution (Obninsk, Russia), $\text{K}_2[\text{H}_3\text{BCO}_2]$ and $\text{BH}_3\text{-NH}_3$. Then citrate buffer or octreotide were added. Radiochemical purity (RCP) was tested by TLC on silica gel - MeOH/HCl 99:1. In vitro experiments carried out with melanoma B 16 and breast carcinoma MCF-7 cells. Twenty-four hours prior treatment, B 16 and MCF 7 cells were seeded on flasks (25 cm^2) and then incubated with 10-100 μCi of ^{188}Re -tricarboxyl complexes (activities contained in 50 μl) for 3 hours. Inhibition of cell viability after influence of [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Cit $_3$ and [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Oct were defined in the test with trypan blue. The results represented as survival percentage and mean lethal dose (D_0). Accumulated activity was expressed in $\%/10^6$ cells. **Results** Maximal cell uptake of [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Cit $_3$ was $3.5\%/10^6$ cells for MCF 7 cells and $5.0\%/10^6$ cells for B 16 after 90 min incubation. Maximal cell uptake of [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Oct was $4.0\%/10^6$ cells and $2.5\%/10^6$ cells for B 16 after 120 min. The number of surviving cells was quantified 48 hours after removal of the radioactive medium. There is no biologic elimination during the incubation time so only physical decay occurs during these periods. The curves of cell survival are described by the equations: $Y_1=100\cdot e^{-0.03x}$ for MCF 7 cells after [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Cit $_3$ influence and D_0 is equal to $9.5 \pm 1.0 \mu\text{Ci}/\text{ml}$. $Y_2=100\cdot e^{-0.0023x}$ for B 16 cells after [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Cit $_3$ influence and D_0 is equal to $11.6 \pm 0.8 \mu\text{Ci}/\text{ml}$. $Y_3=100\cdot e^{-0.0029x}$ for MCF 7 cells after [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Oct influence and D_0 is equal to $9.9 \pm 1.1 \mu\text{Ci}/\text{ml}$. $Y_4=100\cdot e^{-0.0025x}$ for B 16 cells after [$^{188}\text{Re}(\text{CO}_3)_3^+$]-Oct influence and D_0 is equal to $10.7 \pm 1.4 \mu\text{Ci}/\text{ml}$. **Conclusion:** From the preliminary results (accumulation in tumors, cell viability and value D_0) we can conclude that the investigated citrate complexes of ^{188}Re -tricarboxyl can be used as promising agents for nuclear medicine.

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Preparation of [F-18] sodium fluoride for injection, USP and cGMP_s compliance

B. Cordero¹, T. Martinez¹, S. Medin²; ¹Hospital Clínico Santiago, Santiago de Compostela, SPAIN, ²Hospital Universitario Virgen de la Arrixaca, Murcia, SPAIN.

1. INTRODUCTION The favourable imaging performance and the clinical utility of F-18 fluoride PET compared with diphosphonates scintigraphy support the reconsideration of F-18 fluoride as a routine bone imaging agent. Implementation of this nuclear medicine procedure is being considered by our Hospital. We established a fully automated preparation of [F-18] sodium fluoride for injection, USP and cGMPs compliance, including control of residual solvent and sterilization by heat in final vial. **2. MATERIALS AND METHODS** No-carrier-added fluoride-18 was produced by the O-18(p,n)F-18 reaction on a PETtrace cyclotron GEMS. At the end of the bombardment, activity was transferred to a Tracerlab MX module with modified sequence. QMA was preconditioned with 10 cc ethanol plus 10 cc water for injection. The [^{18}F] fluoride was eluted from cartridge with 3mL 0.9% saline solution. The total production time is less than 6

minutes. Nitrogen pushed the 3mL final solution to the Tracerlab dispenser unit. The final solution was dispensed into sterile vials and finally sterilized in autoclave (132°C 3.5 min, $F_0>90$). Quality control was carried out according to the United States Pharmacopeia USP 32-NF 27, including residual solvents. Quality control test were performed 8 hours post preparation. **3. RESULTS AND DISCUSSION** Ethanol levels detected were due to dispenser cleaning procedure, as shown in table 1.

Run	Ppm ethanol predispsing	Ppm ethanol postdispensing
Run 1	0	157
Run 2	0	57
Run 3	20	1140

Table 1 Quality control results for three runs are shown in table 2.

Test USP	Run 1	Run 2	Run 3
Appearance	ok	ok	ok
pH	7.01	7.30	7.68
Radiochemical purity	>99%	>99%	>99%
Chemical purity (Ethanol levels in ppm)	157	57	1140
Radionuclidic purity	ok	ok	ok
Endotoxin levels	<175 UI/ml	<175 UI/ml	<175 UI/ml
Sterility	ok	ok	ok

Table 2 **4. CONCLUSIONS** We have established a rapid, easy and reliable automated method for sodium fluoride F-18 preparation in a modified Tracerlab mx. As a part of cGMPs compliance sterilization by heat in final vial was chosen instead of final filtration. Control of residual solvents was included as chemical purity test to meet USP requirements. The sodium fluoride solution prepared is stable at least 8 hours after preparation.

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Synthesis and biodistribution of ^{99m}Tc -Pheophorbide-a in a model of bacterial infection

F. Yurt Lambrecht¹, K. Ocakoglu², E. Bayrak¹, M. Onursal¹, O. Yilmaz³; ¹Institute of Nuclear Science, Izmir, TURKEY, ²Tarsus Technical Education Faculty, Mersin University, Mersin, TURKEY, ³Department of Animal Research Center, Dokuz Eylul University, Izmir, TURKEY.

Aim: The aim of the current study is to prepare, ^{99m}Tc -Technetium Pheophorbide-a (^{99m}Tc -PH-A) complex, and to evaluate its efficiency as an infection imaging agent. **Materials & methods:** First, PH-A was obtained from *Spirulina maxima algae*, and $^1\text{H-NMR}$ and MS (ESI) methods were used to confirm the product compound. MS (ESI) measured molecular mass as 548 which indicated that the product compound is PH-A. $^1\text{H-NMR}$ analysis also supported the result. **Results:** PH-A was efficiently labeled with ^{99m}Tc with high yield (87 \pm 3.2%). Radiolabeling efficiency was checked by radio thin layer chromatography (RTLC). Biodistribution of ^{99m}Tc -PH-A was investigated in vivo in two groups of rats; bacterial infected rats with *Staphylococcus aureus* (*S. aureus*) and sterile inflamed rats with turpentine oil. These experiments depicted that uptake ratio of ^{99m}Tc -PH-A in bacterial infected muscle to its in normal muscle [target/non-target (T/NT)=5.6 at 1h] was over four times higher than its ratio in sterile inflamed muscle (T/NT=1.29 at 1h) of rats. **Conclusion:** ^{99m}Tc -PH-A prepared with high yield is able to good localize in the bacterial infected muscle of the rats and ^{99m}Tc -PH-A might be developed as a radiopharmaceutical agent for distinguishing the infection from inflammation by nuclear imaging.

P104

Development of EDTMP kit formulation for ^{177}Lu -EDTMP phase III clinical trial

D. Pawlak, A. Jaron, R. Mikolajczak; Institute of Atomic Energy Polatom Radioisotope Centre, Otwock, POLAND.

Introduction. Patients suffering from breast, lung and prostate cancer develop metastases in bone in the advanced stage of their disease. Today ^{153}Sm -EDTMP (ethylenediaminetetramethylene phosphonic acid) and $^{89}\text{SrCl}_2$ are routinely used for pain palliation purposes; however their availability in many countries is still limited. EDTMP has high affinity to the bone tissue and to the tumor metastases to bone accompanied by high stability of EDTMP with a number of metallic cations, including lanthanides. On the other hand the ^{177}Lu is a β^- emitter of moderate radiation energies and a half-life of about one week. These properties make it attractive for internal radiotherapy. It can be produced in the nuclear reactor very effectively due to the high cross-sections for neutrons. The goal of our work was to develop kit for EDTMP labeling with ^{177}Lu produced in the low/medium flux research reactors starting either from natural Lu or ^{176}Lu enriched targets (and with a broad range of specific activities) which could be used for bone pain palliation in IAEA member states, where ^{153}Sm is not easily available. **Materials and Methods.** The formulation of freeze dried kit containing mixed Ca-Na salt of EDTMP (IAE Polatom, Poland) starting from 35 mg of pharmaceutically characterized EDTMP was developed and verified for labeling yield using lutetium chloride, LuCl_3 in diluted HCl (58 μg , 145 μg , 290 μg and 1300 μg Lu) with trace quantity of ^{177}Lu (IAE Polatom, Poland). The content of the kit was incubated for 30 min at RT. Radiochemical purity RCP was checked using ITLC-SA and water-methanol-25% ammonia 50/50/2 v.v. Test for sterility and bacterial endotoxines were performed routinely. **Results and Conclusions.** High RCP over 99% was obtained when EDTMP : Lu molar ratio varied from 232,5 to 10,3. At lower specific activity of ^{177}Lu the turbidity of radiolabelling mixture was observed which disappeared after incubation at elevated temperature 80°C. For the preparation of a single patient dose of ^{177}Lu -EDTMP with 3.7 GBq radioactivity the specific activity of ^{177}Lu should not be less 3.7 GBq/mg Lu, which should be possible in most of nuclear reactors. Experimental data confirmed efficacy of such developed radiopharmaceutical grade ^{177}Lu -EDTMP in pre-clinical evaluation. The kits were delivered to several IAEA member states for early phase clinical trials. **Acknowledgement:** This project was carried out under the IAEA CRP F22042 "Development of therapeutic radiopharmaceuticals based on ^{177}Lu for radionuclide therapy".

P105

Effect of hydroxyl radical scavengers on the radiochemical stability of [¹⁸F]FDG

I. Józszai, M. Svidró, N. Pótári, P. Mikecz, L. Galuska; Institute of Nuclear Medicine, University of Debrecen, Debrecen, HUNGARY.

Aim: The radiochemical purity of [¹⁸F]FDG at high radioactive concentrations decreases in time rapidly due to active species formed during the radiolysis of water. In this study we intended to clarify the effect of selective scavengers of hydroxyl radicals and hydrated electrons on the stability of [¹⁸F]FDG. Our goal was also to examine the stabilization effect of various salts, B-vitamins, sugars and amino acids, which are effective hydroxyl radical scavengers. **Materials & methods:** We studied the impact of stabilizers using 50-100 µL of samples of [¹⁸F]FDG treated with reagents to the concentrations of 50 mmol/L. The initial radioactivity concentrations of samples were approximately 2 GBq/ml. Both treated and untreated [¹⁸F]FDG samples were stored at room temperature (25°C). Stability was tested by analyzing the samples at appropriate time intervals. We determined the radiochemical purity of [¹⁸F]FDG samples by thin layer chromatography method: Merck TLC Silica gel 60, acetonitrile/water 95/5V/V%, ¹⁸F R_F=0, [¹⁸F]FDG R_F=0.45, Acetyl-[¹⁸F]FDG R_F=0.65. **Results:** We found that the radiochemical purity of the untreated [¹⁸F]FDG sample after 210 minutes decreased to 94.70%. In the presence of ammonium formate (selective hydroxyl radical scavenger) and sodium nitrate (selective scavenger of hydrated electrons) the radiochemical purities were 96,76% and 95,35%, respectively. On the other hand the [¹⁸F]FDG sample treated with the mixture of formate and nitrate had a purity of 96,13%. Consequently, selective hydroxyl radical scavengers are the most effective stabilizers for [¹⁸F]FDG. We also investigated the relationship between the effectiveness of stabilizers and the rate constants of their reactions with hydroxyl radicals (k_{OH}). We found that the purity of samples treated with selective OH scavengers, namely with potassium iodide (k_{OH}: 1.1·10¹⁰ L·mol⁻¹·s⁻¹), ethanol (k_{OH}: 1.9·10⁹ L·mol⁻¹·s⁻¹) and sodium acetate (k_{OH}: 7.4·10⁷ L·mol⁻¹·s⁻¹) were 98,90%, 98,74% and 97,96%, respectively. Consequently, the higher the k_{OH} of the stabilizer the more effective for stabilizing [¹⁸F]FDG. In addition, we found that several OH radical scavengers effectively suppress the radiolytic decomposition of [¹⁸F]FDG. For instance, the purity of samples treated with glucose, thiamine and methionine decreased with 1,5%. **Conclusion:** Selective OH scavengers with high k_{OH} should be chosen to effectively stabilize [¹⁸F]FDG against radiolysis. Among the examined stabilizers glucose could be ideal, as it meets the above mentioned requirements and there is no need for a new analytical method for its quantification, since the HPLC method recommended by the Ph.Eur.6.2 for the determination of radiochemical purity of [¹⁸F]FDG can be used for this purpose.

P106

Biological Behavior in vitro of Alpha-Fetoprotein and its sub domain labeled by ^{99m}Tc

V. N. Korsunsky, O. Klementyeva, A. Bruskin, E. Zhilina, O. Egorov, E. Rabinovich, V. Oschepkov, S. Rodionov; A.I. Burnazian Federal Medical Biophysical Center, Moscow, RUSSIAN FEDERATION.

Introduction Human alpha-fetoprotein (AFP), a tumor-associated foetal glycoprotein of 70 kDa, has been recognized for long time as a clinical marker for both foetal distresses as well as for some types of human tumors. It was postulated that growth of some tumor cells occurs, among others, through the interaction of AFP with cell surface receptors. Because breast adenocarcinoma expresses receptors for AFP, we studied ^{99m}Tc radiolabeled AFP and its sub domain (AFP-D) as agents to detect breast cancer. The aim of this work was to evaluate the accumulation and internalization radiolabeled AFP and its sub domain in tumor cells in vitro. **Materials and Methods** Labeling yields of ^{99m}Tc-AFP and ^{99m}Tc-AFP-D >90% were reached. In vitro experiments were carried out with estrogen receptor positive MCF-7 human breast cancer cells. The cell uptake was calculated as percentage of the activity counted in the flasks containing cells relative to the total activity. Studies of internalization were performed as described in (1). The efflux of radioactivity from the cells was determined. The cells were incubated for 60 min to allow cell uptake of tracers to reach a maximal level. The radioactive medium removed and then fresh medium was added to the cells for re-incubation. The cell uptake was determined once again at the end of re-incubation. The cell efflux was calculated as difference of the total activity (cells and medium) and activity in the flasks containing cells (after subtracting the absorbed activity). **Results** Accumulation of ^{99m}Tc-AFP as well as ^{99m}Tc-AFP-D characterized by fast dynamics, which is typical for receptor-specific radiopharmaceuticals. The maximal accumulation in the cells was observed after 60 min from the beginning of incubation. The accumulation of ^{99m}Tc-AFP was about 4.5 % per million cells and for ^{99m}Tc-AFP-D this value was about 3.0% per million cells. In our experiments, we found rapid internalization of the surface-bound ^{99m}Tc-AFP-D into MCF 7 cells. It sharply increased during the first 30 min, reaching its maximal internalization levels of 80%. More than slow internalization of ^{99m}Tc-AFP explained large size of the molecule. This internalization was about 50% during the first 60 min and then slowed to 70%. The levels of internalized activity for both compounds remained constant for at least 2 h. It is shown that cell efflux does not exceed 30% after 2.0 h re-incubation for both complexes. 1. Garcia Garayoa E, Allemann-Tannahill L, et al. *Nucl Med Biol.* 2001;28:75-84.

P107

Identification and quantitation of new chemical impurities in L-[¹¹C-methyl]methionin

D. Szikra¹, I. Józszai¹, T. Miklovicz¹, S. Kéki², L. Galuska¹, P. Mikecz¹; ¹Institute of Nuclear Medicine, Debrecen, HUNGARY, ²University of Debrecen, Institute of Applied Chemistry, Debrecen, HUNGARY.

Objectives: Besides identification- and radiochemical purity confirmation, the chemical impurities has to be determined in L-[¹¹C-methyl]methionin preparations before release, according to PhEur 5.5. We have observed the appearance of an unknown impurity during the chromatographic quality control of L-[¹¹C-methyl]methionine injection, which inhibited the quantitation of the L-homocysteine content. We had to identify this impurity, and modify the HPLC method, in order to be able to quantitate the specified chemical impurities. **Materials and methods:** L-[¹¹C-methyl]methionin was prepared by the methylation of L-homocysteine using [¹¹C]-methyl-iodide in the presence of KF/Al₂O₃ catalyst, as was described earlier by Smítz et al.

and more recently by Mitterhauser et al.. In the beginning for quality control we used Macherey-Nagel Nucleodur C18 Pyramid (5 µm, 4,5x250mm) column with KH₂PO₄ eluent (1,4 g/L, pH=3,3).. When problems had arisen with this method, we switched to Lichrospher 100 RP-18 column with the same eluent. For determination of iodide ions in the product on this latter column the composition of eluent had to be modified by adding 5 % methanol and 0,25nmol tetrabutyl ammonium hydroxide. UV detection was performed on 225 nm in every case. **Results:** The impurity coeluting with homocysteine was identified as iodide ion, formed during the reactions of methyl iodide. We have developed a chromatographic separation for the quantitation of the iodide content, based on the application of an ion-pair reagent. The iodide content of the product was found to be 0,2-2 microgram/ml. The method for amino acid determination was altered in order to eliminate the influence of the iodide ions. On a Lichrospher RP-18 column the iodide is not retained, so it does not disturb the quantitation of the amino acids. The application of this new method revealed the presence of an other chemical impurity, identified as L-homocysteine by mass spectrometry. We have observed the slow oxidation of L-homocysteine to L-homocystine probably by dissolved oxygen in physiological saline solution. **Conclusions:** Our result has shown that in C-11 methylation reaction a few microgram iodide can appear, especially, if the product is not purified by HPLC. The appearance of homocystine in the reaction mixture did not influence the radiochemical yield or the purity of the L-[¹¹C-methyl]methionin.

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Influence of ⁹⁹Tc in the Preparation of ^{99m}Tc Radiopharmaceuticals.

N. Urbano, S. Modoni; Azienda Ospedaliero-Universitaria Ospedali Riuniti, Foggia, ITALY.

Due to the particular branching decay of ⁹⁹Mo, the isomer ^{99m}Tc (T_{1/2}= 2.1·10⁵ yrs, E_βmax= 294 keV) is always present in ⁹⁹Mo/^{99m}Tc generator elution. **Aim** of this work was to: 1) measure ⁹⁹Tc-^{99m}Tc ratio in sodium pertechnetate obtained from two kind of generators; 2) evaluate ⁹⁹Tc influence on radiolabelling yield of ^{99m}Tc-radiopharmaceuticals commonly used in Nuclear Medicine units. **Materials and Methods.** Fifty-seven ⁹⁹Mo/^{99m}Tc wet column generators (thirty loaded with 17.20 GBq and twenty-seven loaded with 10.75 GBq at calibration, respectively) were evaluated over a period of 9 months. From each generator we analyzed the following elutions: A) immediately after generator delivery (1st elution); B) 24 hrs after 1st elution; C) more than 72 hrs after the previous elution. In each elution, ⁹⁹Tc/^{99m}Tc ratio was measured by inductively coupled plasma mass spectrometry (ICP-MS). Obtained ratios were also compared with the respective theoretical values. Each kind of elution was used for the labelling of different pharmaceutical kits (DTPA, HmPAO, DMSA, ECD, Leukoscan, MIBI, MDP, TTR, MAG3, albumin colloids). **Results.** Specific activities (GBq/mL, ±sd) of the eluates from 17.2 GBq generators were: 4.7 ± 0.0004 (A), 3.5 ± 0.08 (B) and 0.54 ± 0.26 (C). Specific activities from 10.75 GBq generators were: 2.1 ± 0.04 (A), 1.7 ± 0.04 (B) and 0.51 ± 0.29 (C). ⁹⁹Tc/^{99m}Tc ratio, determined by ICP-MS, was: 6.28±0.2 (A), 2.1 ± 0.13 (B) and 34.9 ± 21.6 (C) for 17.20 GBq generators; 11.34 ± 0.33 (A), 2.22±0.14 (B) and 17.64 ± 5.45 (C) for 10.75 GBq generators. These results correlated with theoretical ratios values. All radiolabelling yields of ^{99m}Tc radiopharmaceuticals tested resulted above the limit specified by respective manufacturers, even with the greatest ⁹⁹Tc/^{99m}Tc ratio (34.9 ± 21.6) used. HMPAO prepared with the first elution did not result in substandard quality. **Conclusions.** The ⁹⁹Tc/^{99m}Tc ratio is highly dependent on the time elapsed since the previous elution. Nevertheless, radiolabelling yields did not seem influenced by ⁹⁹Tc/^{99m}Tc ratios evaluated, even if further studies are needed to evaluate ⁹⁹Tc contribution to radiation dose to the patient.

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Reliability enhancement and higher production on IBA PET cyclotron

J. Geets, E. Kral, M. Ghyoot; Ion Beam Application, Louvain la Neuve, BELGIUM.

Objectives: To reply to the strong demand of F-18 radio-tracer in PET nuclear medicine and to enhance reliability of cyclotron produced radioisotopes, IBA has finished a development program on the Cyclone® 18 PET cyclotron with the aim of increasing beam current and reliability. **Methods:** This contribution will show the latest results that have been achieved on the IBA Cyclone® 18. A new central region was designed to host two proton ion sources (Cyclone® TWIN) in the cyclotron in order to achieve higher reliability and reduce unexpected downtime of operation especially for commercial FDG suppliers. Doubling the extracted beam current from 80µA to 150µA has been done by developing a new RF amplifier of 16kW and by modification of the central region and ion source. **Results:** The new ion source improves lifetime and have faster maintenance. The stripper system has been reviewed to increase the foil lifetime and to make its replacement easier with a significant maintenance dose reduction. The beam current upgrade is proposed as 'factory upgrade' but was also achieved on multiple machines in the field. The double proton sources (TWIN) has strongly increased uptime and production reliability on Customer's sites, the concept was patented. The Twin proton source is now available on the Cyclone®11 too. **Conclusions:** The latests development in PET cyclotron improved the production capacity from 10 to 18Ci of F-18 in two hours in a reliable manner with both maintenance time and human dose reduction.

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Ga-68 labeling of DOTA coupled peptides: our experience of nearly four years of routine use

M. Aurilio, E. Squame, L. D'Ambrosio, A. Bartiromo, L. Aloj, S. Lastoria; AF Medicina Nucleare, Istituto Nazionale Tumori, Fondazione "G. Pascale", Napoli, ITALY.

Three 1.1 GBq ⁶⁸Ge/⁶⁸Ga generators (Cyclotron Co., Obninsk, Russian Federation) were utilized in our department from June 2006 to December 2009. Five hundred labeling runs were carried out with the use of a manual labeling module, using a well established open pot labeling procedure. All the ⁶⁸Ge/⁶⁸Ga generators employed are based on a TiO₂ stationary phase and are eluted with 7mL 0.1N HCl. The first and third generator utilized performed well within the manufacturer's specifications: elution yields ~ 60%, radiochemical yield ~ 65% and ⁶⁸Ge

breakthrough <0.01%. When utilizing the second generator, elution yields were in the 60% range, however the radiochemical yield decreased sharply over the first five months of use and 68Ge breakthrough values as high as 0.02% were observed. In typical use in our department, the 68Ge/68Ga generator is eluted 5/6 times a week for production of Ga-68 labeled peptides. When preparing 68Ga-DOTATATE, the peptide most utilized, final yield of the product (end of synthesis) ranged from 18 to 466 MBq, average 157MBq, total synthesis time 20 min. This overall yield was highly generator dependent with the first generator we used performing better than the others. Generator n. 1 and n. 3 were in service for well over 12 months each. Generator n. 2 was replaced after 7 months of use. 68Ga-DOTATATE yields per labeling were 175 ± 99 MBq (mean ± SD, range 48-466 MBq) for generator n.1, 158 ± 41 MBq (mean ± SD, range 40-444 MBq) for generator n. 2 and 141 ± 90 MBq (mean ± SD, range 18-459 MBq) for generator n. 3. We are currently on our fourth generator and are experiencing similar problems as with generator n. 2 in that after only three months of use the overall 68Ga yield is 36% lower than expected. Employing this type of commercially available TIO₂-based 68Ge/68Ga generator, we have been able to label 7 different DOTA coupled peptides in high yield. Our experience indicates that the labeling method used is generally applicable with minor modifications to all DOTA coupled peptides. We have found erratic behavior of the generators used thus far with consequent high variability in overall yields from generator to generator.

P111

Preliminary in vivo study on ³²P-chromic phosphate-poly (L-lactic) acid seeds in experimental mice

L. Liu, J. Sun, H. Gao, Z. Yang, Q. Wu, P. Huang; Southeast University, Nanjing, CHINA.

Objective Targeted positioning is one of the important characteristics of radionuclide brachytherapy. This study was to investigate the feasibility of preparation of ³²P-chromic phosphate (CP) with polymer materials poly (L-lactic) acid (PLLA) seed and to observe its in vivo degradation and metabolism in experimental mice. **Methods** ³²P-CP-PLLA seeds (with radioactivity of 20.44 - 25.14 kBq) were implanted into 72 KM mice through laparotomy or percutaneous puncture to the liver, abdominal cavity or limb muscles. The experimental mice were executed within 30 days at different time points. The seeds were taken out. ³²P radioactive counting rate (min⁻¹) in main organs was determined and the percentage of injection dosage in one gram tissue (%ID/g) was calculated. The morphological change of seeds was observed by electron microscopy scanning. The seeds were also implanted into the liver of five SD rats bred in metabolic cage, the radioactive counting rate in 24 h feces and urine was determined and the 30d ³²P excretion rate was also calculated. **Results** The biodistribution in KM mice revealed no displacement of seeds occurred. The released radioactivity of ³²P in main organs or tissues was slightly higher than that of background level. The culminated counting rate in organs or tissues within 30 days changed in different phases: the aggregated uptake in liver was very low during 1-5 d, slightly increased during 6-10 d, decreased during 11-20 d and increased again during 21-25 d to reach its peak value, and then slightly decreased during 26-30 d; the changes in muscle were similar to those in liver but the peak appeared earlier (15 d) with relatively lower value. In abdominal cavity group, the uptake value in feces and urine appeared on 16 d and 19 d, the rates of whole 30-day excretion were 4.08% and 1.33%, respectively. **Conclusions** ³²P-CP-PLLA seeds can be newly prepared implants for the potential treatment of malignant tumor. The seeds remained inside the implantation organs with slowly phased degradation, excreting through feces and urine different from colloid implantation with high liver intake. ³²P-CP-PLLA seeds presented fairly stability and targeting orientation.

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Internal Solid Scintillator - The New Dimension in RadioHPLC.

H. J. Machulla, N. Malik, F. Arndt, T. Kull, B. Zlatopolskiy, C. Solbach, S. N. Reske; Clinic for Nuclear Medicine, Ulm University, Ulm, GERMANY.

Aim. Metabolic studies directly depend on the availability of tracer labelled with PET radionuclides and compounds with the "traditional" radionuclides as carbon-14 and tritium. On-line detection of both β⁺/β⁻ emitting radionuclides is highly desirable for HPLC analytic. Since special Li-glasses (GS1) are available for use as internal solid scintillators. The aim of this work was to evaluate the applicability of that type of detector in case of metabolites labelled with nitrogen-13, carbon-14 and tritium as well as in dual isotope studies. Furthermore, the detection limits of these radionuclides should be determined. **Materials and Methods.** For calibration and testing a HPLC system (Dionex) was used with a Ramona as β-detector (Raytest, Germany) in line. For calibration, ¹⁴C-aspartic acid (3.7 MBq/mL) and ³H-acetic acid (185 MBq/mL) were used. For analysis of ¹⁴C-labelled and ³H-labelled amino acids, SCX Partisil anion exchange column was used. ¹⁴C-proline, ¹⁴C-glutamic acid, ¹⁴C-aspartic acid, ¹⁴C-glutamine, ¹⁴C-alanine, ¹⁴C-urea (37 MBq/mL), ³H-Glutamic acid, and ³H-Alanine were used for analysis. Glutamic acid, glutamine and alanine labeled with nitrogen-13 were separated similarly. For simulation of dual isotope studies, a mixture of ¹³N- and ¹⁴C-aminoacids was analysed by the same HPLC separation. **Results and Discussion.** With Ramona as the on-line β-detector, radio-HPLC was applied for quality control of commercially available ¹⁴C- and ³H-labelled compounds. Although certified with a purity of 99%, ¹⁴C-glutamic acid, ¹⁴C-aspartic acid and ¹⁴C-proline showed impurities of 20%, 10% and 72%, respectively. Calibration was carried out for ¹³N with ¹³NH₃ (linear response interval was 0.7-10 kBq). A good recognition of an activity peak was possible at 40 Bq for ¹³N and ¹⁴C and 5 kBq for ³H. Analysis of a mixture of ¹³N and ¹⁴C amino acids was performed by measuring the mixture. In dual isotope studies with ¹³N- and ¹⁴C amino acids, the mixture of β⁻ and β⁺-emitters was registered and after decay of ¹³N analysis was repeated for registration of ¹⁴C that type of radiochemical standard approach allowed to apply and detect even low activities of ¹⁴C i.e. 40 Bq. **Conclusion.** Detection of β⁺/β⁻ by Ramona as an on-line detector in radio-HPLC under typical flow conditions performed with a high sensitivity substituting the need of final liquid scintillation counting. For biological application, purity of commercially obtained ¹⁴C- and ³H-compounds must be checked critically.

P113

Study on Pharmacokinetics and acute toxicity of hTERT antisense oligonucleotide molecular probe

R. Wang, M. Liu, C. Zhang, P. Yan, M. Yu, Y. Cui; Department of Nuclear Medicine, Peking University First Hospital, Beijing, CHINA.

Objective To study the pharmacokinetics and acute toxicity of human telomerase reverse transcriptase mRNA antisense oligonucleotide molecular probe labeled with technetium-99m (^{99m}Tc-hTERT ASON). **Methods.** ^{99m}Tc-hTERT ASON was prepared. The biodistribution, pharmacokinetics, and the acute toxicity test of ^{99m}Tc-hTERT mRNA ASON were performed. **Results:** The labeling efficiencies of ^{99m}Tc-hTERT mRNA ASON reached (76±5)%, the specific activity was up to 1,850 kBq/μg, and the radiochemical purity was above 96%. ^{99m}Tc-hTERT ASON accumulated mainly in liver and kidney. Radioactivity counts per minute (cpm) versus time profiles for ^{99m}Tc-hTERT ASON were biphasic, indicative of a three-compartment model. The pharmacokinetics parameters of half-life of distribution (T_{1/2d}), the half-life of elimination (T_{1/2e}), the total apparent volume of distribution (Vd) and the total rate of clearance (CL) were 2.04 min, 74.94 min, 969.66 ml, 28.85 ml/min respectively. Kinetic formula of function relationship of drug concentration in central compartment (C) vs time (t) as follow: C_t=Axe^{-αt}+Bxe^{-βt}=2.56×10⁶xe^{-20.987t}+0.69×10⁶xe^{-1.785t}. All KM mice were present well after injection of high dose of ^{99m}Tc-hTERT mRNA ASON. **Conclusion:** These results demonstrated widespread tissue availability of ^{99m}Tc-hTERT ASON and suggested its development as a potential tumor imaging agent. **Key words:** Human telomerase reverse transcriptase; Antisense oligonucleotide; Biodistribution; Pharmacokinetics; Acute toxicity test

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[¹⁸F]-FDG for imaging of brain metabolism in animal models of human disease: a comparison between intraperitoneal and intravenous injection

J. Doorduyn, H. C. Klein, R. A. J. O. Dierckx, E. F. J. de Vries; University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS.

Aim: Small animal PET with [¹⁸F]-FDG allows for imaging of brain metabolism in animal models of human disease. For animal imaging, anaesthesia is used during the PET scan to prevent movement. A major disadvantage of anaesthesia is that brain metabolism is decreased, which can interfere with the imaging results. To overcome the influence of anaesthesia on brain metabolism, [¹⁸F]-FDG can be injected intraperitoneally in awake animals. After distribution of [¹⁸F]-FDG, the animal can be anaesthetized for small animal PET imaging and brain metabolism during the awake period can be determined. In the present study, the feasibility of intraperitoneal injection of [¹⁸F]-FDG for imaging of brain metabolism in awake animals was determined in a rat model of herpes encephalitis. **Material and methods:** Rats were intranasally inoculated with 1x10⁷ PFU of the herpes simplex virus type-1 (HSE) or with PBS (CNTRL). At day 7 after inoculation a [¹⁸F]-FDG small animal PET scan was performed. In one group (IV), rats were anaesthetized and positioned in the small animal PET scanner, after which a 60 minute scan was started simultaneously with the intravenous injection of [¹⁸F]-FDG. In the other group (IP), [¹⁸F]-FDG was injected intraperitoneally in awake rats, after which they were placed in a stimulus-free environment. Rats were anaesthetized and scanned for 30 minutes, at 60 minutes post-injection. Two rats were anaesthetized and injected intraperitoneally with [¹⁸F]-FDG simultaneously with the start of a 90 minute scan. **Results:** After intravenous injection, [¹⁸F]-FDG was rapidly taken up by the brain and remained stable over time, from 10 to 60 minutes post-injection. A significantly higher brain uptake of [¹⁸F]-FDG (SUV) (114%, p=0.001) was found in HSE-IV rats, when compared to CNTRL-IV rats. Intraperitoneal injection resulted in a slower [¹⁸F]-FDG brain uptake when compared to intravenous injection and remained stable over time from 60 to 90 minutes post-injection. Brain uptake in IP rats was significantly higher than in IV rats (on average 114%, p<0.05). However, in contrast to IV rats, no significant difference was found between HSE-IP rats and CNTRL-IP rats (37% higher in HSE-IP, p=0.05). **Conclusion:** Intraperitoneal injection of [¹⁸F]-FDG appears not to be suitable for imaging of brain metabolism in animal models of human disease, like herpes encephalitis. Basal brain metabolism of awake rats may have interfered with the disease associated changes in brain metabolism. However, intraperitoneal injection of [¹⁸F]-FDG in awake animals may still be suitable for imaging of brain activation during behavioural tasks.

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Synthesis of 15-(4-[¹³¹I]-iodophenyl)pentadecanoic Acid (IPPA) via Tin-Precursor using Chloramine-T as an Oxidant

E. Al-Momani, B. Zlatopolskiy, C. Solbach, H. Machulla, S. N. Reske; Clinic for Nuclear Medicine, Ulm University, Ulm, GERMANY.

Aim. Radioiodinated 15-(4-iodophenyl)pentadecanoic acid (¹p-IPPA) is known to be well suited for the evaluation of the metabolic fate of fatty acids. Various radioiodination procedures were published in the past but all they suffer from disadvantages such as long reaction times, the need for high reaction temperatures and/or require use of very toxic thallium or mercury compounds as precursors for radioiodination. However, a radioiodination was to be developed by combining the advantages of chloramine-T method with the low toxicity of tin precursors. **Materials and Methods.** As a precursor for the radioiodination, 15-(4-tributylstannylphenyl)pentadecanoic acid was synthesized by sequence of steps starting with 15-(4-iodophenyl)pentadecanoic acid by means of a palladium-catalysed cross-coupling with hexa-n-butyliditin after esterification into methyl ester, followed by basic hydrolysis, resulting in the known tin compound. According to Hunter-Greenwood method, the radioiodination was performed using chloramine-T and non-carrier-added Na¹³¹I to generate electrophilic iodine for labeling of the tin compound in presence of acetic acid and ethanol. **Results.** [¹³¹I]-p-IPPA was obtained from the corresponding tin precursor and [¹³¹I]-iodide with chloramine-T as an oxidant in a high radiochemical yield (89.6±1.4 %) and radiochemical purity (>99 %), when performing the labeling at room temperature within a reaction time of 3 min. The study of dependences on temperature (0 °C, 20 °C and 80 °C) and reaction time (1, 3, 5, 10 and 30 min) showed no yield increase but the formation of side products at higher temperatures and with prolongation of the reaction time. **Conclusion.** By combining the advantages of tin compounds as a labeling precursor with those of the radioiodination method by using chloramine-T as an oxidizing agent, a fast method was developed for the radiosynthesis of 15-(4-iodophenyl)pentadecanoic acid (p-IPPA) with an isolated radiochemical yield of more than >80 % within 25 min including HPLC purification and formulation. Moreover, another attractive aspect is the low toxicity of the tin precursor when compared to mercury and thallium used in the majority of the previous labeling procedures.

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Suppression of radiolysis on the FASTlab 18F-FDG synthesizer by the addition of ethanol.

M. L. Olesen, H. Hjortsballe Salomonsen, J. H. Dam, K. Nægren; Odense University Hospital, Odense, DENMARK.

The high clinical demand of 18F-FDG has motivated development of new targetry and more efficient synthesis devices. As a result, production of several hundreds of GBq of 18F-FDG in one synthesis batch is often feasible. These high amounts of radioactivity can only be handled by a fully automated synthesis device in a heavily shielded environment. Radiolysis of the product during and after synthesis also becomes a significant problem when working with these high amounts of radioactivity. The aim of this study was to investigate the effect of the radiolysis scavenger ethanol on the radiochemical purity and the shelf-life of 18F-FDG produced in batches of more than 200 GBq. 18F-Fluoride was produced by simultaneous irradiation of two niobium targets at 16.5 MeV and 60 μ A for up to 3 hours. 18F-FDG was subsequently produced on a GE FASTlab device with or without addition of ethanol in various amounts up to 0.5% v/v to the sterile water in the FASTlab system. The sterile water is used to rinse the cassette, to transfer the reaction solution between the compartments of the cassette, and finally to recover 18F-FDG from the cassette to the product vial. Several batches of 200-220 GBq of 18F-FDG were produced and the radiochemical purity of the product was measured at intervals from end of synthesis (EOS) up to 10 hours after EOS. Without addition of ethanol to the sterile water, the radiochemical purity at EOS was 78%. With addition of 0.5% v/v to the sterile water, the radiochemical purity at EOS was higher than 99%, decreasing to 96.5-98.0% at 10 hours after EOS. The addition of ethanol also had a positive effect on the radiochemical yield of 18F-FDG obtained by the FASTlab device. Without ethanol, the yield was 60-75% (not decay corrected, ndc), and with ethanol the yield was 71-75% (ndc). In conclusion, we found that it is possible to reduce radiolysis of 18F-FDG to acceptable levels during the shelf-life of 18F-FDG by addition of ethanol (0.5% v/v) to the sterile water in the FASTlab system. The addition of ethanol also had a positive stabilizing effect on the radiochemical yield of 18F-FDG.

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68Ga-DOTATOC: Experiences in the routine application of the Obninsk 68Ge/68Ga-generator and the EZAG ModularLab synthesis module in Basel

A. Bauman, F. Forrer, M. Fani, H. Maecke, T. L. Mindt; Clinic of Radiology and Nuclear Medicine, Basel, SWITZERLAND.

Aim: The imaging of somatostatin receptor expressing tumours with ^{68}Ga -DOTATOC offers advantages over ^{111}In -OctreoscanTM in terms of affinity to sst2 receptor subtype, sensitivity in detection of NET lesions and clinical management [1]. Therefore the positron emitter ^{68}Ga ($t_{1/2}$ =68 min) deserves special attention, also because of its convenient availability from $^{68}\text{Ge}/^{68}\text{Ga}$ generators. The ^{68}Ga -eluates still contain measurable activities of ^{68}Ge ($t_{1/2}$ =270.8 d) and are contaminated with cations. Several strategies have been reported to purify ^{68}Ga -eluates [2, 3]. In Basel, we have been producing ^{68}Ga -DOTATOC for clinical routine application for 9 months using an automated system based on the cationic purification procedure with the newly introduced single-use StrataX-C cartridges. This work describes our practical and clinical experiences. **Materials and Methods:** ^{68}Ga was eluted from an Obninsk 30 mCi generator integrated in a ModularLab automated system (EZAG, Berlin). The synthesis of ^{68}Ga -DOTATOC was performed according to the manufacturer protocol. Aliquots of the generator eluates and samples of the product were analyzed for ^{68}Ge -content (gamma-counter) and residual solvents (GC-MS). **Results:** While we had some synthesis failures in the initial phase using handmade cartridges filled with Bio-Rad resin, the production of ^{68}Ga -DOTATOC has worked reliably since we have changed to the new cartridges. The elution efficiency of the generator at the beginning was ~80% and after 200 days ~65%. Activity is recovered with >95% from the ion exchanger. The ^{68}Ge -content was in a range of $4.86 \times 10^{-7} \pm 2.75 \times 10^{-9}$ % for ^{68}Ga -eluates and $3.82 \times 10^{-5} \pm 3.77 \times 10^{-5}$ % in the product. The radiochemical yield of ^{68}Ga -DOTATOC was 69.2 ± 9.1 % (decay corrected, n=29) with a radiochemical purity of >99%. Residual solvents in the product were within the limits for human use. We examined 62 patients with NET lesions. The injected activity was 100-150 MBq, the uptake time was 30 min prior PET-CT scan. **Conclusions:** The modified setup works both easier and shorter and the use of standardized single-use cartridges results in a more reliable radiotracer production. Compared to the generator-eluate the ^{68}Ge -content in the product was shown to be reduced by a factor 10^{-2} - 10^{-3} . All examined patients showed the expected biodistribution with high sensitivity for sst2-positive tumours. The smallest detected lesion was a lymphnode metastasis of 7 mm diameter. **References:** [1] Buchmann, Eur.J.Nucl.Med.Mol.Imaging 2007; **34**:1617-1626 [2] Zhernosekov, J.Nucl.Med 2007; **48**: 1741-1748 [3] Ocak, Appl.Rad.Isot. 2010; **68**: 297-302

P118

Comparative Evaluation of ^{99m}Tc -labeled DTPA-bis(2-nitroimidazole) and 2-Nitroimidazole for Hypoxia Imaging

A. K. Pandey¹, P. P. Hazari¹, R. Varshney¹, J. K. Uppal¹, R. Patnaik², A. K. Mishra^{1*}; ¹Division Cyclotron and Radiopharmaceutical Sciences, Institute of Nuclear Medicine and Allied Sciences, Delhi, INDIA, ²Institute of Technology, Banaras Hindu University, Varanasi, INDIA.

Aim: Nitroimidazole derivatives are selectively retained in areas of low oxygen tension, and have been used in cancer research to identify and target ischemic cells in solid tumors. Nitroimidazoles are reduced intracellularly in all cells, but in the absence of adequate supplies of oxygen, they undergo further reduction to more reactive products that bind to cell components. The formation of these products is initiated by an enzyme-mediated single-electron reduction of the nitro group to a free radical which is an anion at neutral pH. The reduction pathway can proceed in successive steps past the hydroxylamine derivative to terminate at the relatively inactive amine derivative. DTPA based imaging agents find diverse applications in the field of molecular imaging. The aim of the study was to compare the ^{99m}Tc labeled DTPA-bis(2-nitroimidazole) and 2-nitroimidazole in hypoxia imaging. **Methods:** The desired conjugate (bis-derivative of 2-nitroimidazole) was synthesized by alkylating 2-nitroimidazole with bromoethylamine in presence of catalyst and then reacting it with DTPA anhydride. The purified conjugate was labeled with

^{99m}Tc . The cytotoxicity assay of DTPA-bis(2-nitroimidazole) and 2-nitroimidazole was tested in U87MG cell line and primary cultured hippocampal neurons using MTT assay. Reduced Glutathione assay was carried out and levels of free radicals were measured with nonfluorescent lipophilic DCFH-DA. Cell uptake studies were done and percentage uptake of ^{99m}Tc -labeled compounds were calculated. **Results:** The bis-derivative of 2-nitroimidazole was successfully synthesized with high yield characterised on the basis of spectroscopic techniques. DTPA-bis(2-nitroimidazole) binds with ^{99m}Tc high efficiency at ambient temperature and the radiolabeling efficiency was found to be >95% and the stability in serum indicated that ^{99m}Tc remained bound to the conjugate upto 24h whereas directly labeled ^{99m}Tc -2-nitroimidazole was only stable upto 6h. The estimated IC_{50} was found to be 19.8 μM and 0.22 μM of DTPA-bis(2-nitroimidazole) and 2-nitroimidazole respectively. DTPA-bis(2-nitroimidazole) significantly reduced free radicals as well as reduced glutathione in dose dependent manner which was comparable to 2-nitroimidazole. The cell uptake of ^{99m}Tc -DTPA-bis(2-nitroimidazole) was found to be maximum at 35 min whereas the accumulation of ^{99m}Tc -2-nitroimidazole was maximum at 1h. **Conclusion:** DTPA based 2-nitroimidazole derived imaging agents are of considerable interest in hypoxia imaging because it specifically detects the severely hypoxic viable cells, but not the necrotic cells. Moreover, introduction of polyaminopolycarboxylate based chelating system allows this conjugate to be utilized as a probe for multimodal imaging. **References:** Engelhardt et al. *Journal of Nuclear Medicine* (2002) 43,837-850.

P119

Synthesis and evaluation of the novel F-18 labeled chalcone derivatives for PET imaging

S. Kim¹, H. Kim¹, M. Kinger¹, D. Kim², I. Kim¹, J. Park¹, M. Hur¹, S. Choi¹, S. Yang¹, K. Yu²; ¹Korea Atomic Energy Research Institute, Jeongup, KOREA, REPUBLIC OF, ²Dongguk Univ., Seoul, KOREA, REPUBLIC OF.

Aim : Chalcones (1,3-diaryl-2-propen-1-ones), a naturally occurring flavonoids, have been widely reported to exhibit several biological activities such as brain dysfunction, anticancer and anti inflammation activities. Recent studies showed that radiolabeled chalcone derivatives could be utilized for potent probes for in vivo imaging of beta-amyloids plaques in Alzheimer Disease. We replaced the ring A with furan moiety and introduced the F-18 labeled alkyl chain on the ring B to see the possibility of cancer imaging agent for PET. **Materials & Methods** The tosylated precursor has been synthesized in four steps in 18% yields and reference compound prepared in 9% yields using DAST. The radiolabeling has been done in the presence of Kryptofix-2.2.2 and K_2CO_3 at 85°C for 10 min. The F-18 labeled chalcone has been purified by HPLC (stationary phase: Waters X-terra 5 μm , 250 \times 4.6mm column; mobile phase: $\text{H}_2\text{O}/\text{ACN}(45/55)$ 3ml/min). The cellular uptakes of the F-18 labeled chalcone have been measured on HeLa, C-6, MCF-7 and CT-26. The biodistribution of F-18 labeled chalcone was tested in living balb/c mice. **Results** The F-18 labeled chalcone has been obtained in 6% yields and radiochemical purity was more than 96% after HPLC purification. Two cancer cell lines, HeLa (2.3 %ID at 2 hrs) and MCF-7 (2.8 %ID at 2 hrs), showed significant uptake in a time dependant manner. F-18 labeled chalcone has been identified to be excreted through the kidney from the animal study. **Conclusion** F-18 labeled chalcone showed a possibility as a potent breast and cervix cancer imaging agent. The evaluation of the tumor xenografted nude mice is under process.

P120

Prevision of ^{89}Zr production using the Monte Carlo code FLUKA

A. Infantino¹, G. Cicoria², D. Pancaldi², A. Ciarmatori², S. Boschi², S. Fanti², M. Marengo², D. Mostacci¹; ¹Università di Bologna, Bologna, ITALY, ²University Hospital "S.Orsola-Malpighi", Bologna, ITALY.

Introduction: Zirconium-89 has been proposed for use in nuclear medicine to label monoclonal antibodies as well as to provide the biodistribution of ^{90}Y labeled radiopharmaceuticals. ^{89}Zr ($T_{1/2} = 3.27$ days) is produced by the irradiation of a solid target of Yttrium-89 with protons, according to the $^{89}\text{Y}(p,n)^{89}\text{Zr}$ reaction. In this work we modelled an irradiation line for production of ^{89}Zr using a widely used Monte Carlo code and compare results with experimental findings. **Material and Methods:** The multi-slab target simulated in FLUKA was composed by 25 μm of HAVAR, 1600 μm of He, 500 μm of Aluminium, 150 μm (or 300 μm) of ^{89}Y and a backing of 850 μm of Copper. Simulated beam had an elliptical shape with Gaussian profile on both x and y axis. Cross section of $^{89}\text{Y}(p,n)^{89}\text{Zr}$ reaction was checked in simulations modelling a "stacked foil" target. Experimental irradiations were performed using a 16.5 MeV GE-PETTrace cyclotron. The target is composed from one or two discs of 89-Yttrium ($\phi=14\text{mm}$, depth=0.15mm) placed in a Copper support ($\phi=32\text{mm}$, depth=1mm) with a cavity to host the Yttrium disc. This assembly was covered by an Aluminium degrader ($\phi=32\text{mm}$, depth=0.5mm). **Results and Conclusions:** The results of the simulations showed that the production of ^{89}Zr can be expected with very high radionuclidic purity and a yield of 21 ± 2 MBq/ μAh for the 300 μm thick Yttrium target, in perfect agreement with the analytical model and experimental results. The activation of the foil of Aluminium and Copper is negligible. The cross section obtained with the simulations is in agreement with the literature data. **REFERENCES** [1] Verel I., Visser G., van Dongen G., "The Promise of Immuno-PET in Radioimmunotherapy", *The Journal of Nuclear Medicine*, Vol. 46, No.1 (Suppl), January 2005 pp. 1645-1705 [2] Kandil S., Scholten B., Saleh Z., Youssef A., Qaim S., Coenen H., "A comparative study on the separation of radiozirconium via ion-exchange and solvent extraction techniques, with particular reference to the production of ^{89}Zr and ^{88}Zr in proton induced reactions on yttrium", *Journal of Radioanalytical and Nuclear Chemistry*, Vol. 274, No.1 (2007), pp.45-52

P121

Production and dosimetric aspects of the potent Auger emitter ^{58m}Co for targeted radionuclide therapy of small tumours

H. Thisgaard¹, M. Jensen², D. R. Elema²; ¹Odense PET Centre, Dept. of Nuclear Medicine, Odense University Hospital, Odense, DENMARK, ²Risø National Laboratory for Sustainable Energy, Technical University of Denmark, Roskilde, DENMARK.

Introduction Auger electron emitting radionuclides in cancer therapy offer the opportunity to deliver a high radiation dose to the tumour cells with high radiotoxicity while minimizing toxicity to normal tissue. The Auger emitter ^{58m}Co ($T_{1/2}$: 9.04 h) has previously been identified as a very potent nuclide for targeted radionuclide therapy based on theoretical dosimetry calculations.¹ However in the production of this isotope, the co-production of the long-lived ground state ^{58g}Co ($T_{1/2}$: 70.86 d) is unavoidable and thus, the impact of this γ -emitting impurity should be included in the dosimetric analysis. This critical part has been investigated and a method for producing this potent Auger-emitter with a low-energy cyclotron has been developed. **Materials and methods** The theoretical dosimetry calculations for ^{58m}Co and the unavoidable impurity ^{58g}Co were performed at a subcellular scale as described previously² including calculation of the tumour-to-normal-tissue dose ratios (TNDs) per disintegration. The ^{58m}Co was produced via the $^{58}\text{Fe}(p,n)^{58m}\text{Co}$ nuclear reaction on 5.5 mg highly enriched ^{58}Fe metal electroplated on a silver backing. The target was irradiated with 18 μA for 1 h with 10.1 MeV protons from the GE PETtrace cyclotron at the Hevesy Laboratory and the ^{58m}Co production yield was measured including the radionuclidic impurities. For developing the separation method, produced radio-Cobalt from irradiated ^{58m}Fe was separated from the target material with ^{59}Fe added on an anion exchange column. **Results** 192 ± 8 MBq of ^{58m}Co was produced in the irradiation corresponding to a production yield of 10.7 MBq/ μAh . The activity of ^{58g}Co was measured to be $0.85\% \pm 0.04\%$ of the produced ^{58m}Co activity at the end of bombardment (EOB). Due to this production impurity and because of the ingrowth of the ground state, the TND and the potency of the ^{58m}Co decrease with time after EOB. About 21 hours after EOB, the resulting TND is 50% of the TND of 'pure' ^{58m}Co . In future therapy with ^{58m}Co , preparation and use of the radiopharmaceutical should thus be started immediately after EOB to obtain the best therapeutic results. The radio-Cobalt yields in the separations were measured to be $>97\%$ with no detectable iron contaminations, thus ready for labelling a biovector (e.g. DOTATOC). **Conclusion** ^{58m}Co has been produced with a small PET cyclotron and the impact of the unavoidable radionuclidic impurity ^{58g}Co on the dosimetry has been investigated. 1. Bernhardt P et al., *Acta Oncologica*. 2001;40(5):602–608. 2. Thisgaard H, Jensen M., *Med Phys*. Sep 2008;35(9):3839–3846.

P14 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Radiopharmaceuticals & Radiochemistry & Dosimetry: Radiopharmaceuticals - New

P122

The Comparative Study of BnAO-derivative on Hypoxic Model Imaging and Assess the Effect of Pentoxifylline

C. Hsia¹, F. Huang¹, G. Hung², W. Lin¹, H. Wang³; ¹Institute of Nuclear Energy Research, Tau-Yen, TAIWAN, ²Departments of Nuclear Medicine, Chang-Bing Show Chwan Hospital, Changhua, TAIWAN, ³Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University, Taipei, TAIWAN.

Aim: ^{99m}Tc -BnAO was the first nonnitro-aryl-based radiotracer used for evaluating hypoxic fraction in neoplasm, stroke and myocardium infarction regions. In this study, 3,3,10,10-tetramethyl-1-(2-nitro-1H-imidazo-1-yl)-4,9-diazadodecane-2,11-bionedioxime (BnAO-NI), combined BnAO and 2-nitroimidazole moiety, was compared with BnAO on stroke bearing mice. Pentoxifylline (PTX), a hemorrheologic methylxanthine derivative for improving the peripheral and cerebral microcirculations, was conducted on stroke and tumor bearing mice for evaluating the pharmaceutical's effect in the uptake of ^{99m}Tc -BnAO-NI on hypoxic region. **Materials and Methods:** BnAO-NI was formulated with stannous chloride and buffer to afford kits. After mixing with ^{99m}Tc -pertechnetate, ^{99m}Tc -BnAO-NI could be prepared in formulations achieved high radiochemical purity (98.1%). Cellular uptake assays based on KHT cell under normoxic and hypoxic conditions were performed in an oxygen-controlled CO_2 incubator. Brain stroke mouse model was induced by the electrocautery at the middle cerebral artery on C3H mice. Human breast cancer (MDA-MB-231) cells ($1 \times 10^7/0.1\text{mL}$) were inoculated subcutaneously into the right thigh of nude mice. After intravenous injection of ^{99m}Tc -BnAO-NI or ^{99m}Tc -BnAO into the stroke-bearing mice, SPECT images were acquired and autoradiography was conducted. Parallel studies in the effect of pentoxifylline (100 mg/kg) were injected intraperitoneally prior to ^{99m}Tc -BnAO or ^{99m}Tc -BnAO-NI injection at 15 min in stroke or tumor-bearing mice for comparing target-to-normal (T/N) ratio. **Results:** Cellular uptake assay showed that ^{99m}Tc -BnAO-NI was less selectively retained in hypoxic cells than ^{99m}Tc -BnAO. The hypoxic T/N brain ratios derived from the autoradiograms of the stroke brains were 3.95 ± 0.07 and 6.08 ± 0.10 ($n=3$) at 2 h post injection of ^{99m}Tc -BnAO-NI and ^{99m}Tc -BnAO, respectively. After intraperitoneal treatment of pentoxifylline, the ratios were 3.81 ± 0.08 and 5.18 ± 0.11 ($n=3$), respectively. In tumor-bearing mice model, there was relatively higher uptake of ^{99m}Tc -BnAO-NI in tumor compared to the contralateral thigh. In addition, the tumor uptake of ^{99m}Tc -BnAO-NI had significantly reduced after pentoxifylline treatment. The T/N ratios of ^{99m}Tc -BnAO-NI in pentoxifylline treated group and control groups were 1.95 ± 0.34 and 3.53 ± 0.55 ($n=3$), respectively ($P = 0.01$). **Conclusions:** This study revealed that ^{99m}Tc -BnAO-NI and ^{99m}Tc -BnAO could selectively retain in hypoxic region. ^{99m}Tc -BnAO had higher cellular and brain hypoxic tissue uptake than ^{99m}Tc -BnAO-NI. ^{99m}Tc -BnAO-NI could present the specific pharmaceutical's effect of pentoxifylline in reducing the hypoxic environment on tumor ($P=0.01$). However, it had no apparent usefulness in improving the severity of hypoxia in brain stroke region ($P = 4.66$).

P123

[¹⁸F]-FEAnMGA: an improved PET tracer for extracellular β -glucuronidase (β -GUS)

I. Farinha Antunes¹, H. J. Haisma², P. H. Elsinga¹, R. A. J. O. Dierckx¹, E. F. J. De Vries¹; ¹University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS, ²University Center of Pharmacy, University of Groningen, Groningen, NETHERLANDS.

Aim: To improve the efficacy of glucuronide prodrugs and to stratify patients that are eligible for treatment with these drugs, information about the level of extracellular β -glucuronidase (β -GUS) in a tumor is of utmost importance. Therefore, we developed a PET method for noninvasive

measurement of extracellular β -GUS. Previous studies of our group have shown that the labeled prodrug [¹⁸F]-FEAnGA is a promising PET tracer for imaging of extracellular β -GUS activity. However, [¹⁸F]-FEAnGA showed rapid renal clearance, which resulted in a relatively low tracer uptake in the tumor. To improve the pharmacokinetics of [¹⁸F]-FEAnGA, its more lipophilic methyl ester analog (called [¹⁸F]-FEAnMGA) was prepared. The methyl ester moiety will be hydrolyzed by esterases in plasma, resulting in the in-situ production of the original PET tracer [¹⁸F]-FEAnGA. Since the methyl ester [¹⁸F]-FEAnMGA is anticipated to be much slower cleared from plasma than [¹⁸F]-FEAnGA, its delivery to the tumor and consequently also the retention of radioactivity in the tumor is expected to be increased, resulting in PET images with better quality. **Materials and methods:** [¹⁸F]fluoroethylamine (FEA) was labeled by fluorination of *N*-[2-(toluene-4-sulfonyloxy)ethyl]-phthalimide, followed by deprotection of the amine with hydrazine. [¹⁸F]-FEAnMGA was obtained by alkylation of the O-protected glucuronide methyl ester precursor with [¹⁸F]-FEA, followed by deprotection of the sugar moiety with NaOMe/MeOH. The product was purified by HPLC. The stability of the tracer in PBS was determined by radio-TLC. The conversion of [¹⁸F]-FEAnMGA into [¹⁸F]-FEAnGA by porcine liver esterase (PLE) and, consequently, its cleavage by E. coli β -GUS was measured with UV spectrophotometry and radio-TLC. **Results:** Radiolabeling of the new β -GUS tracer was achieved in 5–18% overall radiochemical yield (corrected for decay, based on [¹⁸F]fluoride) with a total synthesis time of 150 min after HPLC purification. The lipophilicity of [¹⁸F]-FEAnMGA was shown to be about 10-fold higher than the product [¹⁸F]-FEAnGA (log *P* -0.58 ± 0.00002 and -1.61 ± 0.01 , respectively). In vitro, [¹⁸F]-FEAnGA was stable in PBS for 1 h. Preliminary in vitro studies indicated that [¹⁸F]-FEAnMGA is selectively converted into [¹⁸F]-FEAnGA by PLE followed by total cleavage of [¹⁸F]-FEAnGA to [¹⁸F]-FEA by E. coli β -GUS. In addition, the ester [¹⁸F]-FEAnMGA proved not to be a substrate for E.C. β -GUS. **Conclusion:** [¹⁸F]-FEAnMGA was efficiently labeled with fluorine-18 in good yield. Due to the higher lipophilicity of [¹⁸F]-FEAnMGA it is expected that this tracer will have a slower clearance in vivo than the previous tracer [¹⁸F]-FEAnGA and consequently giving better PET images.

P124

In vivo evaluation of carbon-11-labeled N-((S)-1-((S)-methylpiperidin-2-yl)ethyl)acetamide derivatives as a potential radioligands for glycine transporter 1

J. Toyohara¹, M. Sakata¹, K. Ishiwata¹, J. Wu², H. Ohba³, H. Tsukada³, K. Hashimoto²; ¹Tokyo Metropolitan Institute of Gerontology, Tokyo, JAPAN, ²Chiba University Center for Forensic Mental Health, Chiba, JAPAN, ³Hamamatsu Photonics K.K., Shizuoka, JAPAN.

Introduction: Since glycine acts as a co-agonist at the NMDA receptors, glycine transporter 1 (GlyT-1) has been an attractive target in PET studies of recent date. In an effort to develop new GlyT-1 radioligands, we report here the in vivo evaluation of carbon-11-labeled *N*-((S)-1-((S)-1-methylpiperidin-2-yl)ethyl)acetamide derivatives in mice and conscious monkeys. **Methods:** Three ¹¹C-labeled non-sarcosine-based GlyT1 inhibitors, 2-chloro-3-(trifluoromethyl)-*N*-((S)-1-((S)-1-¹¹C)methylpiperidin-2-yl)(thiophen-3-yl)methyl)benzamide ([¹¹C]SA1), *N*-((S)-1-((S)-1-¹¹C)methylpiperidin-2-yl)(phenyl)methyl)thiophene-2-carboxamide ([¹¹C]SA2), and 2-chloro-3-(trifluoromethyl)-*N*-((S)-1-((S)-1-¹¹C)methylpiperidin-2-yl)(phenyl)methyl)benzamide ([¹¹C]SA3) were synthesized by *N*-[¹¹C]methylation of corresponding desmethyl-precursors with [¹¹C]methyl triflate. *IC*₅₀ values of unlabeled compounds were evaluated by [³H]glycine uptake into rat brain synaptosomes. The radiotracer properties were evaluated in mice biodistribution. Effects of receptor blockade were determined by co-injection of the mice with carrier-loading. Metabolic stability was investigated using radio-HPLC. Dynamic PET scans were performed in conscious monkeys with/without a selective sarcosine-based GlyT-1 inhibitor, ALX-5407 (3 mg/kg) treatment. **Results:** *IC*₅₀ values of SA1, SA2, and SA3 were 9.0, 6400, and 39.7 nM, respectively. Most radioactivities in the mouse brain were detected as an unchanged form, although peripherally these compounds were degraded. The regional brain uptake of [¹¹C]SA1 and [¹¹C]SA3 in mice were heterogeneous and consistent with known GlyT-1 distribution: medulla oblongata > cerebellum > cortex. [¹¹C]SA2 showed a low and homogeneous uptake in the mouse brain. Carrier-loading decreased the uptake of [¹¹C]SA1 in GlyT-1 rich regions: medulla oblongata and cerebellum. However, similar reductions were not observed by [¹¹C]SA3. At baseline, radioactivity in the monkey brain peaked at 30–50 min, and then decreased slightly in [¹¹C]SA1, and it increased gradually, and then reached a plateau in [¹¹C]SA2 and [¹¹C]SA3. In [¹¹C]SA1 ($n = 3$), the rank order of standardized uptake value (SUV) at the latter phase (76–93 min) was thalamus (1.8 ± 0.4) > brainstem (1.6 ± 0.4) > cerebellum (1.4 ± 0.3) ~ frontal cortex (1.4 ± 0.3). And the SUVs were decreased at blocking condition in two of three monkeys: brainstem (25%, 19% in each monkey) > thalamus (20%, 11%) ~ cerebellum (19%, 11%) > frontal cortex (10%, 2%). The regional difference of uptake of [¹¹C]SA2 was not clear, and the uptake of [¹¹C]SA3 was clearly increased (about 30% at the latter phase) at the blocking condition. **Conclusion:** The present findings suggest that [¹¹C]SA1 might be a novel useful radioligand for imaging GlyT-1 in the human brain.

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Design and synthesis of novel 68Ga-chelate-conjugated bisphosphonates bone seeking agents for PET.

H. Dozono, J. Suwada, S. Oshikiri, H. Ashino, M. Satake, K. Suzuki, A. Hino, T. Minamizawa; FUJIFILM RI Pharma Co., Ltd., CHIBA, JAPAN.

Objectives: 68Ga is a positron emitter with a short half-life (68 min) which can be produced on-site via a 68Ge/68Ga generator without a cyclotron. We have recently designed and synthesized novel cyclic chelate conjugated bisphosphonates (chelate-BPs) labelled with 68Ga. The aim of this study was to evaluate these 68Ga-chelate-BPs as potential PET tracers for bone metastases. **Materials and Methods:** Chelate-BPs (DOTA-BP and NOTA-BP) were obtained through the deprotection of t-Bu and TBS groups after coupling the cyclic chelators to the bisphosphonate derivatives. Labeling was done by addition of 68GaCl₃ solution (0.1M HCl) eluted from a 68Ge/68Ga generator. Optimum reaction parameters for complex formation were determined by studying the effects of variations in reaction time, temperature, pH and ligand quantities. Labeling efficiency and radiochemical purity were determined by radio TLC and HPLC. Bone affinity in vitro was evaluated by hydroxyapatite binding assays for 14C-pamidronic acid, ^{99m}Tc-MDP and 68Ga-chelate-BPs. Biodistribution and imaging studies for ^{99m}Tc-MDP and 68Ga-chelate-BPs were performed in normal rats. **Results:** The labeled 68Ga-chelate-BPs radiochemical purities were found to be over 95%. In vitro hydroxyapatite assays, chelate-BPs had affinities similar to MDP for hydroxyapatite. In biodistribution studies, 68Ga-NOTA-BP had

faster blood clearance than ^{99m}Tc -MDP and ^{68}Ga -DOTA-BP. Therefore, ^{68}Ga -NOTA-BP exhibited the highest bone-to-blood ratio among the three compounds. In addition, bone structure was clearly visualized by micro PET imaging only 1hr after injection with ^{68}Ga -NOTA-BP radiotracer. **Conclusions:** We have developed a novel ^{68}Ga -NOTA-BP radiotracer with high affinity for bone and high bone-blood ratio. ^{68}Ga -NOTA-BP is thus a promising PET imaging agent candidate for the diagnosis of bone metastases.

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Evaluation of a radiogallium-labeled bifunctional chelate, Ga-DOTA-MN2, for hypoxic tumor imaging

T. Mukai, K. Sano, M. Okada, M. Maeda; Kyushu University, Fukuoka, JAPAN.

Aim: Based on the previous findings obtained by X-ray crystallography of Ga-DOTA chelates and the drug design concept of bifunctional chelates, we successfully designed and synthesized a radiogallium-labeled bifunctional chelate, ^{67}Ga -DOTA-MN2, for hypoxic tumor imaging. As expected, ^{67}Ga -DOTA-MN2 exhibited high stability although two carboxyl groups in the DOTA skeleton were conjugated with metronidazole derivatives. In the present study, we evaluated Ga-DOTA-MN2 as a nuclear imaging probe for hypoxic tumors. **Materials & Methods:** Coupling of DOTA-bis(*tert*-butyl)ester with 1-(2-aminoethyl)-2-methyl-5-nitroimidazole dihydrochloride, followed by deprotection, afforded DOTA-MN2. ^{67}Ga -labeling was carried out by the reaction of DOTA-MN2 with $^{67}\text{GaCl}_3$ under microwave irradiation. To evaluate the pharmacokinetics, ^{67}Ga -DOTA-MN2 was injected intravenously into FM3A tumor-bearing mice. Furthermore, the intratumoral distribution of ^{67}Ga -DOTA-MN2 was examined by the autoradiographic study, and then the same section was subjected to immunostaining for pimonidazole, which is known as a hypoxic marker. **Results:** After purification by HPLC, ^{67}Ga -DOTA-MN2 was obtained with high radiochemical purity (>97%). Radiochemical yields of the final formulated product were >85%. In biodistribution experiments in FM3A tumor-bearing mice, ^{67}Ga -DOTA-MN2 showed rapid blood clearance and low tissue accumulations of the radioactivity. At 24 h, 57% and 10% of the injected radioactivity of ^{67}Ga -DOTA-MN2 were recovered in the urine and feces, respectively. The tumor accumulation of ^{67}Ga -DOTA-MN2 was significantly higher than that of ^{67}Ga -DOTA, and its intratumoral distribution coincided with the hypoxic regions. These results indicate the significant recognition of the hypoxic regions with metronidazole structural units of ^{67}Ga -DOTA-MN2. **Conclusion:** ^{67}Ga -DOTA-MN2 showed not only a significant accumulation in the hypoxic regions of the tumor but also rapid blood clearance and low accumulations in nontarget tissues of the radioactivity, demonstrating its potential usefulness as a nuclear imaging probe for hypoxic tumors. Also, these results suggest that two functional moieties such as a metronidazole in this study can be conjugated to radiogallium-DOTA chelate without reducing the complex stability. The present findings provide useful information about the chemical design of radiogallium-labeled radiopharmaceuticals for SPECT and PET studies.

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Development of radiobromine-labeled 5-bromo-4'-thio-2'-deoxyuridine as a tumor proliferation imaging agent.

Y. Kiyono¹, K. Sano¹, Y. Nakayama¹, T. Mori¹, J. Toyohara², M. M. Ernesto¹, K. S. Mandap¹, T. Asai¹, H. Okazawa¹, Y. Fujibayashi³; ¹University of Fukui, Fukui, JAPAN, ²Tokyo Metropolitan Institute of Gerontology, Tokyo, JAPAN, ³National Institute of Radiological Sciences, Chiba, JAPAN.

Aim: The aim of this study was to synthesize and evaluate radiobromine-labeled 5-bromo-4'-thio-2'-deoxyuridine (BTdU) as a tumor proliferation imaging. **Methods:** Although Br-76 is suitable for imaging, in this study Br-77 was used because long-half life was convenient for basic experiments. Br-77 was produced with Siemens cyclotron (Eclips RD/HP) and extracted with a thermal diffusion method. The radiolabeling of BTdU with Br-77 was achieved by a destannylation reaction of tributylstannyl precursor. Using L-M cells and thymidine kinase deficient mutant L-M(TK-) cells, cell uptake and DNA incorporation experiments were performed *in vitro*. *In vivo* biodistribution experiments in normal mice and L-M cells-bearing mice were also carried out. **Results:** The radiochemical yield of ^{77}Br -BTdU was about 30% and the radiochemical purity was more than 99%. The uptake of ^{77}Br -BTdU was increased with time in L-M cells (8.4 ± 0.3 %ID/g protein at 30 min, 43 ± 3.6 %ID/g protein at 180 min). On the other hand, there was little uptake of ^{77}Br -BTdU in L-M (TK-) cells (1.1 ± 0.3 %ID/g protein at 180 min). In addition, more than 90% of ^{77}Br -BTdU was incorporated in DNA at 120 min. These results show that ^{77}Br -BTdU is incorporated into DNA. In biodistribution experiments, the uptake of ^{77}Br -BTdU in proliferating organs was high (spleen: 13 ± 4.8, small intestine: 4.5 ± 1.0 %ID/g at 6 hr) and that in non-proliferating organs was low (brain: 0.18 ± 0.04, muscle: 0.21 ± 0.04, liver: 0.55 ± 0.10 %ID/g at 6 hr). In tumor bearing mice, uptake of ^{77}Br -BTdU in L-M cells was high (5.7 ± 1.0 %ID/g at 3 hr and 2.6 ± 0.9 %ID/g at 24 hr after injection). The ratio of tumor-to-muscle in L-M cells was more than 20 at 3 hr. These results show that ^{77}Br -BTdU has suitable characteristics for tumor proliferation imaging. **Conclusion:** Radiobromine-labeled BTdU is potentially useful as a tumor proliferation-imaging agent for PET.

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The Revival of multiparticle cyclotron and At-211 production

J. Geets, B. Nactergal, M. Abs, W. Kleeven; Ion Beam Application, Louvain la Neuve, BELGIUM.

Objectives: To reply to the strong demand of researchers and the need of specific radio nuclides for nuclear medicine in the field of therapy, especially ^{211}At for alpha- radio immunotherapy, IBA propose a Cyclone® 30-XP multiparticle cyclotron. ^{211}At is uniquely produced by alpha beam of 29MeV onto natural Bismuth target. However availability of cyclotrons with alpha beam (positive ion) is today very low since many machines were converted in proton only for FDG production or were decommissioned. Availability of deuteron beam of higher energy will also allow exploration of (d,xn) nuclear reaction for new radioisotope production (ex. ^{64}Cu). **Methods:** While proton (15-30 MeV) and deuteron (8-15 MeV) are produced and extracted in the well-known negative ion mode with stripping extraction in the Cyclone® 30, the positive alpha beam (nucleus of helium atom He⁺) is accelerated and extracted in positive ion mode using an electrostatic deflector. The He²⁺ acceleration needs specific external source and adjustments to the cyclotron magnetic field

and acceleration frequency (RF). The energy of the alpha beam will be fixed in the 29-30 MeV range. Redesign of the magnet system was needed to leave free space for the alpha deflector and to reuse magnetic 'flaps' for field correction as it is done on the IBA-Cyclone® 18/9. Pole extensions gradient correctors were reused from the Cyclone®70 to ease alpha beam extraction. **Results:** Some technical challenges were solved to fit the two RF acceleration modes in the same machine with external ion sources platform for the different ions species. The innovative new RF design was patented by IBA to overcome usually problems with moving RF contacts. Another challenge was solved by using the magnetic deep-valley concept which allows housing the deflector to a common exit used for both modes. This allows the use of one common beam line and target for both proton and alpha beams. **Conclusions:** The design is completed, the machining and magnetic mapping is ongoing (march 2010) and the first Cyclone®30 -XP is foreseen for installation at Forschungszentrum Jülich, Germany in the beginning of 2011.

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Evaluation of ^{99m}Tc -TMEOP as Probe for Functional Monitoring of Multidrug Resistance

F. Mendes, L. Gano, C. Fernandes, A. Paulo, I. Santos; Instituto Tecnológico e Nuclear, Sacavém, PORTUGAL.

Aim: Chemotherapy remains an important therapy in many malignant tumours and is used extensively. Resistance to chemotherapeutic agents is a major obstacle in the successful treatment of cancer patients. Therefore, non-invasive detection of multidrug resistance (MDR) to chemotherapeutic agents is highly advantageous to define a successful therapeutic regimen. Cationic radiotracers originally developed as myocardial perfusion agents, such as ^{99m}Tc -Sestamibi, tend to localize in tumour cells due to the increased negative mitochondrial potentials and have been used for both cancer early detection and non-invasive monitoring of MDR by SPECT. Recently, we developed a new ^{99m}Tc -tris(pyrazolyl)methane complex (^{99m}Tc -TMEOP) with potential for myocardial imaging. It presented high initial and persistent heart uptake associated to rapid blood and liver clearance. The goal of this work is to assess the usefulness of ^{99m}Tc -TMEOP for functional assessment of MDR. **Methods:** The *in vitro* uptake and efflux kinetics of ^{99m}Tc -TMEOP was evaluated in human cancer cell lines, H69 (lung small cell carcinoma) and MCF-7 (breast cancer) and the corresponding drug-resistant H69 Lx4 and MCF/MDR-1, which overexpress Pgp, the most widely studied transporter associated to MDR. We have further evaluated *in vivo* the role of Pgp in the efflux of ^{99m}Tc -TMEOP in rats, and its pharmacokinetics and tumour uptake in MCF-7 and MCF/MDR-1 xenografted tumour models. **Results:** The uptake kinetics of ^{99m}Tc -TMEOP is comparable with ^{99m}Tc -Sestamibi, being significantly reduced in the cells over-expressing Pgp and increased in the presence of verapamil, a modulator of Pgp. The biodistribution data of ^{99m}Tc -TMEOP in rats show that the effect of cyclosporine A, a Pgp inhibitor, induces a significant decrease in the washout rate from liver, kidneys and lungs, organs with a high Pgp expression. In nude mice bearing MDR-negative and MDR-positive tumour xenografts, the biodistribution of ^{99m}Tc -TMEOP was similar in noncancerous organs. However, the tumour uptake was almost 2 times higher in the MCF-7 xenografts compared with the MCF/MDR-1 tumours. The *in vivo* MDR phenotype of the tumours was confirmed by detection of protein expression levels by Western blot. **Conclusion:** We have evaluated ^{99m}Tc -TMEOP *in vitro* and *in vivo*, and results in human cancer cell lines and animal models, indicate that it could act as substrate of the Pgp. In summary, ^{99m}Tc -TMEOP is a promising candidate for tumor imaging and functional assessment of MDR mediated drug resistance.

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Development of a Radiosynthesis Module Designed to Produce Florbetapir F 18 (^{18}F -AV-45) for Clinical Trials

G. A. Casale¹, L. O. Silva¹, P. A. Pace¹, C. D. Hormigo¹, P. Zubata¹, M. Zubillaga¹, N. Leonardi¹, J. Nicolini¹, R. Caro¹, M. Nicolini¹, H. Gutierrez¹, A. Delle Chiaie¹, N. C. Lim², T. E. Benedum²; ¹Laboratorios BACON SAIC, Buenos Aires, ARGENTINA, ²Avid Radiopharmaceuticals Inc., Philadelphia, PA, UNITED STATES.

Florbetapir F-18 is a radiopharmaceutical used for imaging β amyloid deposits in clinical trials in Argentina. Laboratorios BACON has pursued producing this imaging agent locally in its cyclotron facility. The IBA Synthera has been a reliable platform for producing 18F-FDG worldwide via nucleophilic exchange of the radionuclide ^{18}F . This reliability, together with its versatility makes an ideal combination for adapting more complicated processes (compared to ^{18}F -FDG production) into the Synthera platform. We report herein, an IBA Synthera platform adapted synthesis of florbetapir F 18 wherein an HPLC semi preparative purification system and a reformulation module has been successfully integrated. The resulting system is highly reliable and capable of producing highly pure product (both radio-chemically and chemically) with high specific activity.

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First Preparation of [^{18}F]FE@PBM, a potential NET-PET ligand

W. Wadsak¹, J. Ungersboeck¹, R. R. Lanzemberger¹, A. Hoepfing², B. K. Keppler³, K. Kletter¹, R. Dudczak¹, M. Mitterhauser¹; ¹Medical University of Vienna, Vienna, AUSTRIA, ²ABX - Advanced Biochemical Compounds, Radeberg, GERMANY, ³University of Vienna, Vienna, AUSTRIA.

Background: Reboxetine [2-(α -(2-ethoxyphenoxy)-benzyl)-morpholine] is known to be a selective antagonist at the norepinephrine transporter (NET) since 1984. Because of its excellent affinity and selectivity for the NET, it was chosen as lead compound for the design of NET-specific radiopharmaceuticals. So far, the application of the reboxetine derivatives, (S,S)[^{11}C]MeNER ([11C](S,S)-2-(α -(2-methoxyphenoxy)-benzyl)morpholine) and [^{18}F]FMeNER-d2 was described. Recently, PBM ((2S,3S)-2-[α -(2-(carbomethoxy)phenoxy)benzyl)morpholine] was introduced as another promising NET-PET-candidate with similar or superior affinity for hNET (Ki=1.32nM) and selectivity over hSERT and hDAT (Ki=614nM and Ki>3000nM, respectively) compared to (S,S)-reboxetine or (S,S)MeNER. (Zeng et al. Bioorg Med Chem 2008;16:783). Evaluating the structure-activity relationships, we concluded that a reboxetine derivative bearing a fluoroethyl-ester moiety ([^{18}F]FE@PBM) should be the ideal compound, combining high affinity and NET-selectivity as well as metabolic stability. Hence, the aim of this work was the radiosynthesis of the

novel potential NET-PET-ligand, [18F]FE@PBM. Methods: [18F]FE@PBM was synthesized using an optimized two-step fluoroethylation method. [18F]fluoride was azeotropically dried, 2-bromoethyl triflate was added and heated for 10min at 100°C. The intermediate, 1-bromo-2-[18F]fluoro-ethane (BFE) was distilled and added to the TBA salt of the protected precursor (N-BOC-PBM-acid; 1.6mg/ml). Conversion was achieved at elevated temperature (100-150°C) within 10-30min and deprotection was performed with trifluoroacetic acid (TFA). Radiochemical yields (RCY) were determined using radio-HPLC (MeOH/0.1M TFA, gradient; flow 2ml/min) and radio-TLC (acetonitrile/water 95/5). Results: So far, depending on the reaction conditions up to 65% RCY was observed. Using radio-TLC, the product (Rf 0.5-0.7) was separated from unreacted [18F]fluoride (Rf 0-0.1) and an unknown by-product (Rf 0.8-1.0). The HPLC chromatogram showed only minor amounts of by-product formation. Conclusions: We were able to prepare [18F]FE@PBM for the first time. Further optimization and chromatographic purification are currently on the way and preclinical testing will start immediately afterwards.

P132

Targeting of Non-Hodgkin Lymphoma with a novel radioimmunoconjugate: Reevaluation of CD37 as target for radioimmunotherapy

J. Dahle¹, Ø. S. Bruland¹, K. B. Melhus¹, C. Mollatt¹, R. H. Larsen²; ¹Oslo University Hospital, Oslo, NORWAY, ²Nordic Nanovector AS, Oslo, NORWAY.

Beta-emitting radioimmunoconjugates possess high clinical activity in patients with relapsed or refractory B-cell lymphomas, including those refractory to rituximab and chemotherapy. Patients treated with CD20-directed radioimmunotherapy often have been treated with several cycles of cold rituximab, which could result in antigenic drift causing reduced expression of CD20. Thus, a novel approach to lymphoma treatment might be to target other antigens than CD20 after some cycles of rituximab treatment. Radioimmunotherapy with CD37 as target has been explored previously using a ¹³¹I-labeled murine monoclonal antibody (MB-1) against CD37 both in a mouse model and in the clinic. CD37 antibodies were compared with CD20 antibodies and a higher grade of internalization and degradation of ¹³¹I-labeled radioimmunoconjugate was found for CD37 than for CD20. Despite clinical responses, the data for CD20 was evaluated to be marginally better than for CD37. As far as we know, no subsequent efforts have been made to target CD37 with other radioimmunoconjugates. At the Norwegian Radium Hospital a monoclonal antibody (HH1) was developed against CD37. To avoid dehalogenation the antibody was labeled with the radiometals ¹¹¹In and ¹⁷⁷Lu using the p-SCN-benzyl-DOTA chelator. Binding properties and biodistribution of ¹²⁵I-labeled and ¹¹¹In-labeled HH1 were compared with radiolabeled rituximab. Daudi cells labeled with ¹⁷⁷Lu-rituximab had twice as much cell-bound activity attached than cells labeled with ¹⁷⁷Lu-HH1. However, the growth delay as compared with untreated cells increased with 107% for cells treated with 2.5 µg/ml ¹⁷⁷Lu-HH1 and only with 52% for cells treated with 2.5 µg/ml ¹⁷⁷Lu-rituximab. Thus, the ¹⁷⁷Lu-HH1 treatment had a significantly higher therapeutic effect than ¹⁷⁷Lu-rituximab.

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Development of Lutebodies: a new class of targeted anti-cancer agents for radionuclide therapy

A. Aerts; SCK-CEN, Mol, BELGIUM.

Aim. Nanobodies are small antigen-binding single-domain proteins derived from unique heavy-chain antibodies that are present in camelidae. Due to their beneficial pharmacokinetic properties, nanobodies are ideally suited to target tumor-associated antigens for therapeutic purposes. In previous studies we showed excellent targeting of CEA, HER1 and HER2 antigen after labeling with ^{90m}Tc. In the current project, we develop Lu-177 labeled nanobodies that could be used for targeted radionuclide therapy. **Materials & Methods.** Nanobodies were conjugated to the bifunctional chelating agents 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid N-hydroxysuccinimide (DOTA-NHS-ester) or 2-(4-isothiocyanatobenzyl)-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (p-SCN-Bn-DOTA). The degree of conjugation was analysed using Mass Spectrometry (MS). We subsequently labeled DOTA nanobody with cold lutetium. Binding specificity of the lutetium-nanobody (Lutebody) was assessed by enzyme-linked immunosorbent assay (ELISA) on recombinant protein and on cancer cells using flow cytometry. **Results.** MS spectra confirmed the conjugation between DOTA and nanobody. On average there was 1.5 DOTA per nanobody. After labeling with lutetium, ELISA studies showed only a minor decrease of the nanomolar affinity of the nanobodies for the antigens. Flow cytometry confirmed these findings. **Conclusion.** In this study we show for the first time the successful coupling between cancer targeting nanobodies, DOTA and lutetium. After these chemical modifications, the Lutebodies still have nanomolar affinity for their target. Labeling with Lu-177 is currently ongoing.

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Radiochemical, Biological and Dosimetric Evaluation of ^{99m}Tc-LBG for use in Colon Transit Scintigraphy

F. Lucena¹, A. M. Abrantes², J. Rio³, L. Gano⁴, M. F. Botelho⁵, A. I. Santos⁶; ¹Higher School of Health Technology of Lisbon; Technological Institute and Nuclear, Sacavém; ²Institute of Biophysics and Biomathematics, IBILI-Faculty of Medicine, University of Coimbra, Lisboa, PORTUGAL, ³Institute of Biophysics and Biomathematics, IBILI-Faculty of Medicine, University of Coimbra, Coimbra, PORTUGAL, ⁴ICNAS; Institute of Biophysics and Biomathematics, IBILI -Faculty of Medicine, University of Coimbra, Coimbra, PORTUGAL, ⁵Technological Institute and Nuclear, Sacavém, PORTUGAL, ⁶Institute of Biophysics and Biomathematics, IBILI, CIMAGO -Faculty of Medicine; ICNAS, University of Coimbra, Coimbra, PORTUGAL, ⁶Garcia da Horta Hospital, Almada, PORTUGAL.

Constipation is one of the most common gastrointestinal complaints. Nuclear medicine techniques are relatively non-invasive and allow the study of abnormal gastrointestinal motility, namely colonic transit. The absence of a gold-standard radiopharmaceutical makes this an

unusual technique in clinical practice and difficult results comparison between different centers. The sensitivity and specificity are therefore, limited. Locust bean gum (LBG) is a polysaccharide with applications in medical imaging since 2003, as an oral contrast agent in the study of the small intestine by NMR, and later, by CT. The aim of this work consists in the synthesis, evaluation of in vivo biological behavior and determination of the associated internal dosimetry of a ^{99m}Tc complex with locust bean gum (^{99m}Tc-LBG), assessing its potential for clinical application in colon transit scintigraphy. In vitro studies were conducted to optimize the experimental conditions of synthesis and evaluation of the radiochemical stability after freezing and variation of volume, pH and temperature of the ^{99m}Tc-LBG. For in vivo studies healthy Balb-c nu/nu (16 g - 34 g) were intragastrically administrated with an average activity of 14 MBq of ^{99m}Tc-LBG. Groups of 3 animals were sacrificed at 30, 60, 120, 240, 360, 480, 720 and 1440 min after administration of the radiopharmaceutical, having been dissected in each time several whole organs, tissues and fluids of excretion. Additionally, images of mice in different times of sacrifice, and of the intestines, after organ dissection, were acquired in gamma-camera, complementing the information on the progression of the radiopharmaceutical. Internal dosimetry was based on the data of the biodistribution study. After the synthesis of ^{99m}Tc-LBG, evaluation of in vitro stability of the compound presented results of radiochemical purity above 90%. The results of the biodistribution study and the acquired images in gamma-camera show the progression of the radiopharmaceutical in the gut over the 24 hours studied. The organs with more radioactivity were the large intestine (33.7%, 24h) and small intestine (8.1%, 24h), with negligible renal and hepato-biliary excretion. The estimated total effective dose is 0.037 mSv/MBq. Biodistribution and gamma-camera image results validate the hypothesis that the complex of Tc-^{99m} synthesized from LBG remains in the gut until its elimination in stool, not suffering digestion and/or absorption along its path. The estimated effective dose is quite favorable compared with other radiopharmaceuticals currently in use in colon transit scintigraphy. Results suggest that ^{99m}Tc-LBG presents favorable characteristics for potential clinical application in colon transit scintigraphy.

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New ^{99m}Tc - Silica Nanoparticles and Fluorescer Biodistribution Studied Through Scintigraphy and Fluorescence Microscopy

C. Stefanescu¹, B. Tamba¹, A. Wirth², U. Pielese², I. Jaba¹, C. Mungiu¹, V. Rusu¹; ¹U.M.F., Medicine Faculty, Iasi, ROMANIA, ²University of Applied Sciences Northwestern Switzerland, Muttenz, SWITZERLAND.

Aim. Silica nanoparticles (SNP) are a new and versatile tool for targeting drug delivery. Our aim was to investigate biodistribution and pharmacokinetics of two new SNP derivatives in guinea pigs and mice, in order to identify the possible uses as a drug carrier. **Material and Methods.** **Material:** SNP were prepared at the Institute of Chemistry and Bioanalytics, University of Applied Sciences Northwestern Switzerland, Muttenz, Switzerland. Two 100 nm size SNP derivatives were used: AA124 - SNP carrying OH groups on the surface and AA115 - SNP carrying amino-groups on the surface. **Methods.** The procedure of ^{99m}Tc - SNP coupling was an in-house preparation performed as follows: 1- first of all, SNP were suspended in EtOH (5mg/ml) and sonicated for 15 or 20 min for better dispersion. 2- to this suspension, 200MBq/1ml of Na^{99m}TcO₄ solution was added and the suspension was stirred gently. 3- an excess of NaBH₄ reducing agent was added quickly to the suspension and stirred for minimum 1 hour. **Scintigraphic study design:** Groups of 4 animals were intravenously administered with 37MBq/kg/animal ^{99m}Tc-coupled AA115 and AA124 SNP. Control groups received 37MBq/kg animal ^{99m}Tc. A dual head Siemens gamma camera with high resolution parallel collimators was used. The image acquisitions protocol started with a dynamic image acquisition for 60 seconds (1 image/sec), followed by a dynamic image acquisition for 4 minutes (1 image/min) and static planar images (256x256 Matrix, Zoom 2) every 15 minutes for a duration of 2h. For fluorescence microscopy studies, groups of four mice were administered with the two different nanoparticle suspensions and a different group of two mice received a similar volume of PBS as control. The animals were sacrificed at several different time points starting with 30 minutes until 72h, and samples of different organs were extracted and treated for analysis by fluorescence microscopy. **Results.** Following the i.v. administration, AA115 SNP did not penetrate the blood brain barrier. SNP were present in all the organs investigated except the brain, with different target/nontarget indexes, that were graphically represented in time for each of them. Data from scintigraphic images were well verified by fluorescence microscopy, being presented. **Conclusion.** These steps represent a promising support for the idea of using the AA115 as container for modular drug delivery system with promising future in therapeutics. **Acknowledgements:** Work partially supported by the Romanian Ministry of Education and Science, grant CNCIS IDEI 1734/ 2009.

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Long-term toxicity studies on interstitial delivery of ³²P-chromic phosphate-poly-L lactic acid seeds in Beagle dogs

L. Liu¹, Z. Liu¹, J. Sun¹, Q. Nie¹, Z. Tan², Q. Wu¹, H. Gao¹; ¹Southeast University, Nanjing, CHINA, ²Nanjing No.1 Hospital, Nanjing, CHINA.

Objective To explore the possibility and safety of ³²P-CP-PLLA seeds administrated through interstitial implantation. **Methods** Thirty Beagle dogs were randomly divided into groups of ten according to different implants (³²P-CP-PLLA seeds or ³²P-CP colloids), different doses (185, 370 or 740 MBq), and different injection sites (gluteus or liver). Dynamic observation was performed including dogs weighting, blood, blood biochemistry and liver fibrosis detection, SPECT imaging and histology examination. The radioactivity of body surface, blood and daily urine and faeces were measured. **Result** γ imaging demonstrated both of ³²P-CP-PLLA groups and ³²P-CP groups had radioactivity congregating in the implantation field, without liver intake. In ³²P-CP group, amounted to 794.28 MBq/m² administration, obvious liver damage appeared with 56 Gy absorbed dose and systemic toxicity. In ³²P-CP-PLLA groups, up to 1588.89 MBq/m², no obvious liver damage was observed with 89.83 ~ 178.68 Gy absorbed dose in implantation liver area and 1.09~2.18 Gy absorbed dose in the rest liver area. Dogs in high-dose ³²P-CP group appeared weight lost progressively and PLT and Hb obviously reduced. AST and ALT sharply increased before dying and the values of liver fibrosis indicators were higher than that of other groups ($F_{PCIII} = 3.727$, $P_{PCIII} = 0.002$; $F_{HA} = 9.856$, $P_{HA} = 0.000$; $F_{CG} = 18.988$, $P_{CG} = 0.000$; $F_{FCIV} = 4.598$, $P_{FCIV} = 0.000$). The results of blood and blood biochemistry among other groups showed no significant differences. Effective half-life of ³²P-CP-PLLA was 11.78 d, while ³²P-CP was 6.82 d through liver implantation, and 8.73 d through gluteus implantation. Within 4 weeks, moderate to serious liver injuries were found in high-dose ³²P-CP group, while mild to moderate liver injury in other liver

implantation groups. Gluteus implantation groups had no significant pathological liver changes. All groups showed no abnormalities in heart, lung, spleen and kidneys. The blood radioactivity showed slowly jagged decreasing in ^{32}P -CP-PLLA groups and exponential decreasing in ^{32}P -CP groups. The mean accumulated radioactivity in urine / feces after 30-day liver or gluteus implantation were 7.31% / 9.86% or 6.75% / 8.46% in ^{32}P -CP-PLLA group, while 23.69%/8.86% or 36.85%/10.93% in ^{32}P -CP groups. **Conclusion** ^{32}P -CP-PLLA seeds have a higher tolerated dose in dogs which can even endure double doses of ^{32}P -CP lethal dose, with mild and reversible injury to target organs and no obvious systemic toxicity. The ^{32}P -CP-PLLA seeds may have better therapy potential to solid tumors than traditional ^{32}P -CP colloids.

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Synthesis of 5- ^{18}F fluoroisoquin-1-ol as potent imaging agent for PET

H. Kim¹, D. Kim², I. Kim¹, J. Park¹, S. Kim¹, M. Hur¹, S. Choi¹, S. Yang¹, K. Yu², ¹Korea Atomic Energy Research Institute, Jeongup, KOREA, REPUBLIC OF, ²Dongguk University, Seoul, KOREA, REPUBLIC OF.

Aim: Poly(ADP-ribose) polymerase-1 (PARP-1) is an enzyme involved in DNA repair and programmed cell death. Inhibitors of PARP-1 play a crucial role in the treatment of breast cancer in monotherapy as well as in combination with chemotherapeutic agents and radiation. Recently PARP-1 inhibitors have revealed the ability to reduce a VEGF-induced proliferation. Therefore PARP-1 inhibitors may be considered as attractive therapeutics. 1,5-isoquinolinediol has been known as a PARP-1 inhibitor. 5- ^{18}F fluoroisoquinolin-1-ol was synthesized to investigate its potential for cancer imaging agent for PET. **Materials & Methods:** The target compound involves the following steps. 1-chloroisoquinoline was treated with $\text{HNO}_3/\text{H}_2\text{SO}_4$ to give 1-chloro-5-nitroisoquinoline followed by conversion to 5-nitroisoquinolin-1-ol and then finally reduction of the nitro group to get the desired compound 5-aminoisoquinolin-1-ol. 5-fluoroisoquinolin-1-ol was prepared by the Balz-Schiemann reaction using HBF_4 with 5-aminoisoquinolin-1-ol. Subsequently the preparation of H^{18}F from ^{18}F fluoride and HCl , 5- ^{18}F fluoroisoquinolin-1-ol was prepared by H^{18}F with NaNO_2 and 5-aminoisoquinolin-1-ol. These radiolabelling have been done in the presence of Kryptofix-2.2.2 and K_2CO_3 at 120°C for 15 min. **Results:** Radiolabelling was achieved by the reaction of 5-aminoisoquinolin-1-ol with ^{18}F fluoride in acetonitrile/conc.HCl and NaNO_2 at 120°C . On purification using HPLC 5- ^{18}F fluoroisoquinolin-1-ol was obtained in 10% radiochemical yield and in 95% radiochemical purity. (stationary phase: Perkin-Elmer SPHERI-5 RP-18 $5\mu\text{m}$, $250\times 4.6\text{mm}$ column; mobile phase: $\text{H}_2\text{O}/\text{EtOH}(70/30)$ 1mL/min; R_f : 15min). **Conclusion:** The Balz-Schiemann reaction allowed the addition of fluoride into the aromatic compounds without an electron withdrawing group. It has a crucial limit in the radiofluorination due to low specific activity because fluoride and ^{18}F fluoride coexisted for the Balz-Schiemann reaction. We used HCl instead of HBF_4 to overcome this problem. 5- ^{18}F fluoroisoquinolin-1-ol has been developed as a PET imaging probe for the diagnosis of cancer. Further investigation of the method will be performed using various Lewis acids for better radiochemical yield.

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Synthesis of ^{18}F JN-(2-fluoroethyl)clotrimazolium as a potential PET imaging agent

S. Jung¹, I. Kim¹, J. Park¹, S. Kim¹, M. Hur¹, S. Choi¹, S. Yang¹, K. Yu², ¹Korea Atomic Energy Research Institute, Jeongup, KOREA, REPUBLIC OF, ²Dongguk University, Seoul, KOREA, REPUBLIC OF.

Aim: Clotrimazole [1-(2-chlorophenyl)-diphenylmethyl]-1H-imidazole] has been known to inhibit the proliferation of vascular endothelial cells and act as an anti-VEGF drug in vitro, also prevent the angiogenesis in animals. In this study, we synthesized ^{18}F -fluoride labeled clotrimazole derivative as a novel PET radiotracer for breast cancer. **Materials & Methods:** Ethylene glycol was reacted with tosyl chloride in pyridine to give 1,2-ditosyloxyethane. The 1,2-ditosyloxyethane was converted to 2-fluoroethyltosylate on reaction with TBAF. The synthesis of standard compound, N-(2-fluoroethyl)clotrimazolium, was prepared by refluxing with clotrimazole and an excess of 2-fluoroethyltosylate in acetonitrile for 36 hrs. The precursor, N-(2-tosyloxyethyl)clotrimazolium, was prepared by refluxing with clotrimazole and an excess of 1,2-ditosyloxyethane in acetonitrile for 36 hrs. The labeling was done with K^{18}F /Kryptofix 2.2.2 in acetonitrile at 80°C for 10 min to provide a radiolabeled ^{18}F JN-(2-fluoroethyl)clotrimazolium. The radiochemical purity of ^{18}F JN-(2-fluoroethyl)clotrimazolium was > 90%. **Results:** The standard compound was synthesized with a 45% yield and the ^{18}F JN-(2-fluoroethyl)clotrimazolium was synthesized with a 25% yield. Acetonitrile and DMSO have been used as solvent in radiofluorination step and the higher yield observed was of acetonitrile (25%) in comparison to DMSO (5%). Therefore acetonitrile is suitable for radiofluorination step. **Conclusion:** F-18 labeled clotrimazole derivative was synthesized as a novel potential PET radiotracer. These results provide the foundation for further evaluation of ^{18}F JN-(2-fluoroethyl)clotrimazolium as a potential imaging for PET.

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Evaluation of Acute Toxicity of ^{188}Re -BMEDA-liposome in Rats

C. M. Liu¹, C. H. Chang¹, Y. J. Chang¹, C. W. Hsu¹, L. C. Chen¹, H. L. Chen², C. L. Ho¹, C. Y. Yu¹, T. J. Chang¹, T. C. Chiang¹, T. W. Lee¹, ¹Institute of Nuclear Energy Research, Taoyuan, TAIWAN, ²Development Center for Biotechnology, Taipei, TAIWAN.

Liposomes can selectively target cancer sites and carry payloads, thereby improving diagnostic and therapeutic effectiveness and reducing toxicity. To evaluate therapeutic strategies, it is essential to use animal models reflecting important safety aspects before clinical application. The objective of this study was to investigate acute radiotoxicity of ^{188}Re -N,N-bis(2-mercaptoethyl)-N',N'-diethylethylenediamine (BMEDA)-labeled pegylated liposomes (^{188}Re -BMEDA-liposome) in Sprague-Dawley rats. Rats were administered with ^{188}Re -BMEDA-liposome, normal saline as blank or non-radioactive liposome as vesicle control via intravenous injection and observed for 14 days. Examinations have been conducted with respect to mortality, clinical signs, food consumption, body weights, hematological and biochemical analyses. In addition, gross necropsy, histopathological examinations and cytogenetic analyses were also performed at the end of the follow-up period. None of the rats died and no clinical sign was observed during the 14-day study period. Rats administered with ^{188}Re -BMEDA-liposome at dosage of 185 MBq displayed a

significant weight loss compared with the control from study day (SD) 1 to SD 4, and the white blood cell count reduced to 5-10% of initial value (female: 18.55 ± 6.58 to $0.73 \pm 0.26 \times 10^7/\mu\text{L}$; male: 14.52 ± 5.12 to $1.43 \pm 0.54 \times 10^7/\mu\text{L}$) 7 days post injection, but found to recover on SD 15. There was no significant difference in biochemical parameters and histopathological assessments between the ^{188}Re -BMEDA-liposome-treated and control groups, the frequencies of dicentric chromosomes (DCs) were associated with dosage of ^{188}Re -BMEDA-liposome. The information generated from this study on acute toxicity will serve as a safety reference for further subacute toxicity study in rats and human clinical trials.

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Synthesis of ^{68}Ga -labelled porphyrin derivatives for PET imaging agent

E. Lee¹, I. Kim¹, J. Park¹, S. Kim¹, M. Hur¹, S. Choi¹, S. Yang¹, K. Yu², ¹Korea Atomic Energy Research Institute, Jeongup, KOREA, REPUBLIC OF, ²Dongguk University, Seoul, KOREA, REPUBLIC OF.

Aim: ^{68}Ga ($t_{1/2} = 68$ min) is an attractive radionuclide for positron emission tomography (PET) because it can be easily obtained from $^{68}\text{Ge}/^{68}\text{Ga}$ generator without a cyclotron on site. Porphyrin is planar macrocycle incorporating four pyrrole rings joined by methine bridges. Hydrophobic porphyrin derivatives has been known to be localized in tumor tissue due to increasing blood vessel penetrability after binding with albumin in vivo and sufficient lymph conditions caused from inflammation of tumor regions. Furthermore porphyrin derivatives exhibit intracellular uptake into NPC/CNE2 cells, a poorly differentiated human nasopharyngeal carcinoma. Hence ^{68}Ga labeled porphyrin derivatives will be promising as a novel potent PET radiotracer for tumor imaging. **Materials and Methods:** Hematoporphyrin was added to a solution of orthoformate and methanol. Concentrated sulfuric acid was added slowly into the mixture under ice bath and the solution was stirred at room temperature for 45 minutes. The mixture was diluted with water and the pH was adjusted to 4.5 by addition of sodium hydroxide followed by extraction with dichloromethane. Hematoporphyrin dimethyl ester was purified by column chromatography. $^{68}\text{GaGaCl}_3$ is obtained from $^{68}\text{Ge}/^{68}\text{Ga}$ generator eluted with 0.1 N hydrochloric acid. Further $^{68}\text{GaGaCl}_3$ was taken in pyridine followed by addition of porphyrin derivatives and reaction mixture was refluxed for one hour at 100°C . Subsequently ^{68}Ga -porphyrin derivatives was purified using HPLC. **Results:** hematoporphyrin dimethyl ester was obtained in 43% yield. Temperature and pH play an important role in the increasing yields on esterification procedure. The radiochemical yield of ^{68}Ga -hematoporphyrin dimethyl ester and ^{68}Ga -protoporphyrin dimethyl ester were 24% and 18%, respectively. **Conclusion:** ^{68}Ga -hematoporphyrin dimethyl ester and ^{68}Ga -protoporphyrin dimethyl ester were carried out as a tumor imaging agent for PET. The biological evaluation is going on.

P141

Influence of phosphonate-hydroxyapatite microparticle interaction on the delivery of radiation and drugs

N. S. Nikolic, S. D. Vranjes-Djuric, D. L. Jankovic, D. D. Djokic; Vinca Institute of Nuclear Sciences, Belgrade, SERBIA.

Aim Radiosynovectomy (RSV) is a method for treatment of some joint disorders, and involves local intra-articular injection of suitable β -emitting radionuclides in the form of radiocolloids or radiolabelled particulates into the affected synovial joints. In our researches calcium hydroxyapatite (HAP), was studied as a particulate carrier for β -emitting radionuclides in RSV. Particles were radiolabeled with ^{90}Y and their in vivo safety was studied following intra-articular injection into knees of normal rats. The aim of our researches was to explore the factors influencing the labeling yield and particle size distribution of ^{90}Y -labelled HAP particles. We examined the influence of different phosphonates: 1-hydroxyethylidene-1,1-diphosphonate (HEDP), methylenediphosphonate (MDP) and 2,3-dicarboxypropane-1,1-diphosphonic acid (DPD) as chelators in the yttrium-90-labelled HAP particles. In our experiments we used HAP of different particle sizes in order to investigate their biological behavior. Organ distribution studies are performed via intravenous application. Material and Methods $^{90}\text{YCl}_3$ in 0.05 M HCl (Polatom, Poland) Organ biodistribution studies: health Wistar rats (four weeks old) Micro hydroxyapatite powders was synthesized in our Laboratory HEDP and MDP was obtained from Sigma, DPD was synthesized in our Laboratory PCS - Zetasizer Nano ZS (Malvern Instruments, England) TEM, Philips EM 400T, U.K. Results and Discussion Radiolabeling yields of 97-99 % was achieved in all particles preparations. Radiochemical purity of labelled HAP particles was >99% as confirmed with ITLC-SG strips in 80% methanol and saline as mobile phases. The stability of ^{90}Y -labeled particles was studied in saline and in 1% human serum at 37°C , the ^{90}Y -labeled particulates showed excellent in vitro stability, > 98% in both media at 37°C during 5 days. Our results show how organ distribution of radiolabeled particles depends from the way of drug administration and particle sizes. **Conclusion** Biological studies carried out in Wistar rats showed complete retention of injected radioactivity within the synovial cavity of normal animals for up to 96 h post-injection. Stability of ^{90}Y -yttrium-HAP complexes increases with introducing diphosphonates as chelators, especially in presence of MDP. These studies reveal that the ^{90}Y -HA particles offer potential as a suitable agent in the management of RSV of small joints and therefore warrant further investigation.

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A Novel Strategy in the Development of L-[^{18}F]-Labeled Methionine as a PET Tracer for Tumor Imaging

J. Schulz¹, D. Vimont¹, M. Allard¹, P. Panwar², A. K. Mishra², ¹Institut des Neurosciences de Bordeaux, Bordeaux, FRANCE, ²Institute of Nuclear Medicine and Allied Sciences, Delhi, INDIA.

Introduction: In brain tumors, the most widely used tracers are [^{18}F]-fluorodeoxyglucose (FDG) and 11C-methionine (MET). The major metabolic functions of methionine are in protein synthesis and conversion to S-adenosylmethionine, which is required in multiple metabolic pathways. Because the uptake of amino acid in normal tissue is low and increases across glioma capillaries and tumors, the contrast between tumor and normal tissue is generally better with amino acid scanning as compared to FDG-PET. L-[methyl- ^{11}C]-methionine (11C-MET) is the most popular amino acid imaging modality to image the size and spread of gliomas, as MET-PET has the

advantage of showing selective uptake in the brain tumor compared with normal brain tissue. The aim of our study was to synthesize a new L-[18F]methionine derivative and to evaluate its utility as tracer for methionine dependent human tumors firstly because the physical half-life of L-[18F]methionine is considerably longer (109.4 versus 20.4 min) than [11C]-MET. Secondly, L-[18F]-methionine is more stable against metabolic degradation in vivo. Methods: We developed the synthesis of a new 18F labeled L-methionine. We used the amine function of the methionine to incorporate a Si atom. This new methionine derivative was then fluorinated with nucleophilic 18F by Si-18F bond formation. Transmutation studies of 18F labeled L-methionine derivative with 35S-L-methionine were done to evaluate the uptake in U-87MG human tumor malignant glioma cell line. Cytotoxicity studies in BMG, U-87MG and Neuro-2A cell lines were carried out. Animal PET imaging was done in athymic mice grafted with U-87MG tumors. Results: We first modified the methionine to obtain a silylated precursor via the formation of a peptidic bond with a good yield (75 %). This precursor was then used to incorporate an 18F atom via the formation of a Si-18F bond with nucleophilic 18F. Good to excellent radiochemical yields (35%) were obtained starting from high activities (120 GBq). High specific activity in range of 95-110 GBq/ μ mol was obtained. 35S-methionine efflux was trans- stimulated by L-[18F]methionine demonstrating concentrative transport. The mean SUVs of the contralateral muscle was 1.08 ± 0.19 and T/NT ratio was found to be 18.9 ± 0.40 . Conclusion: We have synthesized 18F labeled methionine with good radiochemical yields and high specific activity showing substantial promise for tumor scintigraphy as significant accumulation was observed in athymic mice bearing U-87MG cell line. This system has got an added advantage over 11C-methionine due to the longer half life. References: Kato et al American Journal of Neuroradiology 29:1176-1182 (2008).

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Early detection of radiation induced apoptosis by ^{99m}Tc -Annexin V and ^{201}Tl Thallium-Chloride in a lung cancer cell line

S. Ha-Kawa, M. E. Khoda, K. Utsunomiya, S. Sawada; Kansai Medical University, Hirakata, JAPAN.

The efficacy of ^{99m}Tc -HYNIC-coupled Annexin V (TAV) and ^{201}Tl Thallium-Chloride ($^{201}\text{TlCl}$) in the early detection of radiation induced apoptosis, a proxy indicator of radiation therapy (RT) efficacy, in a lung cancer cell line was investigated. TAV accumulation and $^{201}\text{TlCl}$ accumulation and efflux in non small cell lung cancer, transfected with the wtp53 gene (H1299/wtp53), were measured 24 and 48 hours post irradiation at 5 different gamma ray doses. Radioactivity of this cell line was measured in a gamma well counter. Apoptotic cells were detected employing the TUNEL method. The replication rates (RR) of the cell lines were also measured at 24 and 48 hours after irradiation. Radioisotope accumulation was measured after addition. $^{201}\text{TlCl}$ accumulation was measured at 1, 10 and 30 min after switching to fresh media for efflux study. Cell RR decrease with increased radiation dose was observed 48 hours after irradiation. Apoptotic cell number was found to be increased in response to 9 Gy and 12 Gy radiation dose as compare to the control and other radiation doses (3 - 6 Gy). At 24 hours post irradiation no dose dependent difference in Annexin V accumulation was observed at any time points from 1 - 90 min. However, at 48 hours post irradiation, with 9 Gy and 12 Gy, doses, Annexin V accumulation was found to be higher than in the control and 3 - 6 Gy irradiated groups. No significant Annexin V wash-out was observed in any irradiated and non-irradiated cells. $^{201}\text{TlCl}$ accumulation in the 9 and 12 Gy irradiation groups was found to be higher than in that of the 0 Gy, 3 Gy, or 6 Gy irradiation groups. Quick $^{201}\text{TlCl}$ efflux was observed in the 9 Gy and 12 Gy irradiated cells. TAV may prove to be an effective radiotracer for early assessment of radiation therapy efficacy, via apoptosis, in human lung cancers.

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Uptake of ^{99m}Tc -chondroitin sulfate in thoracic and articular cartilage. A suitable and promising tracer for imaging of osteoarthritis.

G. Sobal, R. Dorotka, J. Menzel, H. Sinzinger, R. Dudczak; Medical University of Vienna, Vienna, AUSTRIA.

Aim: Chondroitin sulfate (CS) is an endogenous component of cartilage and used for treatment of osteoarthritis. We investigated direct in-vitro uptake of $^{99m}\text{TcCS}$ in thoracic and even more important articular cartilage. Materials and Methods: CS (25mg) as Condrosulf (IBSA, Lugano, Switzerland) was radiolabeled using $^{99m}\text{TcO}_4$ -(120-150 MBq) / tin method (pH 5.0, 0.5M Na acetate). Uptake of $^{99m}\text{TcCS}$ (10 μ Ci) was performed in tissue pieces (3-4 mg) from age matched individuals (78a and 63a) post mortem and in articular cartilage from individuals (66a-79a, n=4) undergoing knee arthroplasty. In parallel, uptake of $^{99m}\text{TcCS}$ by autoradiography in frozen tissue sections (10 μ m) derived from the same tissues in both cartilage specimens was investigated too. Specific uptake was evaluated from 10 min. up to the saturation (max. uptake). Non-specific uptake in the presence of 50-fold excess of cold CS was investigated too. The wash-out of the tracer was examined after uptake experiments at 3h and 24h, respectively. Results: Labelling efficiency in all experiments amounted to a max. of 95.0%, specific activity to 6.0mCi/ μ M, (n=6). Uptake in tissue pieces was increasing with time up to saturation in both cartilage specimens, reaching the max. of 50.6-98.8 % already at 30h (thoracic cartilage). Using articular cartilages, uptake amounted to 53.2-88.8 % and saturation was achieved at 24-96h. While the uptake in the thoracic cartilage is quite homogeneously distributed, in contrast, in articular cartilage uptake is higher in the superficial zone as compared to the subchondral one. This correlates with pathological pattern of articular cartilage degradation. Non-specific uptake for both did not exceeded 15%. Autoradiography for both cartilage specimens paralleled uptake in tissue pieces and showed the max. uptake at 72h in thoracic, followed by 48-96h in articular cartilages. Using autoradiography, non-specific uptake ranged below 10%. The wash-out of the tracer in thoracic cartilage amounted to a max. of $3.8 \pm 1.5\%$, in articular to $1.6 \pm 0.3\%$, after 3h. After 24h wash-out for both was even lower. Conclusions: High uptake of $^{99m}\text{TcCS}$ in cartilage proves its chondrotrophic effects. Therefore, $^{99m}\text{TcCS}$ seems to be a suitable and specific tracer to image cartilage degeneration in osteoarthritis.

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Synthesis and Biological evaluation of SPECT radioligand ^{99m}Tc -DTPA-bis(2-methoxyphenyl piperazine) for brain receptor imaging

N. Singh¹, P. P. Hazari¹, P. Panwar², R. Varshney¹, K. Chuttani¹, A. K. Mishra¹. ¹Division Cyclotron and Radiopharmaceutical Sciences, Institute of Nuclear Medicine and Allied Sciences, Delhi, INDIA, ²Delhi Technological University, Delhi, INDIA.

Aim : There is considerable evidence that a variety of functions and disorders of the central nervous system (CNS) is linked to the serotonergic and dopaminergic systems in brain. The practicality of non-invasively studying serotonin/dopamine receptors in vivo has been successfully demonstrated by PET imaging. However, the application of PET imaging agents demands inhouse cyclotron facility. As SPECT is more widely available than PET, many efforts have been focused on the development of agents based on ^{99m}Tc for brain receptor imaging. In our search for effective SPECT radioligands for the serotonin receptors, we synthesized new ligand by coupling alkylated 2-methoxyphenyl piperazine (MPP) with Diethylenetriaminepentaaceticacid. This compound is useful as a probe for the development of radiotracers for studying brain receptor regulation in vivo with the functional imaging technique, SPECT. . Method: DTPA-bis(MPP) was synthesised by conjugating two molecules of 2-methoxyphenyl piperazine to DTPA. Boc protected 3-bromopropylamine was used for alkylation of 2-methoxyphenylpiperazine(MPP) in 2-butanone. The boc protected alkylated product was then cleaved with trifluoroacetic acid to yield MPP-propylamine. The resulting compound (2 mmol) was further conjugated with DTPA anhydride (1mmol) in DMF in presence of triethylamine. The desired conjugate DTPA-bis(MPP) was labeled with ^{99m}Tc and evaluated in vitro in rat hippocampal cultures. Results: The synthesis, characterization and biological evaluation of ^{99m}Tc -labeled DTPA-bis(MPP), bearing the 1-(2-methoxyphenylpiperazine) moiety was carried out. Labeling was performed with high yield (>95%) and radiochemical purity (>98%) using very low ligand concentration. In vitro binding assays in rat hippocampal cultures demonstrated the affinity of this complex for 5-HT1A receptors (IC_{50} to be 27nM). Our results demonstrated the potentiality of the approach for the design of ^{99m}Tc -radioligand DTPA-bis(MPP) derivative with the ability to bind neuroreceptors for studying brain receptor regulation in vivo with the functional imaging technique, SPECT. References: Chu et al *Biorganic & Medicinal Chemistry* (2005) 13, 77-87. Leo'n et al *Nuclear Medicine and Biology* (2002) 29, 217-226.

P146

Radiolabelling proteins with stabilised hypervalent astatine-211: feasibility study and evaluation of the in vitro stability

F. Guérard¹, H. Rajerison¹, A. Favier-Chauvet¹, J. Barbet¹, G. J. Meyer², F. Haddad³, I. Da Silva⁴, J. F. Gestin¹; ¹Centre de recherche en cancérologie Nantes-Angers, Inserm U892, Nantes, FRANCE, ²Klinik für nuklearmedizin, Medizinische Hochschule Hannover, Hannover, GERMANY, ³Subatech, IN2P3/CNRS/EMN, Nantes, FRANCE, ⁴CEMHTI, CNRS UPR3079, Orléans, FRANCE.

Aim: Astatine-211 has become of major interest for alpha immunoradiotherapy thanks to its best adapted radiophysical properties compared to the other alpha emitters. Unfortunately, the described procedures for the radiolabelling of proteins with astatine-211 have shown a lack of in vivo stability, particularly in the case of small proteins such as IgG fragments. We recently developed an original radiolabelling procedure providing aromatic rings radiolabelled with hypervalent astatine. The aim of this study was to develop a bifunctional tin precursor allowing the radiolabelling with hypervalent astatine-211 and the coupling to proteins for stability evaluations. Materials & methods: The relatively hard conditions necessary to introduce astatine on such hindered precursor (100°C in methanol/acetic acid) led us to develop a bifunctional compound able to resist to the radiolabelling procedure prior to the coupling to proteins. It is composed of a tin group on a hexafluorocumylalcohol group and of a maleimide function allowing introduction of stabilised hypervalent astatine and protein coupling. Astatine-211 was prepared by the $^{209}\text{Bi}(\alpha, n)^{211}\text{At}$ reaction at the CNRS cyclotron of CEMHTI and/or at the Klinik für Nuklearmedizin's Hannover's cyclotron and dry distilled from the target. The radiolabelled compound was prepared in two steps. In the first step, the tin precursor and N-chlorosuccinimide in MeOH/ACOH (95/5) were incubated at 100°C over 30 min with astatine-211 recovered in methanol to form the monovalent radiolabelled compound. In the second step N-bromosuccinimide in chloroform and traces of hydrochloric acid were added to form the hypervalent species. The monovalent and the hypervalent astatinated compounds were then incubated with bovine serum albumin (first treated with dithiotreitol) in 0.2M carbonate buffer pH 8.0 over 1h at 37°C for coupling. After purification over a PD10 gel permeation column, the human serum stability was evaluated at 4°C, 20°C and 37°C over 12h by gel permeation chromatography. Results: The two-steps radiolabelling procedure of the tin precursor gave excellent yields (85-90% overall yield) in 1h. Both monovalent and hypervalent astatinated compounds were coupled to BSA with good yields (respectively 96% and 81%). The radiolabelling was stable with more than 99% of the activity remaining on the BSA for both compounds at the temperatures studied. Conclusion: This study demonstrates the possibility to radiolabel a prosthetic group with hypervalent astatine with preservation of the maleimide reactivity for protein coupling. The excellent in vitro stability of BSA labelled with this method encourage us to continue this study with the evaluation of the in vivo stability.

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Experimental study on ^{89}Zr production

G. Cioria, A. Ciarnatori, D. Pancaldi, A. Infantino, S. Boschi, S. Fanti, M. Marengo; Policlinico S.Orsola-Malpighi, Bologna, ITALY.

Aim: Immuno-PET as a scouting procedure before radioimmunotherapy (RIT) aims at the confirmation of tumor targeting and the accurate estimation of radiation dose delivery to both tumor and normal tissues. Immuno-PET with ^{89}Zr -labeled monoclonal antibodies and $^{90\text{Y}}$ -mAb RIT might form such a valuable combination. In this work we evaluated a method for the routine production of high-purity and high-specific-activity ^{89}Zr using a biomedical cyclotron. Materials and methods: Irradiations were performed using a 16.5MeV GE-PETrace cyclotron. Our previously developed research solid target station is able to contain discs of 32 mm of diameter, with a thickness ranging from 0.1 to 2.0. One or two thin discs (depth=0.15 mm, ϕ =14 mm) of ^{89}Y have been placed in a copper backing support (ϕ =32mm, depth=1mm) having a cavity (ϕ =14mm, depth=0.15 or 0.30 mm). This assembly was covered by an Aluminium disc degrader of 32 mm diameter and 0.5 mm thickness. In this way, the incident energy on the Yttrium target results to be 12.7 MeV, lower than the energy threshold of undesired $^{89\text{Y}}(\text{p}, n)^{89\text{Zr}}$ reaction

Synthesis of a [18F]fluoroalkylamine and reaction with an activated ester; 5.) Alkylation of a phenol with 2-[18F]fluoroethyltosylate; The precursors and non-radioactive reference compounds were synthesised in multi-step syntheses. Non-carrier-added [18F]fluoride was used and the identity of the labelled radioligand was confirmed by HPLC co-elution with the non-radioactive reference compound. Bio-distribution of labelled compounds was measured in Sprague-Dawley rats. **Results** - Radiochemical yields ranged between 5 and 8% for [18F]radioligands and 37-39% for [123I]radioligands. Radiochemical purity was greater than 95% in all cases. All compounds gave less than 10 nM Ki. The bio-distribution of five radioligands was measured. In vivo brain uptake was very low for 4-quinolones and up to 1.16% for carbolines. No difference in uptake or retention between GABAA rich and poor regions could be detected. Autoradiography showed specific binding to GABAA rich regions. **Conclusion** - A diverse range of radiochemistry was investigated. For 4-quinolones, direct labelling with fluorine-18 was not successful. Alternative approaches using four different synthons and iodine labelling were successful. These compounds were not suitable for development as PET imaging agents.

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Might Re-188 be more effective for boosting therapy of breast cancer using the IART approach?

A. Duatti¹, A. Boschi¹, M. Pasquali¹, E. Janevik², R. Guernini¹, C. Trapella¹, L. Uccelli¹; ¹University of Ferrara, Ferrara, ITALY, ²University "Goce Delcev", Stip, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF.

A key step in establishing a therapeutic approach based on the internal delivery of radioactivity through a radiopharmaceutical is the choice of a radionuclide having the most appropriate nuclear and chemical properties for selectively depositing the highest dose in the target tissue. Y-90 and Lu-177 are, currently, among the most utilized therapeutic radionuclides for the treatment of different tumors. Though their nuclear characteristics span a broad range of β energies, the chemistry of these radioelements does not allow a large variation of possible chemical vectors as it is mostly relies on the use of DOTA as chelating system. Re-118 is a generator-produced radioisotope and shares with Y-90 and Lu-177 several interesting nuclear properties. In contrast, Re-188 displays a far richer chemistry, thus allowing a broad selection of the most effective chemical vectors for the efficient and target-specific delivery of radioactivity. Intra Avidination for Radionuclide Therapy (IART) is a new therapeutic approach recently proposed for the treatment of residual malignancies after surgical removal of a primary breast cancer lesion. This therapeutic strategy involves local deposition of avidin in the surgical bed followed by intravenous injection of labeled biotin that is, subsequently, captured by cancerous cells after selective uptake of avidin. In this work, we describe the design and preparation and first biological evaluation in animal models of a large class of Re-188 biotin conjugates having different molecular structures, but all showing high affinity for avidin both in vitro and in vivo. The basic structural motif of these new Re-188 radiopharmaceuticals is formed by a Re-nitrido core linked to a biotin residue through both linear and cyclic oxygen-carbon chains tethered to an amino-acid chelating group for the metal. The molecular development of this class of novel biotin-derived bifunctional ligands has been designed by considering current models of in vivo stability and mechanisms of biotin affinity for avidin. Chemical modifications of the molecular structures of Re-188 complexes mostly gave rise to a different in vivo biodistribution behavior while keeping the high affinity of the resulting Re-188 radiopharmaceuticals for avidin after in situ deposition by intramuscular administration. Comparison with biotin-derivatives labeled with Y-90 and Lu-177 showed that the new Re-188 biotin derivatives exhibit a higher in vivo affinity for locally deposited avidin and a broad spectrum of biological behavior that may allow to overcome all problems associated with the retention of the radioactive compound in non target organs such as liver and kidneys.

P15 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Radiopharmaceuticals & Radiochemistry & Dosimetry: Radiopharmacy

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Regulation for the "small scale" preparation of PET Radiopharmaceuticals in Spain: light at the end of the tunnel?

L. López Sánchez, M. Sánchez Martínez, G. Quincoces, C. Vigil, I. Domínguez Prado, J. Richter, I. Peñuelas; University Clinic of Navarra, Pamplona, SPAIN.

As radiopharmaceuticals (RP) are medicinal products (MP) for human use, they are regulated by Directive 2001/83/CE and Regulation No 726/2004. However, these regulations only apply to those RP that are prepared under an industrial process and are intended to receive a marketing authorization (MA) but not for those prepared in small-scale. On the other hand, small scale in house preparation is the most common practice for PET RP, since their special nature makes complicated commercialization for most of them. Nevertheless, no binding regulations have already been set in Europe in this regard, implying a great variability in radiopharmacy practice among European countries, as well as, a generalized ignorance of other Member States' regulations. However, in the framework of the European Union, equity in the access to MP must be guaranteed. So, we consider it might be of interest letting others know the changes that have taken place in Spanish regulations in the last years, as they open up new horizons for small-scale preparations of RP. In first place, the main Spanish regulation concerning MP (Law 29/2006) considers preparation of PET RP in radiopharmacy units, out of the industrial manufacturing track. However, neither the basis to inspect and authorize these units, nor the requirements for the preparation have been still set. In this respect, the Spanish Society of Radiopharmacy is drafting a document based on the Guidance on Current good radiopharmacy practice for the small-scale preparation of radiopharmaceuticals. However, competent authorities will have to give it validity. Secondly, the Spanish Medicines Agency has opened up the possibility of creating protocols for the use of PET RP that will probably never have a MA, but in contrast, have demonstrated their clinical usefulness. This is actually of utmost importance, since only ¹⁸F-DG is registered in Spain nowadays. The Competent Authorities will hopefully approve such protocols. Nevertheless, guidelines referring to the way of preparation and quality control of PET RP

produced in house should also be stated. In conclusion, although latest regulatory approaches symbolize a breakthrough in the preparation and use of PET RP in small scale, there is still a great lack of legislation in this field mainly caused by the "commercial approach" of European regulations. However, the competent authorities start to be aware of this situation and are working together with the Spanish societies of Nuclear Medicine and Radiopharmacy to solve this problem.

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How to reach compliance for manufacturing of PET-radiopharmaceuticals under current EU-GMP regulations: an approach for University Hospitals

H. H. Boersma¹, P. H. Elsinga¹, J. Medema¹, G. Luurtsema¹, M. N. Lub-de Hooge¹, A. M. J. Paans¹, G. Siegers², R. A. J. O. Dierckx¹, J. G. W. Kosterink¹, M. G. G. Sturkenboom¹; ¹University Medical Center Groningen, Groningen, NETHERLANDS, ²University of Ghent, Ghent, BELGIUM.

Aim: Within EU, manufacturing of radiopharmaceuticals, e.g. on-site compounding of tracers, has to comply with current regulations on Good Manufacturing Practices (EU-GMP). Recently, annex 3 on radiopharmaceuticals was updated. As a result, annex 1 on sterile manufacturing must be implemented explicitly for radiopharmaceuticals. Furthermore, radiation regulations are to be met. In order to comply with EU-GMP, a new PET-GMP-facility was planned in our university hospital. Over the last years, a project team has dealt with many challenges on design, development, and building of a novel PET-GMP facility. **Methodology:** A validation model was used as major guideline in the development of the facility. This model describes all development/validation stages: determination of specifications, design, development/ construction, acceptance of the finalized product as well qualification, and validation (Initial Qualification, Operational Qualification, Performance Qualification, IQ/OQ/PQ). These steps are to be met in design, building, validation, and maintenance of the whole facility (building, premises, staff). **Results:** The project team oriented on the requirements which were to be met. Design of the facility, including cleanrooms, grade A and C hotcells as well as the specification of all required equipment (e.g. PET-synthesis modules, analysis equipment, monitoring systems) was performed. Special attention was paid to the air classification of the cleanrooms in order to meet both GMP and radiation regulations and laws. The result of the facility design was drafted into several User Requirement Specifications (URS). Several potential suppliers made offers on the respective parts of the facilities. After acceptance of the offer, a discussion with the supplier was started on the realization of the particular item. Special attention was paid to design details (e.g. architecture, air classification in hotcells and cleanrooms, conditions to monitor) as well as validation aspects of the novel facility. The latter resulted in a finalized URS for each part of the facility. Subsequently, construction took place. In the meantime, a validation plan was made. Finally, all procedures intended to use were written or adapted to the new facility. **Conclusion:** We showed that design, development and construction of an EU-GMP compliant PET facility, the use of validation approaches is essential. Furthermore, to ensure successful validation and qualification of the facility, close collaboration between facility staff and suppliers is another cornerstone.

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The Molybdenum shortage and its effects on a large radiopharmacy

J. Thom; Southampton General Hospital, Southampton, UNITED KINGDOM.

The Molybdenum shortage caused by the temporary closures of some of the reactors producing medical isotopes combined with the routine maintenance program of others has been a worldwide problem. Southampton General Hospital radiopharmacy supplies Technetium based products to 7 hospitals preparing over 5000 products per annum for approximately 50,000 patients, as well as supplying 6 veterinary practices. The shortages have made the co-ordinating role of the centralised radiopharmacy paramount to ensure a continuous supply to the customers so ensuring patient scans continue. The shortages have been alleviated by: 1. Good communications from industry. 2. Good communications to customers. 3. Working in partnership with customers to maximise use of available 99mTc. 4. Good procurement practices. 5. Reducing availability to veterinary practices in times of shortage to maintain human requirements. 6. Isolators designed to take multiple generators from any manufacturer. What have been the effects to our service? 1. Minimal disruption to patient numbers. 2. Increase in customer numbers. 3. Little effect in activity prepared on a daily basis. What does the future hold? 1. The shortages will continue until new reactors are built and commissioned. 2. The shortages will continue until two reactors are repaired. 3. Technetium will no longer be cheap and readily available. 4. To maintain a supply to customers more dialog between supplier and end user to ensure the best use of available Technetium. 5. National strategy to be able to distribute spare activity. 6. Rise of central radiopharmacies?

P157

Therapeutic potential of radiolabeled HSP90 inhibitor on lung cancers

J. Sun, L. Lu, Q. Wu, Z. Yang; Southeast University, Nanjing, CHINA.

The results of clinical trials showed the tumor treatment using HSP90 inhibitors may combine with other treatments. **OBJECTIVE:** To study the therapeutic efficiency of radionuclide-labeled HSP90 inhibitor on human lung cancers. **METHODS:** Three lung cancer cells of A549, H460 and SPC-A-1 were compared and evaluated *in vitro*. Immunofluorescent localization and western blotting of total HSP90 expression were performed. Radionuclide iodine-131 labeled HSP90 inhibitor 17-AAG was achieved. Growth inhibition following *in vitro* exposure to 17-AAG or ¹³¹I-17-AAG were evaluated. BALB/c nude mice bearing human lung cancer tumor xenografts were used for *in vivo* studies. Comparison studies was performed between intravenous administration (i.v.) and intratumoral administration (i.t.). Twenty-four xenografts were randomly divided into two groups with ¹³¹I-17-AAG applied through i.v. or i.t. at the dose of 1.85MBq in 0.1ml solution per mouse. The mice in each group were sacrificed at 0.5, 4, 24 hours or 1 week postinjection. The blood and major organs and tissues were obtained for radioactivity measurement.

Immunohistochemistry of tumors was examined for Ki-67 expression using one-week groups. **RESULTS:** Elevated levels of Hsp90 expression were implicated in these cancer cells compared to normal endothelial cell. Tumor cells showed more sensitivity to ^{125}I -17-AAG of only 25 pmol in 500 μCi than to 17-AAG of 17 nmol. *In vivo* biodistribution assay indicated higher tumor uptake and longer appeared in ^{131}I -17-AAG i.t. injection group with lower-radioactivity distribution in the whole body. While tumor uptake through i.v. injection/vein injection group was not obvious but with a rapid systemic clearance, and Na^{131}I control group had a rapid radioactivity clearance without tumor retention. The Ki67 expression of i.v. one-week group and i.t. one-week group was (39.67 \pm 3.65)% and (52.13 \pm 3.19)%, respectively. **CONCLUSIONS:** ^{131}I -17-AAG may have a good therapeutic potential to human lung cancer cells. Radiolabeled HSP90 inhibitor can be treated as a supplement of HSP90 inhibitors treatment on lung cancer. Intratumoral administration could be recommended, as i.v. administration may have more side effects.

P158

Synthesis and first radiopharmaceutical investigation of 5-[125I]Iodo-SU11248, a potential radiotracer for imaging VEGFR

T. Kniess¹, C. Oliveira², M. Kuchar¹, L. Gano², J. Santos², J. Steinbach¹, ¹Forschungszentrum Dresden-Rossendorf, 01314 Dresden, GERMANY, ²Instituto Tecnológico e Nuclear, 2686-953 Sacavém, PORTUGAL.

Aim: Due to the fact that receptor tyrosine kinases (RTKs) are overexpressed in some tumour entities, they might be a suitable target for PET or SPECT imaging. Then, tyrosine kinase inhibitors labeled with a radioisotope could represent a useful tool for monitoring levels of RTKs in tumour tissue giving valuable information for anti-angiogenic therapy. SU11248 (Sunitinib[®]) is a novel highly potent RTK inhibitor targeting vascular endothelial growth factor receptor (VEGFR) (IC50=0.08 μM) [1]. We report here the synthesis of a 125I-labeled derivative of SU11248 and its first radiopharmaceutical characterization. **Materials and methods:** 5-[125I]Iodo-SU11248 was obtained via destannylation of the corresponding tributylstannyll precursor with [125I]NaI in the presence of H2O2. The radioiodinated compound has been purified by RP-HPLC with UV and radioactivity detection using methanol/0.1% TFA (85:15) as eluent. Determination of human plasma protein binding at time intervals of 0; 1; 2; 4 and 24h was accomplished by incubation of the radiotracer in fresh human serum at 37°C. Preliminary biodistribution studies were carried out in healthy CD-1 mice and in vivo stability was assessed by HPLC analysis of urine samples collected at sacrifice time. **Results:** 5-[125I]Iodo-SU11248 could be obtained in high radiochemical yield (>95%). After HPLC purification the radiochemical purity exceeded 98%. The identity of the radiotracer was confirmed by co-elution with 5-Iodo-SU11248 as reference compound [2]. Lipophilicity of 5-[125I]Iodo-SU11248 has been assessed using the octanol/PBS partition coefficients (logPo/w) and was found to be 2.25. Determination of human plasma protein binding suggested a low non-specific binding of 5-10%. Biodistribution studies showed a relatively high uptake in VEGFR-2 rich tissues like kidney and lung, followed by rapid washout (9.6 and 9.7; 4.5 and 3.8% ID/g kidney and lung at 1 and 4 h, respectively). **Conclusion:** The new 5-[125I]Iodo-SU11248 was synthesized in high radiochemical yield and purity. The high stability in human serum and urine samples, suggests that the tracer is not significantly metabolized. The ability of 5-Iodo-SU11248 to inhibit tyrosine kinase activity, a mandatory prerequisite for further studies on RTK expressing cells, is underway, to disclose whether this radiotracer would be a useful tool for monitoring VEGFR expression. Ultimately, the radiochemical profile of 5-[125I]Iodo-SU11248 associated to a low non-specific binding and rapid clearance from most tissues encourages further radiolabeling with other radioisotopes, such as 123I for SPECT or 124I for PET. [1] Sun L., Liang C. et al., J. Med. Chem., 46, (2003), 1116 [2] Kniess T., Oliveira C. et al., unpublished results

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Synthesis and evaluation of N-(3-[11C]methoxyphenyl)-4-trifluoromethylcinnamide: a radioligand for in vivo visualization of the TRPV1 receptor using PET

D. van Veghel¹, B. J. Cleyhens¹, K. Van Laere², A. Verbruggen¹, G. Bormans¹, ¹Laboratory for Radiopharmacy; K.U.Leuven, Leuven, BELGIUM, ²Nuclear Medicine; University Hospital and K.U.Leuven, Leuven, BELGIUM.

Aim: The TRPV1 (Transient Receptor Potential Vanilloid subfamily type 1) receptor is a non-selective cation channel, mainly expressed on primary sensory neurons TRPV1 plays a key role in the integration of noxious stimuli of chronic inflammatory pain or tissue injury. TRPV1 expression in several brain regions was demonstrated using *in vitro* autoradiography, but the exact role of these central TRPV1 receptors remains elusive. We have synthesized and evaluated carbon-11 labeled analogs of N-(3-methoxyphenyl)-4-chlorocinnamide which was reported to be a high affinity (18 nM) antagonist for hTRPV1. Here we will discuss carbon-11 labeled N-(3-methoxyphenyl)-4-trifluoromethylcinnamide. **Materials & methods.** N-(3-methoxyphenyl)-4-trifluoromethylcinnamide (**1**) was synthesized by the formation of a peptide bond between 4-trifluoromethylcinnamic acid and 3-methoxyaniline. The labeling precursor N-(3-hydroxyphenyl)-4-trifluoromethylcinnamide (**2**) was synthesized in four steps starting from 3-acetamidophenol and 4-trifluoromethylcinnamic acid. Both compounds were purified by column chromatography on silica gel and their structures were confirmed by MS and ¹H NMR. Carbon-11 was produced by a ¹⁵N(p, α)¹²C nuclear reaction in a Cyclone 18/9 cyclotron (IBA, Louvain-la-Neuve, Belgium) yielding [¹¹C]CH₃, which was converted to [¹¹C]MeI or [¹¹C]MeOTf in a home-built recirculation module. The obtained [¹¹C]MeI or [¹¹C]MeOTf was then bubbled through a solution of **2** in DMF in the presence of Cs₂CO₃. The reaction mixture was heated at 70 °C, diluted with water and purified with RP-HPLC, yielding [¹¹C]-**1**. The biodistribution in mice at 2 and 60 min p.i. of [¹¹C]-**1** was studied. **Results.** [¹¹C]-**1** was obtained with a radiochemical yield of \pm 80 % and the radiochemical purity was over 98 %. After intravenous injection of [¹¹C]-**1** in mice, brain uptake was high (1.8% ID at 2 min p.i.) and wash-out was rapid (0.2% ID at 60 min p.i.). [¹¹C]-**1** was also efficiently cleared from plasma (2 min p.i.: 6.0% ID; 60 min p.i.: 1.9% ID), mainly by the hepatobiliary pathway. Prominent is the retention of [¹¹C]-**1** in bone tissue (2 min p.i.: 0.7 % ID/g; 60 min p.i.: 0.7 % ID/g). **Conclusion.** N-(3-hydroxyphenyl)-4-trifluorocinnamide (**2**) was synthesized and efficiently labeled with carbon-11 to obtain compound [¹¹C]-**1**, which has favourable biodistribution characteristics in normal mice. Work is in progress to further evaluate the biological properties of [¹¹C]-**1**.

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Large scale SPECT isotopes production with IBA 30 MeV cyclotron

J. Geets, B. Nactergal, C. Fostier, M. Abs, W. Kleeven; IBA, Louvain la Neuve, BELGIUM.

Objectives: To reply to the increased demand of SPECT isotopes production, mainly 201-Tl to cope with 99Mo/Tc shortage for cardiac studies but also a high demand for 123-I, IBA has accomplished a development program on the Cyclone[®] 30 cyclotron with the aim of increasing beam current and lifetime. **Methods:** This contribution will show the latest results that have been achieved on the IBA Cyclone[®] 30 enhancement program. A new external powerful H⁻ ion source was used, a redesigned injection line and central region was installed onto a standard 30 MeV cyclotron. The new source is an external filament multicusp source. The acceleration power (RF) was upgraded using the IBA in-house expertise to 100 kW giving the power reserve for acceleration of 2mA of proton beam. Auxiliaries systems were upgraded (extraction, collimators,...) to cope with the new beam power. Consequently, the high power solid target system is developed with an optimised full process (plating, separation and recovery of isotope) for 201-Tl, 67-Ga and 111-In. **Results:** Major improvements are the results of a better vacuum and a short line with a good matching to cyclotron central region that enhance the beam current available in the machine. The inflector itself was improved to reach the highest injection possible in the cyclotron. The behaviour of the new ion source was excellent and showed an extended lifetime during factory testing. This high current Cyclone[®] 30 was shipped to the Customer in early 2010. **Conclusions:** The latests development has doubled the beam current available on Cyclone[®]30 cyclotron to 1.6 mA on target with a double production rate on new solid target (mainly for 201-Tl solid target). Target for 123-I production are adapted however the current limitation is lower on the 124-Xe gas target.

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Minimising radiation exposure of PET radiopharmacists following implementation of Tema uDDS-A automatic dose dispensing system and optimising work practices

J. G. Chan, K. J. Hickson, G. J. O'Keefe, K. Young, H. J. Tochon-Danguy, S. S. Poniger, A. M. Scott; Austin Health, Heidelberg VIC, AUSTRALIA.

Production of PET radiopharmaceuticals is increasing annually and this growth can potentially cause unnecessary increases in radiation exposure to staff if work practices are not reviewed. Currently the Radiopharmacy at Austin Hospital's Centre for PET draws around 4,500 doses per year of which over 4,000 are FDG doses. There has been an observed increase in finger dose to the radiopharmacist due primarily to the increased handling of manually dispensed FDG doses. It was for this reason that an automatic dose dispensing system was installed for the dispensing of FDG. The μ DDS-A Automatic Dose Dispensing System from Tema Sinergie allows the safe and rapid dose drawing of radiopharmaceuticals with high precision into shielded syringes or vials. Offering operator safety, the μ DDS-A also preserves the sterility of the radiopharmaceutical being dispensed as well as providing good data traceability. The μ DDS-A has been installed into a shielded laminar flow BSCII which is situated adjacent to hotcells containing FDG automated synthesis modules all within a dedicated clean-room. This poster presents the results of measured radiation exposure prior to and following the installation of the μ DDS-A. **Aim** To optimise the work practices of the PET radiopharmacist involved with FDG production to minimise radiation exposure. **Method** Radiation measurements have been performed using real time (calibrated AGEIS ED2-D) and passive (TLD) dosimeters. Measurements included a radiation survey of the ambient levels in the radiopharmacy and personal monitoring of the radiopharmacists. Levels have been compared pre and post optimisation. **Results** The determination of the yearly projected radiation dose to the radiopharmacist for FDG production was performed utilising real time monitoring methods. For whole body exposure this was approximately 4.1 mSv per year and a dose of 221 mSv per year to the hands. The radiation dose burden from all duties was recorded using TLD's and was found to be 4.5 mSv and 321 mSv for whole body and hand radiation doses respectively. Since the implementation of an automatic radiopharmaceutical dose dispenser, radiation exposure recorded to the hands by TLD measurements have fallen by 39%. Further optimisation has seen the ambient radiation levels fall by 15%. **Conclusion** It has been shown that by reviewing work practices that a significant decrease to radiation exposure can be achieved for the PET radiopharmacist enabling exposure rates to remain well below the radiation dose constraints required by law. Continued review of optimisation ensures that radiation exposure is kept as low as reasonably achievable.

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The study of Pharmacokinetics on ^{99m}Tc-N-ethyl-N₂S₂-Memantine with Pharmacokinetics Local Model

G. Cao¹, X. Zhou¹, Y. Liu², Y. Kong³, J. Zhang¹; ¹Jiangsu Institute of Nuclear Medicine, Wuxi, CHINA, ²Jiangnan University, School of Medicine and Pharmaceutics, Wuxi, CHINA, ³Department of Nuclear Medicine, Huashan hospital, Fudan University, Shanghai, CHINA.

Aim: To study pharmacokinetics of ^{99m}Tc-N-ethyl-N₂S₂-Memantine in the blood and the brain of mice with our pharmacokinetics local model. ^{99m}Tc-N-ethyl-N₂S₂-Memantine, a potential NMDA receptor imaging agent, was prepared in our laboratory. **Methods:** ^{99m}Tc-N-ethyl-N₂S₂-Memantine (0.2ml, 9.25MBq) was injected through tail vein into the mice(20-22g), which were divided into 8 groups (five per group, one group for the blood and the other for the brain) randomly. 10 μL blood samples were withdrawn from the tail vein at 5, 15, 30, 60, 120, 180 and 360min post-injection. The other groups of mice were sacrificed at the same time intervals post-injection, and tissues of the brain(thalamencephalon, hippocampus, frontal cortex, parietal cortex, temporal cortex, striatum and cerebellum) were removed and weighed. Radioactivities were counted with the γ -counter. Kinetic equations and parameters were calculated by our pharmacokinetics local model, which not only can calculate pharmacokinetics of the blood, but also can calculate pharmacokinetics of any tissue. **Results:** According to the calculation of pharmacokinetics local model, kinetic equations are: blood C = 3.8630e^{-0.050048t} + 1.4883e^{-0.000454t}, thalamencephalon C = 0.0597e^{-0.050048t} + 0.1274e^{-0.000454t}, hippocampus C = 0.0477e^{-0.050048t} + 0.0655e^{-0.000454t}, frontal cortex C = 0.0925e^{-0.050048t} + 0.1104e^{-0.000454t}, parietal cortex C =

$0.0611e^{-0.050048 t} + 0.0774e^{-0.000454 t}$, temporal cortex $C = 0.1192e^{-0.050048 t} + 0.0801e^{-0.000454 t}$, striatum $C = 0.0386e^{-0.050048 t} + 0.0645e^{-0.000454 t}$, and cerebellum $C = 0.0879e^{-0.050048 t} + 0.0488e^{-0.000454 t}$, respectively. Pharmacokinetics parameters of the blood were also calculated, k_{21} 0.0375 min^{-1} , k_{31} 0.0109 min^{-1} , k_3 0.0021, CL 0.0427 $\text{ID}\% \cdot \text{min}^{-1}$, AUC 2344 $\text{ID}\% \cdot \text{min}$, $t_{1/2\alpha}$ 13.8 min, $t_{1/2\beta}$ 1527.5 min and etc. Based on kinetic equations, pharmacokinetics parameters of the brain tissues were also calculated, such as peak value, peak time, half-excretion time and etc. **Conclusion:** The study of Pharmacokinetics shown that $^{99\text{m}}\text{Tc}^{\text{m}}\text{-N-ethyl-N}_2\text{S}_2\text{-Memantine}$ can accumulated in some brain tissues of mice, i.e. in thalamencephalon, frontal cortex and temporal cortex. The favourable uptake and suitable retention in these brain tissues confirmed that it may be a potential NMDA receptor imaging agent. **Acknowledgement:** This study are supported by the Jiangsu Natural Science Foundation (BK2008111) and the National Natural Science Foundation of China (30770602).

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A software for automated calculations of technetium-99m generator

J. L. Gómez-Perales¹, A. Varcía-Mendoza², M. E. Alcántara-Vargas¹,
¹Servicio Andaluz de Salud, Cádiz, SPAIN, ²Servicio Andaluz de Salud, Almería, SPAIN.

Introduction: In the day-to-day practice of a radiopharmacy it is important to know at every moment the available activity in a $^{99\text{m}}\text{Mo}/^{99\text{m}}\text{Tc}$ generator. The calculation of such activity is not too complicated, but it is annoying and time-consuming. **Objective:** The aim of this project is to develop a software to calculate $^{99\text{m}}\text{Mo}$ and $^{99\text{m}}\text{Tc}$ activities, elution efficiency, specific activity and other parameters in a $^{99\text{m}}\text{Mo}/^{99\text{m}}\text{Tc}$ generator. **Materials and methods:** We have written the solutions of the Bateman equations and other equations in Visual Basic 6.0 $A_{99\text{mMo}} = A_{99\text{mMo}}(0) \cdot \exp(-\lambda_{99\text{mMo}} t)$ $A_{99\text{mTc}} = A_{99\text{mMo}} \cdot 0.86 \lambda_2 [(\exp(-\lambda_1 t) - \exp(-\lambda_2 t)) / (\lambda_2 - \lambda_1)]$ $m_{\text{Tc}} (\mu\text{g}) = 1.9 \cdot 10^{-4} A_0 (m\text{Ci}) / F$ $F = \lambda_1 [(\exp(-\lambda_1 t) - \exp(-\lambda_2 t)) / 1.162 (\lambda_2 - \lambda_1) \exp(-\lambda_1 t)]$ where $\lambda_1 = ^{99\text{m}}\text{Mo}$ and $\lambda_2 = ^{99\text{m}}\text{Tc}$. **Results:** We have developed a form called Generator Calculator for automatic calculation of $^{99\text{m}}\text{Mo}$ and $^{99\text{m}}\text{Tc}$ activities, elution efficiency, specific activity and eluted mass of $^{99\text{m}}\text{Tc}$ and $^{99\text{m}}\text{Mo}$ in a $^{99\text{m}}\text{Mo}/^{99\text{m}}\text{Tc}$ generator. This form is included in as software called Nucleolab, which is freely available at <http://www.radiofarmacia.org/nucleolab-english/>. **Conclusion:** Generator Calculator is a new software, with an easy-to-use interface, that makes the calculation complexity of $^{99\text{m}}\text{Mo}/^{99\text{m}}\text{Tc}$ generator activities completely hidden for the user, saving you the time that you previously spent on these laborious calculations and reducing the risk of error.

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Software Tool To Ensure Traceability In The Prescription And Preparation Of Radiopharmaceuticals In A Hospital Radiopharmacy Unit

B. Martínez de Miguel, C. de Gracia González, R. Pérez Pascual, J. Vicente Castañeda, E. Martínez Montalbán, L. Roque Caballero, L. M. Martín Curto; Hospital Universitario La Paz, Madrid, SPAIN.

INTRODUCTION In a hospital radiopharmacy unit (URF) is very important the radiopharmaceutical traceability or audit trails of all elements involved in the preparation of radiopharmaceuticals. Our Unit receives a large number of prescriptions of radiopharmaceuticals by the Nuclear Medicine Department. (NMD) AIM implement the computerized control to ensure the traceability of medical prescriptions and preparation of radiopharmaceuticals in our URF. **MATERIALS AND METHOD** In the program for the prescription two applications are developed, one for the prescription by the nuclear medicine physician and the second one for the receipt of applications in the URF. In the program for the preparation it is a specific section for extemporaneous preparations, one for PET radiopharmaceutical and a third for in vivo-in vitro tests. **RESULTS** In the application of the nuclear medicine physician, it records patient identification, seeking radiopharmaceutical, dose and day of housing management. The program limits the prescription itself according to the agenda of the NMD and the time limitation set by laboratories. In the implementation of the URF are displayed in real time the different orders, which once required dose is recorded calls based on the calibration, date of arrival and order number, plus the signing of radiopharmaceutical. We can also have a history of all prescriptions and their status. In the program for the preparation introduces the daily work list from the requirements of the nuclear medicine physician. Write down the generator elution data (batch, quality control, activity eluted ...) and labelling (kit, batch, eluate used, and volume of activity and labelling responsible). Each individual dose of a particular patient is assigned to the corresponding radiopharmaceutical and also recorded dose. The same goes for live-vitro techniques. PET patients were assigned to a particular radiopharmaceutical and shipping (batch arrival activity, data quality control), noting activity and volume prepared and the calibration time and responsible for the preparation. It allows us to obtain a history of all the preparations and each patient, so knowing the identification number of the patient, we can get all the data on prescribing and preparing dose, as the name of kit, laboratory, batch, eluate used, quality control, responsible for the preparation, ensuring traceability. We can also obtain statistical analysis expenditure per patient and total spending. **CONCLUSION** This confirms the adequacy of programs to ensure traceability of products, becoming also an effective tool for a proper statistical analysis and maintain a history of a patient.

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Rules for a good preparation of radiopharmaceuticals in nuclear medicine. Structural and organizational adjustments at Villa Sofia Hospital, Palermo.

R. Badagliacca, F. Colombo, S. Carluccio, S. Ialuna, A. Moreci; O.U. Nuclear Medicine, Villa Sofia Hospital, Palermo, ITALY.

Background and Objective: A good preparation of radiopharmaceuticals in Nuclear Medicine (Italian Pharmacopoeia) require that the Nuclear Medicine departments individuate within July 1st 2010 a responsible for radiopharmaceuticals (RPs) Preparation, Quality Control (QC) and Certification to realize a "Quality System". Design: Quality, requirement for safety and efficacy, must be granted through a Certification Quality System which always allows to obtain a product pursuant to predetermined specifics. Nuclear Medicine departments where RPs are prepared

must organize and manage RPs preparation with the following activities: Quality Management, Staff, Documentation, Laboratory and Equipment, starting Materials, Preparation Operations, Preparation QC, Confection and Labelling, Preparation Stability, Microbiological Aspects of the RPs. Setting: Nuclear Medicine Department of Villa Sofia Hospital has identified the elements functional to the Department requalification and the placing in safety of radiochemistry patterns, has provided for a specific nominative organization chart and endowed itself with a documentation system of RPs preparations. Main Outcome Measures: The flow-chart includes: a general responsible person; a responsible for quality certification; a person responsible for preparation operations; a person responsible for quality controls; a person responsible for the final authorization. The person responsible for the final authorization controls that the preparation is pursuant to CQ specifics necessary to the authorization and that the preparation has been made according to the present rules for a good preparation. An appropriate set of preprinted forms has been arranged in order to identify the various parts of the production process and to allow the filing and documentation of every preparations (preparation, confection, labelling and quality controls, the management of every organizational and logistic aspects necessary to grant, with respect of environmental and sterility conditions, the compilation of periodical maintenance programs for the preparation control instruments in conformity with pharmacopoeia and/or supplier firm's provisions). Results: every preparation and RPs QC phases has been described in Standard Operative Procedures (SOP) updated and reviewed. Batch records and CQ documentation are stored for at least a year after the limit date of patient administration in case of well established preparations, and for at least two years for preparations in progress. Conclusions: In our experience SOP allowed to realize RPs preparations in accordance to good laboratory and clinic practice rules. The work continues in order to optimize the activities of the Nuclear Medicine Department, with respect to the rules of patients and workers safety in a sustainable way from both an economical and an organizational point of view.

P166

Alternative method thyroid block with iodine solution prior to the administration of 123I-lofupane

J. P. Diaz Alarcon, M. Bermudez Morales, M. J. Urena Lara; Complejo Hospitalario De Jaen, JAEN, SPAIN.

INTRODUCTION Blocking the uptake of radionuclides by the thyroid is used to reduce radiation dose. Of the radionuclides commonly used in nuclear medicine, only technetium and iodine are concentrated by the thyroid, although technetium no need to use blocking agents. **OBJECTIVES** - Check whether a single administration of iodine solution (Lugol's Iodine) (0.8 ml) 90 minutes prior to administration of 123I-lofupane, is sufficient to cause thyroid blockade, compared to the traditional administration of potassium iodide (specified in the technical leaflet of the Datscan®) or iodine solution (5 drops every 8 hours) 48 hours prior. - Assess the benefits of this new method. **MATERIAL AND METHODS** The thyroid blocking was conducted by administrating the patient 0.8 ml of 5% oral iodine solution, equivalent to 100 mg of Iodine, 90 minutes before the injection of 123I-lofupane and 24 hours thereafter. Finally, in a number of patients randomized block effectiveness checks by planar scintigraphy focusing on thyroid area (Siemens Gamma camera and dual-cam head). **RESULTS** 281 patients were treated with iodine solution and 20% (56 patients) found thyroid blocking. In 100% of cases the blockade was effective. **CONCLUSIONS** 1. - Applying this procedure we get an effective thyroid blocking. 2. - We improve the design and cost, as the iodine solution is more stable than the potassium iodide (date of expiry of 3 months vs. 15 days). 3. - We increase security and patient comfort, since its administration in the Department of Nuclear Medicine is making sure the intake and at the same time we avoid a previous posting, the days before the test, to collect iodine.

P167

Stability of 99mTc-DTPA and 99mTc-Rhenium Sulfide Nanocolloid. A Comparison for Solid Gastric Emptying Studies

G. Pla, B. López, S. Aguadé, M. Quera, B. Soriano, J. Castell; Vall d'hebron, Barcelona, SPAIN.

Aim Solid gastric emptying studies require a meal where the radiolabeled solid is an omelette. Thus the radiopharmaceutical employed should have among other characteristics resistance to heat and gastric pH (1.4-4). This work was set to test and compare $^{99\text{m}}\text{Tc-DTPA}$ (diethylene triamine pentaacetic acid) and $^{99\text{m}}\text{Tc-SC}$ (rhenium sulfide nanocolloid) stability by means of radiochemical purity (RCP) after exposure to heat, whole liquid egg and different hydrochloric acid concentrations (HCl), the latter to determine the range of gastric pH in which they could remain stable. **Materials and methods** Samples of both $^{99\text{m}}\text{Tc-DTPA}$ and $^{99\text{m}}\text{Tc-SC}$ (37 MBq/0.2 mL) were submitted to 15 different combinations with heat to the boiling point, whole liquid egg (0.2 mL) and an excess of HCl (0.2 M; 0.08 M; 0.04 M; 0.01 M). The reaction pH of each series was measured with pH paper. RCP of $^{99\text{m}}\text{Tc-DTPA}$ and $^{99\text{m}}\text{Tc-SC}$ series was tested by the manufacturer's recommended method. The developed test strips were cut into two sections at the middle pencil line and each section was placed into test tubes and counted in a scintillation well counter (LKB-Wallac 1282). The assay was performed three different times and each of these by triplicate. Mean values were calculated. **Results**

Series		% RCP $^{99\text{m}}\text{TcDTPA}$	% RCP $^{99\text{m}}\text{TcSC}$
Control	Control	99.17	98.90
	HCl 0.2 M	56.81	91.23
Room temperature	HCl 0.08 M	83.48	92.87
	HCl 0.04 M	96.19	97.80
	HCl 0.01 M	98.10	97.77
	Control	99.07	97.10
Heat	HCl 0.2 M	57.40	88.27
	HCl 0.08 M	80.00	85.75
Heat	HCl 0.04 M	94.70	96.60
	HCl 0.01 M	98.80	96.00
Room temperature	Control	99.91	98.83

Egg	HCl 0.2 M	63.06	97.70
	HCl 0.08 M	97.99	98.73
	HCl 0.04 M	98.15	98.80
	HCl 0.01 M	99.05	98.43

Conclusion Although better results with ^{99m}Tc -SC than with ^{99m}Tc -DTPA are obtained both radiopharmaceuticals seem to be stable from 0.04 M HCl (pH 1.4) to lower concentrations meaning that they are resistant to gastric pH. Moreover the addition of egg extends their stability due to its buffer effect. Heat seems not to alter any of both radiopharmaceuticals.

P168

Preparation of ^{99m}Tc -PQQ and Blood kinetic studies

X. Zhou, Y. Kong, J. Zhang, G. Cao; Jiangsu Institute of Nuclear Medicine, Wuxi, Jiangsu Province, CHINA.

Objectives: Pyrroloquinoline quinone (PQQ) was identified as a novel co-factor in various bacterial alcohol dehydrogenases. Few data are available, however, on the metabolism of PQQ in mammalian tissues. The absorption, distribution and excretion of PQQ have been studied using ^{14}C labeled. The present study was undertaken to evaluate the blood kinetic of PQQ in mice by labeling ^{99m}Tc with the SnF_2 method. **Methods:** ^{99m}Tc -PQQ was prepared by using stannous fluoride method. A series of studies were performed to optimize labeling efficiency of ^{99m}Tc -PQQ by varying the pH value, varying the amount of PQQ, $\text{SnF}_2 \cdot 2\text{H}_2\text{O}$, EDTA-2Na and GH , labeling yield was measured by RHPLC. 9.62 MBq of the ^{99m}Tc -PQQ (0.2 mL) was administered intravenously through the tail vein to ICR mice ($n=6, 25 \pm 3\text{g}$), 10 μL blood samples were withdrawn from the tail vein at different time after intravenous injection, and radioactivity was measured in the gamma counter. **Results:** The maximum radiolabeling yield of ^{99m}Tc -PQQ was 94% under optimum conditions of 0.99 mg of PQQ, 30 μg of $\text{SnF}_2 \cdot 0.5\text{mg}$ of EDTA and 0.05–0.1 mL of $\text{Na}^{99m}\text{TcO}_4$ (14.8–18.5 MBq) at pH 6.0 and 25 °C with a response volume of 1 mL. ^{99m}Tc -PQQ was stable up to 5 h at 25 °C in aqueous solution and radiochemical purity was over 90% at selected condition. The two-phase blood clearance half-times $[(t_{1/2})_{\text{al}}$ and $(t_{1/2})_{\text{bt}}$] were 18.1568 and 100.4532. A dual-exponential equation was $Y=10.875819e^{(-0.038188t)}+5.214271e^{(-0.0008899t)}$. **Conclusions:** ^{99m}Tc -PQQ was successfully prepared. Labeling yield and radiochemical purity were all over 90% with good stability. The further study on biological evaluation and radioligand receptor binding assays will be needed. **Research Support:** Project supported by National Natural Science Foundation of China (30770602).

P169

Performance analysis of $^{68}\text{Ge}/^{68}\text{Ga}$ generator and radionuclidic purity from the eluate to the final ^{68}Ga -DOTATOC product using a commonly available NaI well detector

S. Papi, F. Botta, A. Di Dia, L. Gariboldi, L. Martano, M. Chinol, G. Paganelli; European Institute of Oncology, Milano, ITALY.

Aim: ^{68}Ga PET radiopharmacy impact is more and more growing due to its favourable characteristics; nevertheless, ^{68}Ge contamination has to be monitored, representing a potential irradiation risk. In this work we analyze the yield performance of our commercial $^{68}\text{Ge}/^{68}\text{Ga}$ generator routinely used for the synthesis of ^{68}Ga -DOTATOC, along with the ^{68}Ge breakthrough both in the eluate and in the final formulation utilizing a low cost NaI well detector. **Materials & Methods:** All the experiments were performed using a 8 months old $^{68}\text{Ge}/^{68}\text{Ga}$ generator (Eckert & Ziegler 1.1 GBq). Elutions were carried out at different times, with different time gap between elutions, to evaluate any possible influence of radiolysis on the release of ^{68}Ge and on elution yield. Activity of ^{68}Ga eluted was counted in a dose calibrator (Isomed 2000), whereas ^{68}Ge was analyzed upon decay of ^{68}Ga inside a NaI well detector (Silena SNIP) coupled with a multi-channel analyzer. Quantitation of the 511 keV photopeak counts was carried out with a dedicated software (Genie 2000) and conversion to Bq of ^{68}Ge was extrapolated by a reference calibration in efficiency. To verify the efficiency (cps/Bq) calibration, the factor was studied by different reference solutions of ^{68}Ga . Since our synthesis module performs a timed fractionated elution, ^{68}Ga was collected in two fractions: a) the activity usually channelled to reactor and b) the activity diverted to waste. After synthesis, a C_{18} light (Waters) cartridge purification is carried out; therefore, different batches of ^{68}Ga -DOTATOC were analyzed upon decay, to evaluate residual ^{68}Ge in the final formulation. **Results:** Efficiency calibration for ^{68}Ga was found constant over decay (median 0.172 cps/Bq, range 0.167–0.180). No correlation was found between total ^{68}Ge leakage and age of the generator, data being in the range $0.3\text{--}1.9 \times 10^{-10}\%$; moreover the reactor fraction of eluate contained only 30–40% of total ^{68}Ge breakthrough (median 227 Bq, range 79–670 Bq). Total elution yield and reactor ^{68}Ga activity were found reproducible (86% and 73% respectively). $^{68}\text{Ge}/^{68}\text{Ga}$ ratio was always below the safe value of 10 Bq/MBq (Eur. Pharm v7 draft) both in the reactor (median 0.5, range 0.2–1.3 Bq/MBq) and waste (median 4.7, range 1.9–7.8 Bq/MBq) fractions. Nevertheless, no ^{68}Ge contamination was detectable in purified ^{68}Ga -DOTATOC. **Conclusion:** The performance of the $^{68}\text{Ge}/^{68}\text{Ga}$ generator fractionated elution is safe and reproducible, giving high ^{68}Ga yields with negligible amounts of ^{68}Ge during synthesis that are discarded after purification. Being ^{68}Ge the only potential radionuclidic contaminant, a NaI well detector seems to be a suitable choice for routine analyses.

P170

Automated Production of N-([^{11}C]Methyl)benperidol ([^{11}C]NMB) for Clinical Application.

S. M. Moerlein, J. LaVenture, G. G. Gaehle, J. Robben, J. S. Perlmutter, R. H. Mach; Mallinckrodt Institute of Radiology, Washington University, St. Louis, MO, UNITED STATES.

Aim: The goal of this work was to develop a reliable means for the routine production of the D2-specific radioligand [^{11}C]NMB for clinical application in human subjects. Although [^{18}F]NMB is used in clinical studies, until now NMB labeled with carbon-11 has not been available for use in humans. **Materials and Methods:** We have adapted our previously-described synthetic pathway (Moerlein, et al. Radiochem Acta 2004; 92: 333–9) to a fully-automated module. The chemistry module is operated using digital and analog I/O modules (Arcus Technology, Livermore, CA)

connected to a PC through a USB port. The device is controlled by a Visual Basic program that requires operator verification of cleaning and setup steps. As the synthesis proceeds, the control software input/output statements systematically verify the process. Components used in the module were selected based on chemical resistance, and are inexpensive to assemble and easily replaced. All supplies, including tubing and reagent containers, are disposable, which greatly simplifies cleaning and maintenance of a sterile, pyrogen-free drug production environment. The labeling precursor (benperidol) for the N-([^{11}C]methyl)ation reaction was obtained from Janssen, and NMB standard was from ABX (Radeberg, Germany). [^{11}C]CO₂ was produced using the Washington University JSW-16/8 cyclotron, and converted to [^{11}C]methyl iodide using a GE PETrace processor. Preparative HPLC was used to isolate the drug product (stationary phase: Phenomenex Luna 5 μm C-18(2) 100 Å 250 x 10 mm; mobile phase: acetonitrile / 25 mM potassium phosphate buffer (1/1); flow rate: 3.5 mL/min). The retention time for NMB is 18–20 min, whereas that for benperidol is 12–13 min. The HPLC eluent containing product [^{11}C]NMB is diluted in aqueous base solution, and the radiolabeled compound is isolated onto a Waters C-18 Sep-Pak cartridge. [^{11}C]NMB was reformulated in 10% EtOH solution. Terminal sterilization of the product was achieved using an in-line 0.22 μm filter, which was tested for membrane integrity prior to drug release. **Results:** Batch yields of 1.5–3.0 GBq of [^{11}C]NMB are routinely obtained using this methodology. The drug is produced with a radiochemical purity exceeding 98.8% and specific activity of 131–158 Tq/mmol. Overall preparation time is 51–53 min after EOB, and the entire procedure is automated to minimize radiation burden to personnel. **Conclusion:** This inexpensive automated module reliably produces [^{11}C]NMB that meets all regulatory requirements for drug purity and suitability for clinical use.

P171

Design and performance of a new automatic radiopharmaceuticals system for patient administration

A. Fedele¹, G. Cicoria², S. Piancastelli¹, M. Marengo², ¹TEMA Sinergie S.r.l., Faenza, ITALY, ²University Hospital "S. Orsola-Malpighi", Bologna, ITALY.

Introduction: The increasing use of radiopharmaceuticals involving significant radiation exposure during administration, both in diagnostic procedures (such as 18F-FDG), and in therapy (such as 90Y-Zealini), leads to an effort to constantly reduce staff's dose. These demands lead to the necessity of developing automatic systems for dispensing of individual patient's doses, reducing the direct exposure of the operator to the radioactive substances during preparations, as well as of automatic system for patient administration. Materials and methods: The Rad-Inject automatic infuser has been built in order to reduce the dose absorbed by the operator during administration. The infuser is set up to be used together with the $\mu\text{DDS-A}^{\text{TM}}$ fractioning unit, that allows to prepare the exact amount of FDG inside dedicated 10 ml syringes. It has been conceived around an approved medical device, by adding the necessary protection in order to allow safe administration of radiopharmaceuticals. The infuser has a double shielding, the first one containing the syringe and that must be inserted inside the second, put on the stand of the system. The resulting assembly has a limited footprint and its use is straightforward by nurses and technologists. The system has been initially tested for administration of 18F-FDG; operational parameters, like infusion time, number of syringe washing cycles, etc. and can be easily configured; not only, but it is easy adapted to other radiopharmaceuticals, including therapeutic beta emitters. **Results:** administration time is 1 minute; the residual activity in the syringe resulted to be around 1 MBq with only 2 washing cycles. In the first operational tests, dose reduction to the technologist/nurse performing the administration showed to be at least 50%, compared to conventional administration procedures. Moreover, even if the possibility of manual preparation of patient doses is preserved, the association with an automatic dose dispensing system assures traceability of doses and substantially reduces the risk of misadministration. **Conclusions:** the Rad-Inject promises to be a powerful tool for radiation protection of the staff in the administration of radiopharmaceuticals and to increase patient's safety; the Rad-Inject has been CE certified as an approved medical device.

P172

A Proposal for Phosphor Imager Acceptance Testing Procedure and Routine Quality Controls in Nuclear Pharmacy Practice.

N. Urbano, G. Nardella, G. Lizzadro, G. Santopietro, S. Modoni; Medicina Nucleare, Azienda Ospedaliero-Universitaria "Ospedali Riuniti", Foggia, ITALY.

The digital autoradiography system (Cyclone, PerkinElmer Inc.) is currently used in nuclear medicine for quantitative imaging of radioactivity distribution (TLC samples, tissue sections, cell cultures). Hence, the quantitative and effective evaluation of instrument performance (Multi-Sensitive Medium phosphor screen and Photometer) is recommended for quality assurance. **Aim** of this study was to define a set of tests (uniformity, resolution, linearity, response) for setting up a specific acceptance testing procedure and routine quality controls for this instrument. **Materials and methods.** Over a 3-months period, we weekly performed the following tests either on the phosphor screen (25.2 * 12.5 cm) and photometer. Quantization was performed by OptiQuant software. Photometer Uniformity was performed by photographic white paper scanned with 600 dpi resolution for 10min. Screen Uniformity was performed by suitable flood phantom filled with de-ionized water containing 3.7 MBq of ^{99m}Tc kept in contact with phosphor screen for 60 sec. In both uniformity measurements, the field of view was subdivided in a grid of squares (46columns - 21rows), each with 0.25 cm² area (UFOV). The central surface of the grid (34columns - 13rows) was CFOV. Uniformity was evaluated by visual inspection and calculation of smoothed (nine-points) Integral (IU) and Differential Uniformity (DU) in UFOV and CFOV, respectively, from the Digital Light Units (DLU) measured in each square. Photometer Geometric Resolution was performed by scanning a photographic black paper with white bars (width 0.5 - 1 - 2 cm) Screen Resolution and geometric linearity were performed by suitable phantom consisting in a lead plate with an array of holes (24 columns - 12 rows; hole diameter 2mm; hole distance 10mm). This phantom was interposed between uniformity flood phantom and phosphor screen. Resolution was expressed as Full Width at Half Maximum (FWHM). Linearity was evaluated by visual inspection. Screen Response Linearity was performed by ^{137}Cs (3.7 MBq) standard source. **Results.** Photometer IU was 17.4±0.2% (UFOV) and 13.7±1.1% (CFOV). Photometer DU ranged between 1.9±0.9% and 2.3±1.2% for UFOV and between 1.9±0.8% and 2.1±1.1% for CFOV. Screen IU was 19.7±2.3% (UFOV) and 11.1±3.7% (CFOV). Screen DU ranged between 1.6±1.1% and 1.8±0.9% for UFOV and between 1.2±0.4% and 1.4±0.6% for CFOV.

Photometer resolution was good (FWHM=0.5±0.076mm). Screen resolution (FWHM) was 1.94±0.08mm. Screen Response Linearity ranged between -3.5% and +2.8% with reference to the mean of measured values. **Conclusions.** Our data suggest that the methodology we propose could be an easy, accurate, quick and low-cost tool for routine quality controls.

P16 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Radiopharmaceuticals & Radiochemistry & Dosimetry: Radiopeptide therapy & dosimetry

P173

The neo-adjuvant role of Peptide Receptor Radionuclide Therapy (PRRT) with ⁹⁰Y-DOTATOC in gastro-entero-pancreatic (GEP) Neuroendocrine tumour (NET): lesion down-staging and surgery chance in patients with a primary diagnosis of inoperable pancreatic NET.

V. Mattone, C. Fabbri, M. Casi, F. De Lauro, M. Agostini, S. Vecchio, G. Marchi, M. Venturi, M. Bartolomei, Bufalini Hospital, Cesena, ITALY.

Aim. We have retrospectively analyzed the outcome of some inoperable patients, affected by GEP NET, who could obtain a surgery treatment after PRRT with ⁹⁰Y-DOTATOC. **Materials & Methods.** During the last 3 years 50 patients (pts) affected by NET (80% with GEP tumour), over-expressing subtype 2 an 5 somatostatin receptors, underwent PRRT with ⁹⁰Y-DOTATOC. Most of them presented metastases principally involving the liver and abdominal lymphnodes. After accurate evaluations (CT or MRI, OctreoScan® or 68Ga-DOTANOC, Blood cell-count and creatinine value) pts received a mean cumulative injected activity of 8.4 GBq (range 6.7-12) divided into 4-5 intravenous administrations, 6-8 weeks apart, and appropriate Lysine infusion for renal protection. We focused on objective response, toxicity and absorbed dose (in terms of biological effective dose - BED) to lesions and kidneys. **Results.** Partial response was gained in 19/50 pts (38%), the same percentage obtained a stable disease, while 12 pts (24%) progressed. The median cumulative BED to tumour and kidney was 133 Gy (range 33-487) and 39.5 Gy (range 9.5-85), respectively. Reversible grade 1 bone-marrow toxicity and mild increase of serum creatinine were reported in 22% and 8%, respectively. Six out the 19 pts, who obtained a partial response, presented, at enrolment for PRRT, a inoperable pancreatic primary tumour with a low grade of proliferation (Ki67 <2%): in 4 of them, hepatic (3 pts) and local lymph node (1 pt) metastases were also present. They received a mean cumulative injected activity of 9.4 GBq (range 7.2-11.5) and median cumulative BED to primary tumour of 279.1 Gy (range 89.2-297.7). Evaluation after PRRT demonstrated a complete resolution of NET-related symptoms, a significant volume decrease of pancreatic lesions, ranging from 60 to 80% (RECIST criteria) and disappearance of metastases. Moreover, no renal and haematologic toxicity was reported (WHO criteria). Subsequently, they were treated with surgery, obtaining further benefits. **Conclusions.** According to the evidence in literature, PRRT with ⁹⁰Y-DOTATOC can be considered, at present, an useful tool to control NET disease. In selected cases, PRRT with ⁹⁰Y-DOTATOC might have an important role as a neo-adjuvant treatment, with the final aim to modify the course of disease by increasing overall survival and improving quality of life.

P174

⁶⁸Ga-DOTATOC PET/CT after 1 cycle of PRRT with ⁹⁰Y-DOTATOC visualizes changes in somatostatin receptor availability in neuroendocrine tumours

S. Van Binnebeek¹, F. M. Mottaghy², M. Koole¹, K. Baete¹, B. Vanbilloen¹, C. Terwinghe¹, P. Clement¹, A. Verbruggen¹, L. Mortelmans¹, E. Van Cutsem¹, K. Haustermans¹, C. Verslype¹, C. M. Deroose¹; ¹UZ Leuven, Leuven, BELGIUM, ²UK Aachen, Aachen, GERMANY.

Aim Peptide receptor radionuclide therapy (PRRT) addressing the somatostatin receptor (SSR) has emerged as a powerful palliative therapy in neuroendocrine tumors (NETs). Different trials showed complete and partial response rates in the range of 10-30%. Approximately 50% of patients show disease stabilization. One important factor predicting response to therapy, is the degree of SSR expression, determined by SSR scintigraphy. There are currently no validated tools that allow early therapy response assessment after 1 treatment. In this prospective study we investigate the early effect of 1 cycle of PRRT with 1.85GBq/m² ⁹⁰Y-DOTATOC on SSR availability as assessed by ⁶⁸Ga-DOTATOC-PET/CT. **Materials and methods** In 11 patients with proven diagnosis of disseminated NET, we compared uptake in metastatic lesions on ⁶⁸Ga-DOTATOC-PET/CT before and 7 weeks after a first cycle of PRRT with ⁹⁰Y-DOTATOC. Both PET/CT scans were dynamically acquired during 30 minutes after injection of 185MBq. In every patient the same 4 to 6 lesions were delineated manually using PMOD-software in both scans and standard uptake values (SUV_{max}) in the last frame were analysed and compared (paired t-test, significant if p<0.05). **Results** In 3 patients, the uptake on ⁶⁸Ga-DOTATOC-PET/CT was significantly lower after one treatment with ⁹⁰Y-DOTATOC. In 2 patients a significant increase was observed. The other 6 patients showed no significant changes between both scans. The change between both scans, on averaged SUV_{max} for all assessed lesions, ranged from -32.5% to +37.2%. **Conclusion** Early imaging after one cycle of PRRT with ⁹⁰Y-DOTATOC reveals changes in SSR availability. The significance of these changes still needs to be determined and correlated with long term ⁶⁸Ga-DOTATOC-PET/CT and clinical therapeutic outcome. If these changes allow to discriminate a fraction of responders or non-responders, early ⁶⁸Ga-DOTATOC-PET/CT may guide a fraction of patients to discontinuation of therapy, limiting thereby toxicity and costs within these patients. Further study in additional 35 patients is ongoing.

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Assessment of effectiveness and toxicity of the therapy with somatostatin analogue labelled ⁹⁰Y-DOTATATE in patients with non-functional pancreatic neuroendocrine tumours (PNT)

A. Sowa-Staszczak¹, D. Pach¹, A. Stefańska¹, M. Tomaszuk¹, R. Mikołajczak², D. Pawlak², M. Trofimiuk¹, M. Opalińska¹, R. Chrzan³, A. Hubalewska-Dydejczyk¹; ¹Nuclear Medicine Unit Endocrinology Department, Jagiellonian University, Medical College, Krakow, POLAND, ²Research and Development, IAE Radioisotope Centre POLATOM, Otwock-Swierk, POLAND, ³Department of Radiology, Jagiellonian University, Medical College, Krakow, POLAND.

Introduction: Therapy with labelled somatostatin analogues is the modern approach to the patients with disseminated or unresectable NETs expressing somatostatin receptors (SSTR). Octreotate is the somatostatin analogue with very high affinity to the SSTR type 2, most commonly present in neuroendocrine tumours. In non-functional PNT, grading and systemic metastases have a significant impact on survival. Up to 60% of non-functioning endocrine pancreatic tumours are already metastasized at diagnosis. Overall, the 5-year survival rate is about 33%. The chemotherapy is the most common treatment approach. **The aim of the study** was to assess the efficacy and toxicity of peptide receptor radionuclide therapy (PRRT) with the use of the high affinity somatostatin receptor subtype 2 analogue, ⁹⁰Y labelled Tyr3-octreotate, (⁹⁰Y-DOTATATE) in non-functional pancreatic neuroendocrine tumours. **Material and methods:** 19 patients with metastatic NET were diagnosed in the Department of Endocrinology UJCM. 5 patients with high proliferation index (Ki >20%, 4- negative SRS, tumour size 3-7cm) were directed to chemotherapy. 14 patients with positive SRS scan due to disseminated and/or inoperable PNTs (2 patients) were qualified to PRRT (6 men, 8 women, mean age 54,7 years old, Karnofsky's index > 70-100%). The size of the tumour was 2,3-12cm, Ki-67 was <15%, the most frequent localization was in the tail of the pancreas. Each patient received 7,4 GBq/m² of PRRT divided in 4-5 cycles (most often 100mCi per cycle), every 6 to 9 weeks. For nephroprotection amino-acids formula Vamin 18, before and after each cycle of PRRT, was administered. **Results:** Among all patients partial remission was observed in 14% of cases, stabilization in 64% and progression of the disease in 22% of patients. 2 patients due to progression of the disease received additional cycles of PRRT. The mean observation time was 17,2 months. The mean time to progression was 14,5 months. 4 patients died. After the treatment the creatinine level was 96,37 umol/l. Mean platelets level was 231 000/ul. Mean hemoglobin level was 10,9 g/l. In one patient the value of Hb was assessed as toxicity grade 3. Mean leukocytes level was 5530/ul. **Conclusion:** 1. After PRRT, stabilization of the disease was observed in the majority of patients. 2. PRRT did not cause myelotoxicity and nephrotoxicity.

P176

The Accuracy of Adaptive Thresholding for Estimating Individual Patient Organ Volumes and Activities for Patient-Specific Dosimetry Calculations

J. Grimes¹, B. Birkenfeld², A. Celler¹, S. Shcherbinin¹, M. H. Listewnik², H. Piwowarska-Bilska², P. Zorga²; ¹University of British Columbia, Vancouver, BC, CANADA, ²Pomeranian Medical University, Szczecin, POLAND.

Aim: In targeted radionuclide therapy, patient-specific dose calculations require accurate region volume and activity estimates. To obtain these estimates, tumour and organ segmentation in SPECT images is commonly done using thresholding. We have used the adaptive thresholding approach, in which the threshold is chosen based on the signal to background ratio (SBR) of activity for each region of interest. The aim of this work was to verify the consistency of SPECT reconstructions and the use of the adaptive thresholding technique by checking reproducibility of source region volume and activity estimates derived from SPECT/CT scans acquired at 2 consecutive time points. **Materials and Methods:** Five patients with suspected neuroendocrine tumours were injected with 810-980 MBq of Tc-99m Tektrotyd followed by a series of nuclear medicine scans that included 3 WB scans at 2, 4 and 24 hours and 2 SPECT/CT scans in succession at 3 hours following injection. The shape of time-activity curves (TACs) were determined from a monoexponential fit through the counts in tumours, kidneys, liver, and spleen on the WB images. These regions were segmented in the SPECT images using three different thresholds of maximum counts: 1) 40%, which is commonly recommended in the literature, 2) the adaptive threshold for estimation of true volume (ThV) and 3) the adaptive threshold for estimation of true activity (ThA). ThV and ThA were each determined using recovery curves (threshold versus SBR) obtained from phantom experiments. For all thresholds, the volumes and activities of each region estimated from the 2 consecutive SPECT images were compared. Activity in each region at the second time point was corrected for decrease of radioactivity using the effective half-life determined from the exponential fit. **Results and Conclusion:** The average percent differences (+/- standard deviation) between volumes segmented in the 2 SPECT images were -1.3% +/- 6.7% using the 40% threshold and -0.7% +/- 4.5% using ThV. Although the 40% threshold produced reasonable reproducibility in organ volume estimates, organ boundaries drawn on CT slices indicated that this threshold underestimated organ volumes. Use of ThV resulted in more consistent organ volume estimates compared to the 40% threshold, in addition to better agreement with the organ boundaries drawn on CT. Activity estimates from both scans, obtained using ThA, differed by 0.2% +/- 6.0% on average. These results indicate that volume and activity estimates determined from SPECT images are reproducible and can be consistently obtained through the use of adaptive thresholding.

Table 1. Percent differences in volume and activity estimates determined from 2 SPECT images

% Difference	Volume		Activity
	40% Threshold	ThV	ThA
Mean +/- SD	-1.3 +/- 6.7%	-0.7 +/- 4.5%	0.2 +/- 6.0%
Range (min - max)	-10.8 -11.3%	-7.8 - 7.3%	-7.9 - 12.9%

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A method of quantitative analysis for patient-specific dosimetry with ¹¹¹In quantitative SPECT-CT imaging

E. Grassi, E. Mezzenga, F. Fioroni, D. Farioli, A. Versari, M. Iori, S. Maria Nuova Hospital, Reggio Emilia, ITALY.

Purpose The important change from planar to hybrid tomographic imaging of SPECT-CT implies a gain in the accuracy of the organ/lesion absorbed dose assessment as highlighted in literature.

For this purpose gamma-camera scanners are to be characterized to obtain a valid quantitative SPECT-CT imaging. The aim of this work is a more accurate computation of the activity retained in organs at risk and in lesions. **Material** An anthropomorphic phantom (Anthropomorphic Torso Phantom, Data Spectrum Corporation, Hillsborough, North Carolina, USA) with organs and added lesions inserts was filled with different activity concentrations of ^{111}In . It was scanned with a hybrid Siemens Symbia T SPECT-CT at different time points over a period of a week. The acquisition parameters for ^{111}In were: matrix 128x128, 32 frames, 40 s/frame, circular orbit. The projections were reconstructed with the Siemens Flash 3D algorithm with a variable number of iterations and subsets (cubic voxel of 4.8mm). Images were corrected for attenuation, scatter and response of the collimator by the reconstruction algorithm. The organs/lesions VOIs around the inserts were drawn on CT slices by means of Siemens Volumetric Analysis software and the mean counts inside these volumes were evaluated by SPECT images. A calibration factor to convert counts in activity was computed in function of insert dimensions and of the algorithm parameters. In accordance with MIRDO pamphlet 16 the time-activity curve of our SPECT phantom was considered to value the physical half-time. **Results** Accuracy on the decay half-time evaluation was around 4 per cent compared to the real value. The calibration factor curve showed a dependence in function of the reconstruction parameters and of the insert dimension. This latter case was evident for smaller volumes (<15cc), because of the partial volume effect. The better compromise between acquisition statistics and subset and iteration number is the combination of 4 iterations and 4 subsets (4i4s), though the combination 8 iterations and 8 subset should be better if a good statistics was available. The extrapolated equation for 4i4s images is: $y=120.149.8*(\exp(-0.133*x))$, where x is the volume (cc) of the organ or lesion considered and y is the counts-to-activity conversion factor (cps/MBq). **Conclusion** The scanner characterization allows us to implement a method to perform a quantitative 3D dosimetry in patient administered with radiolabelled peptides such as DOTATOC. Our work is intended to be completed by testing the method with real patient dosimetry (administered with nearly 185MBq of ^{111}In -DOTATOC) and other isotopes.

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Determination of a SPECT Calibration Factor for Dosimetric Calculation in 177-Lu-Dotatate Therapy

R. de Nijs, S. Holm, T. L. Klausen, T. Heiberg, P. Oturai, J. Mortensen; Rigshospitalet Copenhagen University Hospital, Copenhagen, DENMARK.

Aim Neuroendocrine tumours can be treated with targeted Lu-177-Dotatate therapy. For dosimetric calculations the absolute activity distribution is calculated from the relative count concentration in a SPECT-image. The needed calibration factor was determined in a phantom and five patients. **Materials & methods** Patients were administered 5.3-7.4 GBq Lu-177-Dotatate and scanned on the day of treatment (day 0) and 1, 4 and 7 days later. Planar scans were used for monitoring total activity and for calculating the activity fraction in the SPECT field of view. Normally no SPECT-scan is acquired at day 0. The phantom (NEMA2007/IEC2008), a 10 liter perspex container with six spheres (10-37 mm in diameter), was filled with 550 MBq Lu-177 (55 MBq/L) and the spheres were filled with an activity concentration 8.2 times higher (450 MBq/L). Measurements were performed on a Philips Precedence SPECT/16MDCT scanner. Whole body planar and SPECT/CT scans were acquired with MEGP parallel hole collimators and SPECT scans were acquired over 360 degrees at 128 angles (20 seconds per angle). The main 20% energy window was set at 208 keV with two abutting 10 keV correction windows. CT-images (140 kVp) were used for attenuation correction. SPECT reconstruction with and without scatter correction was performed with 3D-OSEM and Astonish (Philips). The calibration factor was determined for this set-up, but depends on total scan time. **Results** Results are given as mean with population standard deviation for reconstruction with Astonish with scatter correction (3D-OSEM gave similar results). For the phantom study a calibration factor of 3.14 ± 0.16 Bq/count was found for the background and the five largest spheres. The smallest sphere had a calibration factor of 1.95 Bq/count. Based on the known administered activity at day 0, a SPECT-scan and planar scan on day 0, the calibration factor for the five patients was 3.19 ± 0.22 Bq/count. Based on the administered activity at day 0, a SPECT-scan on day 1 (indirect method) and planar scans on day 0 and 1 the calibration factor for five patients was 2.82 ± 0.30 Bq/count. **Conclusion** The calibration factor is rather insensitive to the chosen reconstruction method, if both scatter and attenuation correction are applied, and was found to be comparable in patients and the phantom for different volume sizes. The indirect method gave a slightly lower value. A universal calibration factor can be used, if attenuation and scatter corrections are applied, and this makes needed individualized dosimetry possible.

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Ex-vivo autoradiographic study registered with histopathological sections demonstrates inhomogeneous radioactivity distribution after therapeutic application of $^{90}\text{Y}/^{111}\text{In}$ -DOTATOC

G. Nicolas¹, B. Campana², F. Forrer¹; ¹University Hospital, Institute of Nuclear Medicine, Basel, SWITZERLAND, ²University Hospital, Institute of Pathology, Basel, SWITZERLAND.

Background Efficacy and toxicity of peptide receptor radionuclide therapy using ^{90}Y -DOTATOC in neuroendocrine tumour (NET) patients depends on the uptake of radioactivity in target and non-target tissue. The uptake and the biodistribution are usually evaluated on the ^{111}In -DOTATOC post-therapy scintigraphy. For obvious reasons no autoradiographies of patients are available. Only one report of ex-vivo autoradiographies of healthy kidney tissue using ^{111}In -Octreotide is published to date. We report the case of a 50 year-old woman treated with $^{90}\text{Y}/^{111}\text{In}$ -DOTATOC for a metastatic well differentiated neuroendocrine carcinoma of the pancreas. Sixteen hours post injection the patient passed away after an acute upper gastro-intestinal bleeding from a deep duodenal ulcer. Ex-vivo autoradiographies along with histo-pathological sections of tumours and organs could be obtained. Material and Method Sections from organs of interest and tumours were exposed to storage phosphor screens for post-mortem autoradiographic imaging. After registration of the histopathologic and autoradiographic images a semi-quantitative analysis, was performed evaluating the extent of tumour infiltration and necrosis. The histological features were correlated to the radioactivity density measured in regions of interest and expressed as density light units per mm^2 . Results Co-registration of the information obtained from histopathology and autoradiography demonstrated high and specific accumulation

of radioactivity in all tumours, including micrometastatic tumour foci (< 0.2 mm). The tumor:liver background ratios ranged from 1.8 to 33.5, which is directly correlated to the extent of tumour infiltration while is inversely correlated to the extent of necrosis. As expected, the kidneys accumulated high amounts of radioactivity. The radioactivity was mainly concentrated in the urine collecting system and homogeneously distributed in the cortical and medullary structures, without significant gradient. Conclusion This is a unique case of side by side correlation between histological findings and $^{90}\text{Y}/^{111}\text{In}$ -DOTATOC uptake after targeted radiopeptide therapy in a patient with metastatic neuroendocrine tumour. A good correlation between the tumour uptake and the tumour cell density was found. Most of the radioactivity present in the kidneys was observed in the urine, reinforcing the need for abundant peritherapeutic hydration in receptor targeting radiotherapy. These findings along with recent dosimetric studies emphasise the need of microscopic dosimetry in order to improve the accuracy of dosimetric results and to establish dose-response relations.

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Model of Individualized Radiomolecular Therapy Planning In Neuroendocrine Liver Metastases Coxtails of Y-90-DOTA-TOC/ Lu-177-DOTA-TATE/ In-111- DTPA-Phe¹- Octreotide, after Selective Catheterization of the Hepatic Artery

M. Lyra¹, M. Paphiti¹, I. Karfis², G. Limouris¹; ¹University of Athens, Athens, GREECE, ²NIMITS Military Hosp, Athens, GREECE.

Purpose: To provide the optimal individualized treatment strategy in inoperable neuroendocrine liver metastatic patients. **Materials and Methods:** Tumours should be classified into 3 size categories: those with a diameter up to 2.5 cm (Group A), others with a diameter from 2.5 to 4.0 cm (Group B) and into a last cohort with a diameter over 4.0 cm (Group C). Radiobiological burden of each patient is pre-calculated not to exceed 25 Gy to the kidneys. In cases where the tumour volume exceeds 4.0 cm, Y-90-DOTA-TOC is planned to be infused first. In cases where the tumour volume does not exceed 4.0 cm, Lu-177-DOTA-TATE is decided to be firstly infused. The second infusion is scheduled to be applied according to the tumour-size changes obtained along the time period after the first infusion; so, in case the tumour volume does not exceed 4.0 cm we proceed with Lu-177-DOTA-TATE, and if not??, Y-90-DOTA-TOC infusion is repeated. The third infusion is scheduled to be applied according to the tumour shrinkage degree and the clinical and laboratory findings as well. In cases where the tumour volume becomes less or equal to 2.5 cm, Lu-177-DOTA-TATE in combination with In-111- DTPA-Phe¹-Octreotide should be applied. **Dosimetry:** Planar and tomographic images should be obtained immediately after the infusion and 1, 2, and 3 days thereafter to determine the amount of true activity in preselected regions of interest (liver-nodules) in the relevant Octreoscan. Absorbed doses delivered to metastases and to red marrow are calculated in turn, using the OLINDA/EXM code. The derived values are correlated to the therapeutic benefit. Response assessment is classified according to the Response Evaluating Criteria In Solid Tumours (RECIST 1.0). CT/MRI scans are performed as baseline before, during and after the end of treatment and monthly US images are obtained for follow up measurements. Toxicity (WHO criteria) is measured using blood and urine tests of renal, hepatic and bone marrow function. **Conclusion:** In unresectable metastatic liver lesions, positive for somatostatin receptors a schedule of repeated, trans hepatic, high doses of Y-90-, Lu-177 and In-111 labelled peptide cocktail could be applied for the optimization and the individualization treatment, minimizing in parallel the toxicity of non target tissue tumours in measurable disease.

P17 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Radiopharmaceuticals & Radiochemistry & Dosimetry: Antibodies and peptides

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Evaluation of [^{124}I] scFv ANTI-CEA

D. Martini¹, G. Valentini¹, P. Panichelli¹, G. Montali¹, C. Vesprini¹, L. Castignani¹, M. Paparelli¹, S. Dominici¹, V. Fiori², D. Moricoli³; ¹ACOM spa, Montecosaro, ITALY, ²University of Urbino, Urbino, ITALY, ³Diatheva srl, Fano, ITALY.

Aim Interestingly ^{124}I is one of the most promising candidate between positron emitters for PET with tumour-seeking MAbs (immuno-PET) since antibody fragments in scFv format, have shown fast tumour targeting and blood clearance, a more uniform tumor distribution and a lower potential to elicit a human immune response compared to full length monoclonal antibodies. The procedure described allows to localize tumor masses in particular human metastatic melanoma cancer cells, and follow their evolution during radiotherapy. **Materials and methods** Monoclonal single chain Fv (scFv) antibody fragments was obtained by DNA recombinant techniques, it posses a very high affinity for recombinant CEA antigen and efficient recognition of CEACAM proteins in human metastatic melanoma. Labelling was performed according to the Iodogen-coated MAB protocol. The Pharmacokinetics parameters of scFv anti CEA 124I-conjugated was determined in nude mice (CD-1 Nude) previously inoculated with melanoma cancer cells. Ten mice were injected with a single dose of intravenous scFv CEA 124I and blood sample collected at 0, 5, 10 and 30 minutes and 2, 3, 4, 6, 24, 48 hours, plasma activity was measured by γ -counter. For the MicroPET analysis mice were treated with 10MBq μCi of 124I-scFv anti CEA and analyzed after 4 and 6 hours post injection. The Biodistribution data derived from the mice previously subjected to MicroPET and sacrificed after 4 hours post treatment. The radioactivity of explanted organs (tumor, spleen, liver, kidneys, lung, heart, blood, thyroid, stomach) was assessed by reading the γ -counter. **Results** The Pharmacokinetics parameters of recombinant scFv anti CEA 124I-conjugated showed an optimal clearance, the half life value of $t_{1/2} 8.884 \pm 3.3$ was similar (or superior) to those obtained with diabodies. In comparison with other scFv molecules, the scFv anti CEA 124I reveals lower elimination from circulation and this can contribute to antibody accumulation in the tumor. Selective tumour targeting has been highlighted with immuno-PET in CD-1 nude mice previously injected with melanoma cancer cells, MicroPET imaging have evidenced the large capabilities of this kind of complex in tumour imaging. The immunolocalization on the tumor site of the scFv anti CEA 124I was confirmed with the Biodistribution

data, with indicate values reaching 36% ID/gr. Conclusions The recombinant scFv antibody to the CEACAM1 cell surface determinant specifically delivers 124I on target cells. The data above demonstrate the specificity of antibody as imaging agent for immuno-PET analysis for recognizing CEA + solid tumor including melanoma, lung and gastric carcinomas.

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Optimization of Iodine-124 labeling of L19SIP for PET imaging

M. Aurilio¹, L. D'Ambrosio¹, M. Ventani², J. Piazzzi², L. Giovannoni², D. Neri², L. Aloj¹, S. Lastoria¹; ¹AF Medicina Nucleare, Istituto Nazionale Tumori, Fondazione "G. Pascale", Napoli, ITALY, ²Philogen SpA, Siena, ITALY.

Background: L19SIP is a fully human antibody fragment (small immunoprotein, SIP) directed against the extra domain B (EDB) of fibronectin. EDB is a selective marker for tumor neovasculature, with very low expression levels in normal tissues. Radiolabeled 131I-L19SIP is being developed for radioimmunotherapy (RIT) for various types of cancers. Iodine-124 is a positron-emitter with a half-life of approximately 4 days. We are developing the methodology of using 124I-labelled L19SIP in PET imaging of tumors (immunoPET) and in dosimetry estimation of tumor and organ doses prior to 131I-L19SIP RIT. Methods: Iodine-124 was supplied at a concentration of 74 MBq/ml in 1 mM sodium hydroxide, with no carrier added. Labeling of L19SIP was performed according to the chloramine T method. The radiolabeling procedure consisted of a controlled oxidation step without the use of a reducing agent to stop the reaction. The amount of starting radioactivity utilized was calculated considering the molecular weight of the target and the expected labeling yield. Optimization of labeling conditions was achieved by performing extensive preliminary experiments in small reaction volumes. The target specific activity to achieve was in the order of 1 mCi/mg. The reaction was initiated by adding the Chloramine-T solution (0,24 M, prepared immediately before labeling) directly to the reaction mixture at room temperature. Incubation time was finally set at 1 min. Unbound 124I was measured and removed by gel filtration using prepacked G25 Sephadex columns (GE Healthcare) eluted with phosphate buffered saline. Silica gel thin layer chromatography (mobile phase: methanol/water 85:15) was utilized before and after gel filtration to assess radiochemical purity. The purified reaction mixture was also evaluated for immunoreactivity by measuring radioactivity retained on an antigen affinity chromatography column. Results: The radiochemical yields under the conditions presented were consistently between 80 and 95%. Radiochemical purity above 99.5% was always obtained after gel filtration. The mild conditions of our chloramine T based iodination reaction allowed optimization of labeling yields while maintaining high immunoreactivity (80-99 %). Further investigation of the relationship between incubation time and radiochemical yields showed no significant differences for incubations between 1 and 10 minutes. Immunoreactivity appeared to be more dependent on the concentration of Chloramine T rather than incubation times. Increasing Chloramine T concentrations resulted in decreased immunoreactivity (as low as 23%). Conclusion: We have optimized the labeling conditions of L19SIP with 124I to achieve reproducible yields and immunoreactivity for effective use in clinical PET applications.

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Receptor affinity of ^{nat}Sc and ^{nat}Ga labelled DOTA-TATE

E. Koumariou; IAE, Radioisotope Centre Polatom, Otwock-swierk, POLAND.

Aim: ⁴⁴Sc as positron emitter can be an interesting alternative to ⁶⁸Ga due to longer half life ($t_{1/2}$ =3.9h). Moreover, the β emitter ⁴⁷Sc can be used for therapy using the same peptide vectors. DOTA as chelating agent for Ga and Sc has been proven suitable for the radiolabelling of peptides with receptor mediated function [Viola-Villegas N et al, 2009]. Recently the radiolabelling of ⁴⁴Sc-DOTA-TATE has been reported [proszynski]. In this work we investigated the in vitro receptor affinity of well established somatostatin analog DOTA-TATE labelled with Ga and Sc. **Material and Methods:** Cold complexes of DOTA-TATE with ^{nat}Ga and ^{nat}Sc were synthesized and identified by HPLC and MS analysis. The in vitro studies were carried out in rat pancreatic cancer cell line AR42J. The minimum required concentration of [¹²⁵I-Tyr¹¹]-SST-14 for the binding affinity studies was determined by the saturation curve of [¹²⁵I-Tyr¹¹]-SST-14 in AR42J cells. DOTA-TATE, ^{nat}Sc-DOTA-TATE and ^{nat}Ga-DOTA-TATE in competition to [¹²⁵I-Tyr¹¹]-SST-14 were investigated in reference to Tyr¹¹-SST-14. The concentration peptide in studied complexes was determined in colorimetric assay. **Results-Conclusions:** Our previous in vitro studies of bombesin analog DOTA-BN[2-14]NH₂ complexes with ⁹⁰Y, ¹⁷⁷Lu, ⁶⁸Ga and ⁴⁴Sc [abstract Koumariou et al., 2009] in PC-3 cells indicated that the affinity profile of ^{nat}Y-, ^{nat}Lu-, ^{nat}Ga- and ^{nat}Sc-DOTA-BN[2-14]NH₂ is decreasing in the order ^{nat}Ga>^{nat}Lu>DOTA-BN[2-14]NH₂>^{nat}Y<^{nat}Sc. The comparison of affinities between ^{nat}Sc and ^{nat}Ga DOTA-TATE metal complexes confirmed the higher affinity of Ga labeled peptide. Table 1 presents obtained IC50 values for DOTATATE in comparison to earlier reported IC50 values for DOTA-BN[2-14]NH₂. These findings need further confirmation in *in vitro* and *in vivo* evaluation. Table 1: Binding affinity values (IC₅₀) of M³⁺-DOTA-peptides in respective receptor expressing cell lines.

Derivative	IC ₅₀ ±SEM (nM) PC-3 cells	Derivative	IC ₅₀ ±SEM (nM) AR42J cells
DOTA-BN[2-14]NH ₂	1.78±0.12	Tyr ¹¹ -SST-14	0.67±0.12
^{nat} Y-DOTA-BN[2-14]NH ₂	1.90±0.06	DOTA-TATE	0.64±0.22
^{nat} Lu-DOTA-BN[2-14]NH ₂	1.34±0.11	^{nat} Ga-DOTA-TATE	0.20±0.18
^{nat} Ga-DOTA-BN[2-14]NH ₂	0.85±0.06	^{nat} Sc-DOTA-TATE	0.70±0.20
^{nat} Sc-DOTA-BN[2-14]NH ₂	6.49±0.13		

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[Lys⁴⁰-(Ahx-HYNIC)NH₂-^{99m}Tc]-exendin-4 as potential radiopharmaceutical for insulinoma diagnostics

B. Janota¹, R. Mikolajczak¹, M. Leszczynska¹, E. Jakubowska¹, H. Maecke²; ¹Institute of Atomic Energy Radioisotope Centre POLATOM, Otwock,

POLAND, ²Clinic of Nuclear Medicine, University Hospital, Freiburg, GERMANY.

The aim: The receptors of glucagon-like peptide 1 (GLP-1) are highly overexpressed in insulinomas. In insulinomas, the density of the GLP-1 receptor is higher than any of other peptide receptors. It provides an attractive target for imaging. Exendin-4 is a long-acting potent agonist of glucagon-like peptide 1. It has been shown before, that [Lys⁴⁰-(Ahx-DTPA-¹¹¹In)NH₂]-exendin-4 SPECT localizes insulinomas difficult to imagine with other modalities. However [Lys⁴⁰-(Ahx-DTPA-¹¹¹In)NH₂]-exendin-4 imaging may have some limitation including high kidney uptake and high cost. The aim of this project was to develop the dry kit formula for ^{99m}Tc labeling of [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 and initiate its pre-clinical and investigation. **Materials and methods:** [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 was custom-synthesized by Peptide Specialty Laboratories. Exendin-4 was modified C-terminally with Lys⁴⁰-NH₂, where the lysine side chain was conjugated with Ahx-HYNIC (Ahx is aminohexanoic acid). Wet ^{99m}Tc-labelling of [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 was performed to optimize the amount and concentration of reagents, temperature and reaction time which was then transferred to [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 dry kit formulation. Two-vials dry kits were prepared with the following composition: vial I: 20 µg [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4, 20 µg SnCl₂, 50 mg tricine, 10 mg mannitol; vial II: 10 mg EDDA. Radiolabelling was carried out by the addition 0.3-1.5 ml of ^{99m}Mo/^{99m}Tc generator eluate (10-50 mCi radioactivity) followed by 20 min incubation at 80°C. Radiochemical purity of [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 controlled by TLC and HPLC showed over 90% radiochemical yield and percentage of non-bound ^{99m}Tc-perthetate as well as colloidal forms of ^{99m}Tc was in the range of 5% **Results and Conclusion:** [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 was successfully labeled with technetium-99m with radiochemical yields over 90% and [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 was stable for 6 hours after labeling. Further pre-clinical studies are planned to compare diagnostic potential of [Lys⁴⁰-(Ahx-HYNIC)NH₂]-exendin-4 with [Lys⁴⁰-(Ahx-DTPA-¹¹¹In)NH₂]-exendin-4.

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In vitro comparison of renal accumulation of two gastrin analogs using two renal cell models

Z. Novy, J. Mandikova, F. Trejtnar, A. Laznickova; Faculty Of Pharmacy, Charles University, Hradec Kralove, CZECH REPUBLIC.

Aim: Radiolabeled somatostatin and gastrin analogs have been shown to be useful in scintigraphy and radiotherapy of various malignancies. Maximum dose of radioactivity that can be administered is limited by high and persistent renal retention of the peptides. In this study, renal accumulation and processing of two radiolabeled receptor-specific gastrin analogs, ¹¹¹In-DOTA-minigastrin 45 (¹¹¹In-MG45) and ¹¹¹In-DOTA-minigastrin 47 (¹¹¹In-MG47), were studied. The renal uptake of the ¹¹¹In-minigastrins was compared with that of another group of receptor-specific peptides, somatostatin analogs such as ¹¹¹In-[DOTA⁰, Tyr³]-octreotide (¹¹¹In-DOTA-TATE) and ¹¹¹In-[DOTA⁰, 1-Nal³]-octreotide (¹¹¹In-DOTA-NOC). **Materials & Methods:** Two renal experimental in vitro models were used in the study. The first one was freshly isolated rat renal cells prepared by two-phase collagenase perfusion from native kidneys. The second used cell model was the standard porcine proximal tubular cell line LLC-PK1. Incubation experiments were carried out at 37 °C and under low temperature (4 °C) to determine possible contribution of active transport mechanisms to the renal uptake. ^{99m}Tc-mercaptopropylglycine (^{99m}Tc-MAG3) and ^{99m}Tc-labeled albumin were used as comparative compounds to quantify the cellular uptake of radiolabeled peptides. **Results:** The rate of accumulation of the studied compounds in the LLC-PK1 cells at 37 °C was as follows: ^{99m}Tc-albumin > ¹¹¹In-DOTA-NOC > ¹¹¹In-DOTA-MG45 > ¹¹¹In-DOTA-TATE > ¹¹¹In-DOTA-MG47 > ^{99m}Tc-MAG3. The found rate of accumulation in the primary rat renal cells was: ^{99m}Tc-MAG3 > ^{99m}Tc-albumin > ¹¹¹In-DOTA-NOC > ¹¹¹In-DOTA-MG45 > ¹¹¹In-DOTA-TATE > ¹¹¹In-DOTA-MG47. Accumulation of ¹¹¹In-DOTA-NOC and ¹¹¹In-DOTA-TATE was higher than that of ¹¹¹In-DOTA-MG47 in both models. The lower incubation temperature led to a lower renal accumulation in ¹¹¹In-DOTA-MG45. On the other side, ¹¹¹In-DOTA-MG45 uptake in the renal cells was not affected by the lower temperature. **Conclusion:** Significant differences in renal cellular accumulation were observed between two studied ¹¹¹In-minigastrins. ¹¹¹In-DOTA-MG45 showed significantly higher uptake than ¹¹¹In-DOTA-MG47 in both cell models. A low contribution active transport mechanisms was detected only in ¹¹¹In-DOTA-MG-45. ¹¹¹In-DOTA-MG-47 is accumulated only by passive transport. The renal uptake of ¹¹¹In-DOTA-MG47 was significantly lower than that of ¹¹¹In-labeled somatostatin derivatives in both renal cell models. *The work originated in collaboration within COST BM607 and was supported by grant of Ministry of Education of the Czech Republic No. OC 08006 and by the grant No. 124409/FaF/CEK of the Grant Agency of Charles University.*

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Solid phase synthesis of Gly-(D)Ala-Gly-Gly octreotide conjugated to Paclitaxel for drug delivery and imaging of neuroendocrine tumor

R. Varshney¹, N. Dubey², P. P. Hazari¹, J. Uppal¹, S. Pal¹, P. Trivedi², A. K. Mishra¹; ¹INMAS, Delhi, INDIA, ²RGPV, Bhopal, INDIA.

Objective: Somatostatin (SST) is a neuropeptide that demonstrates a powerful inhibitory action against several endocrine systems. SST is now recognized as a hormone capable of regulating fundamental processes such as secretion, cell division, proliferation and apoptosis. Most neuroendocrine tumors and their metastases express SSTRs to a much greater extent than do normal tissues. For therapeutic feasibility in humans, several synthetic SST analogs (*i.e.* octreotide, an octapeptide) have been created with improved metabolic stability. Octreotide is an octapeptide analog of endogenous SST and binds to SSTR-2, SSTR-3 and SSTR-5. Paclitaxel has demonstrated significant activity in clinical trials against a wide variety of tumors, especially, ovarian and breast cancer in the past 10-20 years. In order to increase therapeutic efficiency and reduce side-effects, much effort has been devoted to the development of tumor-targetable drug delivery system of paclitaxel such as liposomes, nanoparticles, parenteral emulsion, water-soluble prodrugs and conjugates. By virtue of these properties, we hypothesized that octreotide had the potential to be a suitable vehicle for delivering paclitaxel to its intracellular target. Therefore, we have developed modified octreotide and conjugated paclitaxel for targeted delivery. **Methods:** We have modified octreotide at the N terminus by adding a group of amino acids Gly-(D) Ala-Gly-Gly as a chelating moiety that permitted N₄-configuration for ^{99m}Tc binding and evaluated their cytotoxicity. We have synthesized and characterized modified- octreotide by Fmoc solid phase

strategy using rink amide resin. **Results:** Paclitaxel was analyzed using reverse phase HPLC methods and a mobile phase of 58:37:5 acetonitrile:water:methanol at 1 mL/min with UV detection at 232 nm. The ^{99m}Tc complexation was carried out with 98% radiolabeling yield and found stable in human serum under physiological condition up to 24 h. **Conclusion:** We have evaluated Gly-(D)Ala-Gly-Gly-octreotide conjugated to Paclitaxel as a potential conjugate for imaging neuroendocrine tumors.

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Radiolabelling and in vivo evaluation of a collagen-targeting peptide for the isotopic imaging of liver fibrosis in rat

T. Poisson¹, C. Z. Dong², S. Loyau³, A. Meulemans¹, S. Burg¹, J. B. Michel³, P. Billiald⁴, D. Le Guludec¹, M. Jandrot-Perrus³, L. Sarda-Mantel¹; ¹Department of Nuclear Medicine, Hôpital Bichat, Paris, FRANCE, ²Laboratoire ITODYS/CNRS UMR 7086 Equipe Pharmacochimie Moléculaire, Paris, FRANCE, ³INSERM U698, Hôpital Bichat, Paris, FRANCE, ⁴Museum National d'Histoire Naturelle, CNRS-FRE 3206, Paris, FRANCE.

Objectives: Our aim was to study the radiolabelling, the in vivo behaviour, and the isotopic imaging performances of collagen (Col), a peptide mimicking platelet glycoprotein VI (GPVI) (collagen receptor) obtained by screening of a bacterial library for peptides with anti-GPVI monoclonal antibody. **Methods:** We radiolabelled Col with Technetium-99m (99mTc), and DTPA-Col with Indium-111 (111In). The quality control of unlabelled Col and radiotracers was performed using Sep-Pak and/or High Performance Liquid Chromatography (HPLC). The affinity of purified radiotracers for collagen was measured using Ligand Tracer technology. Then they were injected to 10 (5 Tc / 5 In) rats with liver fibrosis (LF) obtained by carbon tetrachloride oral or intraperitoneal administration during 6 weeks, and to 5 (3 Tc / 2 In) control rats. Planar whole-body scintigraphic images (Biospace Lab microSPECT), autoradiographic (Instant Imager Packard) and histologic studies of liver sections were performed. **Results:** Unlabelled Col and DTPA-Col were not degraded in plasma until 120 min. The rate of radiolabelling was 80 to 95% with Tc, and 70 to 85% with In. Dissociation constant was about 1.5 $\mu\text{mol/L}$ for both radiotracers. On imaging, in controls, 99mTc-Col demonstrated a fast blood clearance, early first pass biliary excretion and low renal uptake, whereas 111In-DTPA-Col showed only early renal excretion. Two hours post-IV, 99mTc-Col and 111In-DTPA-Col liver uptakes were increased in respectively 3/5 and 1/5 LF rats compared to controls. Autoradiography reported 43 \pm 13 counts/mm² in LF rats versus 29 \pm 3 in controls ($p=0.05$) for 99mTc-Col, and 23 \pm 10 versus 10 \pm 7 (NS) for 111In-DTPA-Col, the radiotracers activity being grossly correlated with the intensity of fibrosis on histology (Sirius red). **Conclusions:** 99mTc-Col and 111In-DTPA-Col showed similar micromolar affinity for collagen in vitro. In vivo, 111In-DTPA-Col presents the interest over 99mTc-Col of no liver non specific accumulation, but has very quick renal excretion and seems to have lower sensitivity of detection in vivo in a rat model of liver fibrosis. Improved derivatives of Col are now being developed, designed for increased affinity for collagen, and lower renal clearance.

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Gallium labelled NOTA-based RGD-conjugates for targeting $\alpha_v\beta_3$ integrin receptor

M. M. Prata¹, A. Sá², Á. A. Matias¹, C. F. G. C. Galdes³, P. M. T. Ferreira⁴, J. P. André⁵; ¹BILI-FMUC, Coimbra, PORTUGAL, ²Chemistry Department, University of Minho, Braga, PORTUGAL, ³Dep Ciências da Vida FCTUC and CNC-UC, Coimbra, PORTUGAL, ⁴Chemistry Department - University of Minho, Braga, PORTUGAL, ⁵Chemistry Department- University of Minho, Braga, PORTUGAL.

Introduction and Objectives: Ga(III) chelates are of high interest in the field of medical imaging. ^{68}Ga ($t_{1/2} = 68$ min), a β^+ emitter, which can be produced from a ^{68}Ge generator system allowing easy routine manufacture in hospital facilities. The most common chelators for Ga(III) are hexadentate and, among them, triaza macrocycles are particularly suitable due to their high conformational and size selectivity, allowing a good fit of the relatively small cation in the macrocyclic cavity. Peptides have shown to be the most effective targeting moieties known for cellular receptors, drug delivery, molecular imaging and radiotherapeutic applications. The RGD peptide sequence has emerged as one of the most efficient epitopes for targeting the $\alpha_v\beta_3$ integrin receptor. This integrin is highly expressed on activated endothelial cells in neovasculature of various tumors and it has been demonstrated that it is overexpressed on both the endothelial cells and tumor cells in melanoma, glioma, ovarian and breast cancers and the $\alpha_v\beta_3$ expression correlates well with tumor progression and invasiveness of tumors. **Methodologies and Results** In this work we describe the synthesis of two conjugates based on derivatives of NOTA, in which one of the acetate pendant arms displays a α -alkyl substituent with a variable number of carbon atoms, and bearing a RGD peptide moiety. The radiolabelling of **NOTAC6-GRGDG** and **NOTAC8-GRGDG** with [^{67}Ga] has been characterized and the stability and octanol/water partition coefficient (log P) of [^{67}Ga]NOTAC8-GRGDG was obtained. The internalization profile of the radiolabelled bioconjugates was accessed both in breast tumor and glioblastoma cell lines.

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The viennese Ga68-DOTA-NOC production via the Raytest® SynChrom®-Synthesis module.

H. Eidherr¹, J. Ungersböck¹, F. Girschele¹, M. Mitterhauser¹, J. Schmaljohann², K. Kletter¹, R. Dudczak¹, W. Wadsak¹; ¹Medical University of Vienna, Vienna, AUSTRIA, ²Raytest Isotopenmessgeräte GmbH, Straubenhardt, GERMANY.

Aim: Ga68-DOTA-NOC is a sophisticated and innovative tracer for the diagnosis of neuroendocrine tumours like gastrinomas and consequently sufficient and reliable yields of the tracer are needed in our institution. **Materials & Methods:** The radiochemical synthesis was performed on the dedicated Ga68-Synthesis-module (SynChrom® from Raytest®) and consisted of the following key events: Gallium-68 was eluted with 10ml 0.1N HCl from a TiO₂-based

1850MBq Ge68-/Ga68-Generator (Obninsk, Russia). The peak Ga68-activity was subjected to the complexation reaction with 50 μg DOTA-NOC peptide in 50 μl 0.05N HCl and 155 μl 1M NaOAc at 95°C for 5min. Subsequently, the crude product was purified on a C18-SPE column (SepPac light, Waters), eluted with 0.6ml ethanol and rinsed with 2ml saline (0.9%). After pH adjustment to pH 7.4 by addition of PBS, the product was finally 0.22 μm filtrated to prevent bacterial and pyrogenic contamination. In detail, the whole fully-automated synthesis consisted of 44 steps. Quality control included TLC, HPLC, pH-, osmolality-, radionuclidic purity-, sterility- and apyrogenicity control. **Results:** Using the described method, Ga68-DOTA-NOC could be produced in a fast and reliable way in 18 \pm 2min synthesis time (+ 6 \pm 1min OC). After 1.9ml void volume, the following 1.9ml fraction represented the peak Ga68-activity and contained 70-80% of the elutable activity. The radiochemical yield was 50-70% (not decay corrected, based on eluted Ga68-GaCl₃) with a rate of failed syntheses of <1%. Radiochemical purity was 98.0-99.5%, Ge68 contamination was <6x10⁻⁵%, pH 7.0-7.4, osmolality ~290mosmol/kg. Pyrogenic and microbial contamination was not encountered so far (0% of the lots). **Conclusion:** With the presented production mode and synthesis module, sufficient amounts of Ga68-DOTA-NOC in excellent quality could be reliably guaranteed.

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Biodistribution of [^{99m}Tc]-HYNIC-c(RGDyK) in nude rats bearing human breast carcinoma or testicular teratoma

J. Rouvet¹, R. Modzelewski¹, N. Aide², M. Briand², J. Pille³, J. Picquenot³, P. Vera¹, P. Bohn¹; ¹Department of Nuclear Medicine, Henri Becquerel Center and Rouen University Hospital & QUANT.I.F - LITIS EA 4108, Faculty of Medicine and Pharmacy, University of Rouen, Rouen, FRANCE, ²Caen University Hospital and François Baclesse Cancer Center, Caen, FRANCE, ³Department of Anatomopathology, Henri Becquerel Center, Rouen, FRANCE.

Aim: The $\alpha_v\beta_3$ integrin plays an important role in angiogenesis and tumor metastasis. Radiolabeled RGD (Arg-Gly-Asp) peptides that specifically target $\alpha_v\beta_3$ integrin have a great potential for early detection and treatment follow-up of solid tumors. The aim of this study was to evaluate the distribution of [^{99m}Tc]-HYNIC-c(RGDyK) in nude rats implanted with MDA-MB-231 human breast carcinoma or with Ntera-2 human testicular teratoma. **Materials & methods:** Two female nude rats were injected subcutaneously in the right posterior inguinal mammary fat pad with MDA-MB-231 cells and two other in the right hindlimb with Ntera-2 cells. Once tumors reached a diameter ~1 cm, [^{99m}Tc]-HYNIC-c(RGDyK) was intravenously injected (radiochemical purity >95%; 185 MBq/rat) into the tail vein. They were imaged 2h postinjection under a micro-SPECT/CT and subsequently sacrificed. Samples of blood, tumor and tissues of interest (liver, small intestine, colon, muscle, kidneys and feces) were collected in triplicate, wet-weighted, and counted in a gamma-counter. Results were expressed as the percentage of injected dose per gram of tissue (%ID/g) and tumor-to-organ uptake ratios were calculated. Moreover, histological analysis of tumors was performed. **Results:** Retention in all organs was lower than 3%ID/g after 2h. Uptake in the normal tissues was from 0.01 to 2.20%ID/g. The highest values were found in the kidneys (2.13 - 2.20%ID/g) and the liver (0.15 - 1.03%ID/g), the two elimination routes of the tracer. The uptake values in MDA-MB-231 tumor indicated a greater retention in the periphery of the tumor than in the center (0.10 \pm 0.02% versus 0.06 \pm 0.01%ID/g; $p < 0.05$). Tumor to muscle ratio was 5.70. The distribution in Ntera-2 tumor was homogeneous with 1.62 \pm 0.57%ID/g. Tumor to muscle ratio was 9.70. Histological analysis of the tumors showed an angiogenesis localized at the periphery in the MDA-MB-231 tumor, and evenly distributed in the Ntera-2 tumor. **Conclusion:** This biodistribution study showed a significant tracer uptake in the two types of tumors, indicating an overexpression of $\alpha_v\beta_3$ integrin. The MDA-MB-231 cells do not express the $\alpha_v\beta_3$ integrin naturally: the tracer uptake is only due to an angiogenesis stemming from rat tissues, thus more intense in the tumor periphery. Conversely, $\alpha_v\beta_3$ integrin was naturally expressed on the surface of Ntera-2 cells. The high and homogeneous uptake observed must therefore be tempered by the fact that it reflects not only an angiogenic phenomenon, but also the intrinsic expression of this integrin by the tumor.

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Nucleophilic synthesis of the [^{18}F]fluoropropanoyl-Gluc-Lys-TOCA for Somatostatin Receptors Imaging.

L. Prochazka, M. Kropacek, F. Melichar, J. Basta, J. Zimova; Nuclear Physics Institute of the ASCR p.r.i., Rez, CZECH REPUBLIC.

Aim: Imaging of the somatostatin receptors expressed in case of the Gastro-enteropancreatic neuroendocrine tumour, carcinoma tumour or malignant lung tumours is done in the Czech Republic mainly using In-111 labelled OctreoScan and Tc-99m labelled NeoSpect. Presented work is focussed on labelling of peptides with Fluorine-18. These compound could provide more precise three-dimensional localisation of the tumour using PET. On the basis of known background research and agreement with Na Homolce-PET center as well, N²-(1-deoxy-D-fructosyl)-N²-2-[^{18}F]fluoropropionyl]-Lys⁵-Tyr³-octeotrate (Gluc-Lys-TOCA) was chosen as a suitable peptide. **Materials & Methods:** Synthesis is carried out according to modified method previously published by the authors Guhlke S., et al. Appl. Radiat. Isot. 45, 715, 1994 starts from 9-anthrylmethyl-2-bromopropionate precursor using tetrabutylammonium hydroxide as the catalyst. Hydrolysis of labelled intermediate is done by tetramethylammonium hydroxide, dimethyl sulfoxide is added in order to prevent 2-fluoropropionate from evaporation loss. Bis-(4-nitrophenyl) carbonate is added in order to react with the intermediate to form 4-nitrophenyl-2-[^{18}F]fluoropropionate, which is then separated using HPLC, trapped from the acquisition fraction on the graphitic carbon column and eluted by methanol with addition of tetramethylammonium hydroxide back to the reactor vessel. Methanol is evaporated and KOBt (benzotriazole salt) and peptide precursor are added. Labeled peptide is purified using reverse phase HPLC, trapped on the LiChrolute EN column and eluted by methanol. Solvent is evaporated and the residue is finely re-dissolved in the saline solution. **Results:** Main work was focussed on preparation of 4-nitrophenyl-2-[^{18}F]fluoropropionate acylating agent by the three-step synthesis simplified by omitting the HPLC separation of 9'-anthrylmethyl-2-fluoropropionate as intermediate. Synthesis time was cut down from 90 to 60 minutes, while decay corrected radiochemical yield was from 60% to 65%. Suitable agent for hydrolysis of the intermediate in the primary reaction mixture before entering reaction with bis-(4-nitrophenyl) carbonate was found. The separation column for preparing of acylating agent in the form suitable for further reaction with peptide containing

protecting groups was found. **Conclusion:** Acylation reaction of the protecting groups containing peptide known from literature was modified to be applicable using TracerLab Mx FDG commercial automatic module. Total synthesis time of the labelled peptide (starting from target material) was cut down from already published 180 minutes to 120 minutes. Decay corrected radiochemical yield was from 25% to 30%. Newly developed synthesis procedure allows production of F-18 labelled peptide with the radioactive concentration sufficient enough for screening of several patients.

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Relations between receptor affinity of radiolabeled somatostatin analogs and the peptide radioactivity uptake in somatostatin receptor-rich organs in rats

M. Laznicek, A. Laznickova; Faculty of Pharmacy, Charles University, Hradec Kralove, CZECH REPUBLIC.

Aim: Radiolabeled somatostatin analogs became an accepted diagnosis and treatment for neuroendocrine tumors. Optimal structure of the peptide is still under debate as there are still potential improvements in the field of somatostatin receptor targeting. The aim of this study was to determine whether receptor affinity determined in *in vitro* conditions correlates with the radioactivity uptake in tissues with a high density of somatostatin receptors in series of radiolabeled somatostatin analogs in preclinical experiments. **Materials and Methods:** For the study, eight somatostatin analogs (namely octreotide, octreotate and Tyr³-octreotate derivatives) labeled either with Y-90 or In-111 were employed. The peptides were administered to male Wistar rats intravenously in the dose of 0.2 µg per animal. Organs bearing a high density of somatostatin receptors, namely the adrenals and pancreas, served as endogenous indicators of the specific binding of the peptide in *in vivo* conditions. Receptor affinity *in vitro* (the values of IC₅₀ to somatostatin receptor subtype sstr2) were taken from literature. **Results:** Radioactivity accumulation values in the adrenals and pancreas at 24 h and 48 h after dosing of the peptides under study were used, whether there are any correlations between radioactivity uptake *in vivo* and receptor affinity to sstr2 was investigated. Significant, but moderate correlations were found between the organ radioactivity uptake and two descriptors: 1/IC₅₀ and log (IC₅₀). When the value for ¹¹¹In-DOTA-1-Nal³-octreotide (a high affinity ligand of the sst2 and also sstr3 and sstr5 subtype), which was an outlier from the regression line, was omitted, higher correlation coefficients were produced. **Conclusions:** Moderate correlations between affinity of selected radiolabelled somatostatin analogs to sstr2 (IC₅₀ values) and peptide radioactivity uptake in somatostatin receptor-rich tissues were found in rats. Radioactivity accumulation in these organs is probably affected not only by the specific binding to sstr2, but also by the peptide binding to other somatostatin receptor subtypes, peptide lipophilicity and probably also by a rate of peptide-receptor binding and its consequent internalization, as the blood radioactivity decrease is relatively rapid. The study was supported by the Grant Agency of the Czech Republic - grant No. P304/10/1738. Research originated in collaboration within COST BM0607.

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Comparison of distribution profiles of two minigastrins labeled with In-111 in rats

A. Laznickova, L. Melicharova, P. Barta, M. Laznicek; Faculty of Pharmacy, Charles University, Hradec Kralove, CZECH REPUBLIC.

Receptors for regulatory peptides are expressed by a number of human neoplasms and can be visualized *in vivo* with peptide receptor scintigraphy. CCK-B/gastrin receptors have been shown to be expressed in several types of human cancers and are a potential target for peptide receptor radionuclide therapy. In the present study distribution and elimination characteristics of two ¹¹¹In-labeled minigastrin analogs modified with DOTA-chelator namely MG 11 (D-Glu-Ala-Tyr-Gly-Trp-Met-Asp-Phe-NH₂) and MG 47 (D-Gln)₆-Ala-Tyr-Gly-Trp-Met-Asp-Phe-NH₂ were compared in intact rats. **Materials and Methods:** Radiolabeling of DOTA-minigastrins with ¹¹¹In was carried out by adding of 10 µg of the peptide (in 10 µl of water solution) to 100 µl 0.4 M acetate buffer pH 5 together with 2 mCi of ¹¹¹InCl₃ (in 2 µl of 0.05 M HCl, PerkinElmer). After incubation at 95 °C for 30 minutes, the radiochemical purity was determined by ITLC-SG and HPLC analysis. Radiolabeled ¹¹¹In-DOTA-minigastrins were administered to male Wistar rats in the dose of 2 µg per kg of body weight. **Results:** Both ¹¹¹In-DOTA-minigastrins exhibited rapid clearance of the radioactivity from the blood and most other organs of rats. Higher and comparable radioactivity concentrations in organs over-expressing CCK-B/gastrin receptors were found for both agents under study. The *in vitro* experiments confirmed significant internalization of radioactivity into CCK-B/gastrin receptor expressing cell lines. Radioactivity uptake in the kidney after ¹¹¹In-MG 11 was about twice of that for ¹¹¹In-MG 47, but still substantially lower in comparison with radiolabeled somatostatin derivatives. Radioactivity was eliminated from the body mostly by urine. **Conclusion:** The radiolabeled peptides from group of gastrin derivatives are promising tools in scintigraphy or radiotherapy of the carcinomas. The advantage of ¹¹¹In-DOTA-minigastrins is their rapid radioactivity clearance from non-target organs and tissues and relatively low radioactivity uptake in the kidney. The research originated in collaboration within Action COST BM0607 and was supported by grant of Czech Ministry of Education OC08006 and by Grant Agency of Czech Republic, grant No. P304/10/1738.

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Renal accumulation of DOTA-conjugated minigastrin 11 labeled with indium-111 in vitro

F. Trejtnar, Z. Novy, J. Mandikova, A. Laznickova, M. Laznicek; Charles University in Prague, Faculty of Pharmacy, Hradec Kralove, CZECH REPUBLIC.

Aim: Radiolabelled CCK-B/gastrin receptor-targeting peptides may be a new class of receptor binding peptides for radiodiagnosis and radiotherapy of some malignancies, namely medullary thyroid carcinoma. As potentially useful compounds to image CCK-B/gastrin receptors were shown gastrin derivatives with shorter peptide chain, minigastrins, connected to a convenient chelator. The aim of the study was to investigate renal accumulation and mechanism of membrane transport of a newly developed gastrin analogue, DOTA-minigastrin 11, labeled with indium-111 (¹¹¹In-DOTA-MG11), using an *in vitro* renal cellular model. **Materials & Methods:**

Freshly isolated rat renal cells were used as the experimental renal model to study renal accumulation of the radiolabeled peptide. The rat renal cells were isolated from rat kidneys by two-phase collagenase perfusion method. The standard porcine proximal tubule cell line LLC-PK1 was used as a comparative model. Renal accumulation of ¹¹¹In-DOTA-MG11 was compared with that of DOTA-MG11 labeled with lutetium-177 to evaluate influence of the used radionuclide on the renal uptake. Incubation under low temperature was used to reveal possible contribution of active transport mechanisms to the renal transport. Renally accumulated compounds as ^{99m}Tc-mercaptoacetyltryglycine (^{99m}Tc-MAG3) and ^{99m}Tc-dimercaptosuccinate (^{99m}Tc-DMSA) were used as comparative compounds to quantify the cellular uptake of the radiolabeled peptide. In addition, ¹¹¹In-MG-11 cellular accumulation was compared with that of ¹¹¹In-[DOTA⁰, Tyr³, Thr⁸]-octreotide (¹¹¹In-DOTA-TATE), a typical member of another group of receptor-specific peptides. **Results:** The found rate of ¹¹¹In-DOTA-MG11 accumulation in the isolated rat renal cells was relatively low. ¹¹¹In-DOTA-MG11 accumulation was similar to that of ¹¹¹In-DOTA-TATE, ^{99m}Tc-MAG3 and ^{99m}Tc-DMSA were accumulated in rat renal cells in a non-comparable higher rate. The incubation under low temperature leads only to a nonsignificantly lower accumulation of ¹¹¹In-MG-11. No evident differences in accumulation in the rat renal cells were found between ¹¹¹In-MG-11 and ¹¹¹Lu-MG-11. The results on renal accumulation of the studied radiolabeled peptides obtained in LLC-PK1 cells were analogical. **Conclusion:** Using a rat cellular experimental model, a similar renal uptake of ¹¹¹In-DOTA-MG11 was demonstrated in comparison with that found for ¹¹¹In-DOTA-TATE. Passive transport seems to be responsible for the renal accumulation of ¹¹¹In-DOTA-MG11. A dependence of then renal uptake of DOTA-MG11 on the used radiolabel was not proved. The work originated in collaboration within COST BM0607 and was supported by grant of Ministry of Education of the Czech Republic No. OC 08006 and by the grant of Czech Science Foundation No. P304/10/173

P18 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Cardiovascular: Methods in nuclear cardiology

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Half Dose MIBG Cardiac SPECT Clinical Evaluation of Resolution Recovery Methods

H. Pena¹, G. Cantinho¹, D. Cerqueira², J. Clemente², M. Wilk³, Y. Srour³, F. Godinho¹, ¹Atomedical, SA & Instituto de Medicina Nuclear da Faculdade de Medicina de Lisboa, Lisboa, PORTUGAL, ²Atomedical, SA, Lisboa, PORTUGAL, ³UltraSPECT, Haifa, ISRAEL.

Introduction: The tomographic reconstruction by iterative methods, as WBR, allows acquisition's time or activity reduction in perfusion scans, issues with an increasing importance in NM departments. We've also been witnessing a growing interest in the use of 123I-MIBG cardiac SPECT, especially in familiar amyloid polyneuropathy (FAP). To process tomographic studies, we used WBR methodology and the more recently developed Xpress3, itself an improvement of WBR. We evaluated the possibility of performing the 123I-MIBG cardiac SPECT studies, using lower activity than the usually recommended. **Material & Methods:** 50 patients (pts) with FAP or high blood pressure (HBP) were randomly studied. We sequentially acquired tomographic studies at 30 minutes and at 3 hours after e.v. 185-222 MBq 123I-MIBG: A1 (30 s/view/60 views) and A2 (15 s/view/60 views). A1 studies were processed by FBP and A2 by WBR and Xpress3. The 100 studies were analyzed by two independent observers who classified the slices in very good (VG), good (G) and sufficient (S) quality. For quantification purposes, we analyzed all the studies and then, separately: abnormal studies, FAP studies and HBP patients' studies. To quantify LV radiopharmaceutical distribution, the 3 main vascular territories were considered, using Germano's QPS method to assess lesions score, severity and area. Paired Student t test (p) and Pearson correlation coefficient analysis (r) were used for statistical purposes. **Results:** In none of the studies did the visual analysis modify the final report. On the qualitative analysis of the tomographic slices, the two observers always found a better quality when WBR or Xpress3 was used, compared to the FBP processed studies, with an inter-observer agreement >96%. Half of the FBP studies were classified as S, while none of the WBR or Xpress3 was. On the quantitative lesion and score analysis, the correlation coefficients was always > or = 0.96 for the all patients group. On the 21 abnormal studies (FBP score > 4), the quantitative analysis didn't show any statistically significant difference [table1]. On FAP abnormal studies, the results were similar [table2]. All the HBP studies were normal and statistically similar. **Conclusions:** We can conclude that the use of WBR and Xpress3 for 123I-MIBG cardiac SPECT doesn't affect the results, with important advantage on time and administered activity reduction and at last, but not less importantly, less expensive.

Table 1 - Score Comparison - Abnormal cases

	FBP vs WBR	FBP vs Xpress3	WBR vs Xpress
p	0.89	0.96	0.68
r	0.95	0.95	0.99

Table 2 - Scores Comparison - Abnormal FAP cases

	FBP vs WBR	FBP vs Xpress3	WBR vs Xpress3
p	0.36	0.39	0.80
r	0.95	0.96	0.99

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Reverse of stress/rest Lung/ Heart Ratio relationship as a prognostic factor of Coronary Disease

I. Karfis¹, I. Kotsalou¹, M. Poulakis², P. Xaplanteris², J. Karydas², A. Zoumboulidis¹, K. Lazaridis², N. Dimakopoulos¹; ¹NIMTS Hospital, Nuclear Medicine Dept., Athens, GREECE, ²NIMTS Hospital, Cardiology Department, Athens, GREECE.

AIM : Lung/ Heart Ratio (LHR stress) increase in stress myocardial perfusion imaging (MPI) is considered as a marker of exercise- induced left ventricular systolic and diastolic dysfunction and high risk coronary artery disease (CAD). The respective ratio measured in rest study (LHR rest) is normally greater than the LHR stress (S<R), due to proportionally increased blood supply during stress test. In this study we aimed to identify any correlation between the LHR stress/LHR rest ratio and the extent of coronary heart disease defined by ^{99m}Tc- tetrofosmin myocardial perfusion imaging. **METHODS - MATERIALS :** We correlated the clinical and demographic characteristics, the SPECT images and quantitative lung/heart ratio in 82 patients undergoing stress (treadmill or adenosine) ^{99m}Tc- tetrofosmin perfusion testing, due to anginal symptoms. LHR was defined on the anterior planar image obtained during exercise ^{99m}Tc- tetrofosmin SPECT acquisition as the mean counts per pixel in an entire left lung field region of interest (ROI) divided by the mean counts per pixel in the hottest myocardial wall ROI. Normal values were stress LHR ≤ 0,49 and S <R (LHR stress / LHR rest < 1). **RESULTS :** The 55 (67%) of 82 individuals had reverse of LHR stress / LHR rest index, with similar proportions in single (68%), 2-vessel (68%), 3-vessel (63%) disease, making remarkable that reverse of S/R ratio (normal s<r) was very often evident even single - vessel disease. On the other hand, although 57 (70%) of the patients had pathologically increased LHR stress, 55 (67%) of the total had S>R, including both those with normal and abnormal LHR stress. Multivariable analysis revealed statistically significant correlation between presence of multivessel disease and increased stress LHR, something which was not proved for single-vessel disease. **CONCLUSIONS :** Stress Lung/ Heart Ratio (LHR) is a common finding in multi- vessel coronary disease indicating ventricular dysfunction. Reverse of normal sLHR<r LHR relationship might be the sign of early ventricular dysfunction, present even from the beginning of single- vessel disease.

S<R	SPECT (no. vessels)			Total
	1	2	3	
Normal	6 (32%)	14 (32%)	7 (37%)	27 (33%)
Abnormal	13 (68%)	30 (68%)	12 (63%)	55(67%)
Total	19 (23%)	44 (54%)	19 (23%)	82

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Stress Lung/ Heart Ratio as an index of left ventricular dysfunction and multi-vessel Coronary Disease

I. Kotsalou¹, I. Karfis¹, M. Poulakis², J. Karydas², P. Georgoulas³, A. Zomboulidis¹, K. Lazaridis², N. Dimakopoulos³; ¹NIMTS Hospital, Nuclear Medicine Dept., Athens, GREECE, ²NIMTS Hospital, Cardiology Department, Athens, GREECE, ³University of Larissa, Nuclear Medicine Department, Athens, GREECE.

AIM : Increased Lung/ Heart Ratio (LHR) in Myocardial Perfusion studies is a predictor of adverse cardiac events and identifies people with extensive coronary artery disease (CAD). In this study we aimed to evaluate the degree of correlation between the Lung/ Heart Ratio and the presence of multi-vessel coronary disease defined by ^{99m}Tc- tetrofosmin myocardial perfusion imaging (MPI). **METHODS - MATERIALS :** We reviewed the records and images of 82 consecutive subjects, without previously known coronary artery disease, who underwent exercise or adenosine ^{99m}Tc-tetrofosmin perfusion testing. LHR was defined by the ratio of the mean pulmonary counts and the mean myocardial counts assessed from corresponding regions of interest (ROI's) positioned over the left lung and the heart respectively, in the anterior view of the tomographic data acquisition procedure. Normal values were stress LHR ≤ 0,49 and S <R. All patients were subjected to coronary angiography post the MPI study. **RESULTS :** The 57 patients (70%) had LHR greater than 0,49 and 82% of them had perfusion abnormalities indicating multivessel coronary disease, whereas the respective proportion for patients with normal LHR (n=25) was 64%. Multivariable analysis revealed statistically significant correlation between presence of multivessel disease and increased LHR, something which was not proved in single-vessel disease. On the other hand, reverse of stress/ rest ratio (normal s<r) was very often evident of single - vessel disease. **CONCLUSIONS :** Stress Lung/ Heart Ratio (LHR) is a common finding in multi-vessel coronary disease indicating ventricular dysfunction and predictor of adverse cardiac events. Reverse of normal sLHR<r LHR relationship might be the sign of early ventricular dysfunction, present even from the beginning of single- vessel disease.

LHR	SPECT (no. vessels)			Total
	1	2	3	
Normal	9 (47%)	13 (29%)	3 (17%)	25 (30%)
Abnormal	10 (53%)	32 (71%)	15 (83%)	57(70%)
Total	19 (23%)	45 (55%)	18 (22%)	82

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Influence of different reconstruction algorithms on quantitative parameters of myocardial perfusion SPECT

O. Lang¹, I. Komorousova², H. Balon¹; ¹Charles Univ., 3rd Medical Faculty, Prague 10, CZECH REPUBLIC, ²Center for Nuclear Medicine, Prague 9, CZECH REPUBLIC.

Objectives: Software for quantitative evaluation of myocardial perfusion scans was developed in the era of filtered backprojection for tomography reconstruction. However, newer processing stations use iterative reconstruction algorithms. Our goal was to assess the differences in image patterns between the two reconstruction methods and to compare data derived from quantitative analysis. **Methods:** We analyzed myocardial perfusion scans of 32 pts (19 male, 13 female, avg age 63 y) evaluated for suspected or known ischemic heart disease. Standardized protocol with Tc99m-MIBI was used. Data were processed twice on all pts; first with filtered backprojection (FBP), then with OSEM/MLEM algorithm (IR). Emory Cardiac Tool Box was used for quantitative analysis; data were compared with paired t-test. **Results:** Upon visual assessment, the image quality was better with IR. By quantitative analysis, the respective parameters for FBP and IR were: mean SSS 6.3 vs. 7.3, SRS 4.3 vs. 4.5, SDS 2.0 vs. 2.8, total perfusion defect 11.8% vs. 12.7%, LAD defect 11.3% vs. 11.9%, LCx defect 6.6% vs. 7.3%, RCA defect 15.4% vs. 13.8%, EF 56.3% vs. 55.9%, EDV 98.3 vs. 91.9 and ESV 45.2 vs. 42.6. None of the

differences were statistically significant (p ranged from 0.435 to 0.926). **Conclusions:** Image quality of myocardial perfusion was found to be better using iterative reconstruction. The results of quantitative analysis were similar; the differences did not reach statistical significance. Therefore, current commercially available normal databases can be used without limitations regardless of the reconstruction algorithm.

P200

Half-time cardiac imaging acquisition- A comparative study

R. Muzaffar¹, D. Oliver², A. Abdelmalik¹, P. Fajnwaks¹, N. Nguyen¹, M. Osman¹; ¹Saint Louis University, St. Louis, MO, UNITED STATES, ²Cancer Center- Saint Louis University, St. Louis, MO, UNITED STATES.

Purpose: Myocardial perfusion SPECT imaging is a well-established clinical discipline, with over 5 million studies performed annually. However, it is a relatively long examination requiring a few hours to complete; therefore, the number of studies performed per day is restricted by the duration of imaging. Astonish (Philips Medical Systems) is a new recovery algorithm with iterative reconstruction that aims to reduce the duration of image acquisition by 50%. We wished to evaluate the reproducibility of image interpretation and image quality using full-time data without Astonish (FT) and half-time data with Astonish (HTA). **Methods:** Thirty-three consecutive patients (20 M, 13 F; mean age 58.2 yrs) underwent rest/stress Tc-99m ECG-gated SPECT. FT data sets included acquisition of 64 projections and processing with filtered backprojection. The HTA data was created by retrospectively extracting 32 projections from the FT data and processed with Astonish algorithm. FT and HTA images were reviewed in a random sequence by a board certified nuclear physician blinded to clinical history. Image quality was scored on a 4-point scale (0 = poor, 1 = fair, 3 = good, 4= excellent). Also, certainty of the presence of coronary artery disease was scored on a 5-point scale (0 = definitely normal, 1 = probably normal, 2 = equivocal, 3 = probably abnormal, 4 = definitely abnormal). Kappa statistics were used for evaluation of agreement. **Results:** HTA processing with Astonish resulted in an improvement in image quality compared to FT processing with FBP (82% HTA was considered excellent quality vs 24% FT; 15% HTA was considered good quality vs 67% FT). Image interpretation was relatively consistent with a normal vs abnormal interpretation of 42%/58% HTA and 33%/67% FT. The measurement of agreement for diagnostic impression revealed a kappa value of 0.833. **Conclusion:** Image acquisition and processing with Astonish provides improved image quality without losing diagnostic accuracy. This promising new technique will allow for greater productivity without the loss of interpretive certainty.

P201

Comparison Of Filtered Back Projection And Iterative Reconstruction Methods In Myocardial Perfusion Scintigraphy

E. Öztürk, D. Kuslu; UFUK University Medical Faculty, Ankara, TURKEY.

AIM: One of the most important problem during interpretation of Tc99m labelled radiopharmaceutical myocardial perfusion scintigraphy is the diaphragmatic attenuation or the high gastrointestinal activity that masks the inferior wall. In recent years, iterative reconstruction (IR) has been used increasingly in reconstruction of myocardial perfusion SPECT images instead of filtered back projection (FBP). However, there are limited numbers of studies that shows role of IR especially in the evaluation of inferior wall. In this study we compared IR method and FBP for both visual interpretation and segmental myocardial tracer uptake values. **MATERIALS AND METHODS:** The study group comprised 148 consecutive patients (94 M, 54 F) who underwent 1-day 99m-Tc MIBI rest/stress myocardial perfusion imaging. Images were reconstructed with both iterative reconstruction (IR-OSEM) and FBP and compared. The images from two methods were interpreted both semi quantitative visual analysis (normal-0, mild-1, moderate-2, severe-3 ischemia, scar-4, diaphragmatic/breast attenuation-5 and increased gastrointestinal activity-6) and segmental myocardial tracer uptake values (percent of maximum). The uptake values and visual assessment scores obtained from the filtered back projection images were compared with the ones obtained from images reconstructed with iterative method. Data of PBP divided in to three groups: 1- All patients, 2-Patients interpreted as inferior wall abnormality, 3- Patients interpreted as diaphragmatic attenuation. 68 patients underwent coronary angiography and results of these patients also compared. Statistical analysis was made using Wilcoxon (sig. p<0.05) and Paired T-test (sig. P<0.01) **RESULTS:** Results are shown in the table

Group	1 (N=148)		2 (N=86)		3 (N=24)	
	REST	STRESS	REST	STRESS	REST	STRESS
Semiquantitative	APICAL*		APICAL AND INFERIOR**		-	
Visual	Inferior mid-bazal*	Midinferoseptal*	Midinferior inferoapical*	Bazal, midanterior r*	Inferior apical	Inferoapical
Quantitative	inferoapical	inferoseptal	anteroapical**	anteroapical, apical*	anteroapical r	midinferior
	apical**	apical**			*	anteroapical *

* (p<0.01) ** (p<0.05) 33 of 68 patients underwent coronary angiography had RCA stenosis and similar curves have been obtained in ROC analyses of two methods. **CONCLUSION:** IR can be useful especially in apical and inferior wall interpretation except in the cases inferior wall interpreted as diaphragmatic attenuation. Because of the routine protocol used in our department, the number of cases with high GIS activity is limited in our group and the potential impact of this method need to be evaluated in more patients with especially high GIS activity and RCA stenosis.

P202

The diagnostic potential of summed stress scores and defect extent in myocardial perfusion SPECT

T. Rösner¹, J. Streich², W. Kaiser³; ¹NuCom Software, Rohlstorf, GERMANY, ²Leibniz-Institute for Zoo and Wildlife Research, Berlin, GERMANY, ³Nuklearmedizin, Stuttgart, GERMANY.

Myocardial perfusion SPECT studies are commonly processed using the Bulls Eye plot, followed by calculation of Summed Stress Scores (SSS) and defect extent (DE). Initially, every single pixel value in the Bulls Eye is normalized to a reference area, sometimes performed as a normalization to the maximum pixel value. In this normalization procedure, the localization of the reference area in the Bulls Eye plot is not taken into account, thus potentially reducing the diagnostic potential of SSS and DE calculation. We compared three normalization procedures more or less depending on the localization information. Patients were examined using a double head gamma camera and rectangular head position, without ECG gating and with 180° scan arc. A patient group with normal perfusion scintigrams and a group with moderate or serious findings in stress examination were selected for calculation of sensitivity and specificity. Patient studies were processed fully automatically using filtered backprojection and reorientation as well as Bulls Eye calculation and segmentation. 3 Methods were used to normalize the Bulls Eye: 1. 4DMSPECT method: The Bulls Eye is normalized to the maximum perfusion value of 42 pre-defined segments. This method depends on the segment setting and the localization of the maximum segment. 2. The mean of the uppermost 30% Bulls Eye normalized pixel values is used as reference. The pixels taken into account might have been widely spread across the Bulls Eye plot. Therefore, the effect of localisation information is less than in method 1. 3. The mean pixel perfusion serves as reference. It does not depend on localization information. All 3 methods show comparable sensitivity and specificity and we conclude, that localization information has minor relevance for Bulls Eye normalization. In all methods the SSS specificity is higher than for DE (defect extent). To avoid false positive results, one should prefer SSS. In contrast, one should use DE to achieve a higher sensitivity and to avoid false negative results.

P203

Impact of the use of Attenuation-Correction in G-SPECT myocardial perfusion imaging interpretation: results of multicenter SPAG (SPECT Attenuation-correction vs Gated) study

D. Genovesi¹, A. Giorgetti¹, A. Gimelli¹, G. Cannizzaro², R. Giubbini³, F. Bertagna³, G. Fagioli⁴, M. Rossi⁴, A. Romeo⁴, P. Bertolaccini⁵, R. Bonini⁵, E. M. Ferdeghini⁶, P. Marzullo⁷; ¹Fondazione Gabriele Monasterio, Pisa, ITALY, ²A.O. V. Cervello, Palermo, ITALY, ³Spedali Civili, Brescia, ITALY, ⁴Ospedale Maggiore, Bologna, ITALY, ⁵Ospedale Ss Giacomo e Cristoforo, Massa, ITALY, ⁶IFC-CNR, Pisa, ITALY.

Purpose Attenuation artifacts cause reduction of specificity of stress-rest gated single photon emission computed tomography (G-SPECT) myocardial perfusion images. The purpose of this multicenter study is to assess the real improvement in diagnostic accuracy due to the use of Attenuation Correction (AC) differentiated by coronary territory, patient's sex and body-mass-index (BMI). Methods The effect of AC was evaluated in a group of 104 patients (pts) (Age: 64±10 years; 82 male, 22 female; BMI: 27±4) with known coronary artery disease (CAD) studied by coronary angiography (CAG) within one month from the SPECT study; in particular 61 pts had a positive CAG (≥50%) while 43 pts had not significant coronary stenosis. G-SPECT images attenuation-corrected and not attenuation-corrected (NC) were randomly interpreted by 3 blinded readers. Results The use of AC did not improve the overall accuracy both for women (AC: sens. 85.7%, spec. 62.5%; NC: sens. 92.9%, spec. 62.5%) and for men (AC: sens. 72.3%, spec. 91.4%; NC: sens. 87.2%, spec. 94.3%); while it demonstrated a significant accuracy improvement in the evaluation of inferior wall in over-weighted men (AC: sens. 80%, spec. 100%; NC: sens. 80%, spec. 66.7% - $p = 0.04$). Unexpectedly the use of AC did not cause any improvement of accuracy in the evaluation of anterior wall in women (AC: sens. 72.7%, spec. 63.6%; NC: sens. 90.9%, spec. 63.6%). Conclusions. CT-based AC of G-SPECT images consistently improved diagnostic performance of readers in the evaluation of right coronary territory of over-weighted men, while it could be avoidable in normal-weighted men and in women at all. The extensive use of CT-based AC of G-SPECT causes an overall reduction of sensitivity as well as an unjustified increase of global radioexposure.

P204

Comparison of Gated Myocardial Perfusion SPECT Using Tl-201 and Tc-99m-Tetrafosmin to Evaluate Left Ventricular Function

E. Takács, A. Radácsi, M. Janecskó, P. Sárman, I. Szilvási; Semmelweis University Kútvolgyi Clinical Center, Budapest, HUNGARY.

Aim: Tc-99m-tetrafosmin (TF) ECG-gated SPECT (GSPECT) is a generally accepted method for simultaneous evaluation of myocardial perfusion and left ventricular (LV) function. Because of the Mo-99 crisis demand for Tl-201 is increasing. Aim of this study was to compare the diagnostic value of TF GSPECT and Tl-201 GSPECT in the assessment of global and regional LV function. Patients and methods: 15 patients (14 men, 1 woman) with known ischemic heart disease underwent TF stress-rest GSPECT and Tl-201 rest-redistribution GSPECT (110 MBq for viability). Results of resting GSPECTs of both examinations were analysed. Global (ejection fraction: EF) and regional function (wall motion and thickening) of the LV were evaluated using a quantitative software (QPS/QGS, 20 segments model, scoring system). Results were related to segmental myocardial perfusion and echocardiographic findings. Results: LV EF values determined by Tl-201 and TF correlated well (50.7 ±10.2 % vs 53.8±12.6 %, $r=0.82$). Both EF were significantly lower than by cardiac ultrasound (64.3±8.1 %, $p<0.05$). Segmental wall thickening scores were similar on both GSPECT examinations ($r=0.59$), but wall motion scores were less reliable by Tl-201 than by TF GSPECT ($r=0.44$). Conclusion: Tl-201 GSPECT is reliable for assessment of LV EF and seems to be appropriate to investigate regional wall thickening. It is less reliable in evaluating regional wall motion. GSPECT of the standard Tl-201 myocardial scintigraphy is recommended.

P205

Regional left ventricular myocardial mass assessment by scintigraphy in coronary artery disease

M. Zigman¹, S. A. Rogan², D. Planinc³, Z. Kusic²; ¹Dpt. of Oncology and Nuclear Medicine, University Hospital "Sestre milosrdnice", Zagreb, CROATIA, ²Dpt. of Oncology and Nuclear Medicine, University Hospital,

Zagreb, CROATIA, ³Dpt. of Internal Medicine, University Hospital, Zagreb, CROATIA.

The aim of the study was to evaluate possibility of non-invasive quantitative determination of viable regional left ventricular mass (rLVM) in patients (pts) with different type of coronary artery disease (CAD) using perfusion myocardial scintigraphy. Patients: Study population consisted of 90 pts with established CAD and 34 pts with non-ishaemic cardiomyopathy who underwent complete cardiologic evaluation and gated stress/rest SPECT perfusion scintigraphy using ²⁰¹Talium. According to diagnose pts were divided into the groups: A) pts with anterior myocardial infarctions (n=36); B) pts with inferior infarcts (n=34); C) pts with verified CAD without infarct (n=20) and group D) pts with non-ishaemic cardiomyopathy (n=34). Methods: Voxel based analysis was used for estimation of rLVM on tomographic slices by manually defined region of interest in LV myocardium on perfusion scintigraphy (Hermes software package). Five parallel planes on horizontal long axes were used for assessment of rLVM: upper mid-wall slice (I), upper endocardial slice (II), central LV slice (III), lower endocardial (IV) and lower mid-wall (V) slice. Slice width is 5.3 mm. Results: Mean±SD of rLVM (gram per slice) was estimated in the groups as follow: in group A myocardial mass was significantly lower in regions I and II compared to groups B, C and D ($p<0.001$; 11.2±2.0 and 8.5±3.0 gram vs 17-19.0±3.5 gram). In group B greater mass difference was found in lower planes (III, IV) compared to group A and D ($p<0.001$; 8.2±2.0 gram and 7.0±2.0 vs 13.5-18.0 gram). Group C and D showed higher myocardial mass in central region compared to groups A and B but without statistically significance. Group D shows in all planes higher mass values except in lower slices (19-23.0±5.0 vs 11-18±2.0 gram). Based on scintigraphic analysis of 128 myocardial regions without any perfusional defects we found that mean values of rLVM is 16.5±3.0 grams, thereby hypertrophy is considered when region mass is more than 20 grams. Regions with rLVM from 10-13.5 grams had preserved function although altered (hypokinetic). Myocardial mass under this value is connected rather with scar and severe regional myocardial wall motion abnormalities. Conclusion: in vivo regional mass estimation based on scintigraphy method could be very useful in follow-up of pts with CAD for monitoring of quantitative changing in myocardial viability during medical therapy or after coronary artery intervention.

P206

A decision support system in myocardial perfusion scintigraphy: The advice may save unnecessary rest studies

K. Tagil¹, D. Jakobsson², M. Lomsky³, J. Marving⁴, S. Svensson⁵, B. Hesse⁶; ¹Clinical Physiology and Nuclear Medicine, Malmo University Hospital, Malmo, SWEDEN, ²EXINI Diagnostics, Ideon Science Park, Lund, SWEDEN, ³Department of Clinical Physiology, Sahlgrenska University Hospital, Gothenburg, SWEDEN, ⁴Department of Clinical Physiology, Gentofte Hospital, Copenhagen, DENMARK, ⁵Department of Clinical Physiology, Karlskrona Hospital, Karlskrona, SWEDEN, ⁶Department of Clinical Physiology and Nuclear Medicine, Rigshospitalet, Copenhagen, DENMARK.

Aim: It is often a practical question in myocardial perfusion scintigraphy (MPS) whether to continue with the rest study after termination of a fairly normal stress study, the question being more difficult with less experience. The purpose of this study was to analyze the value of a decision support system (DSS) as an aid to answer this question. Methods: Nine physicians, all trainees in nuclear medicine, interpreted 100 MPS stress studies in patients with low-intermediate likelihood of coronary disease, first without and then with the advice of a DSS. Each study was interpreted regarding the necessity to continue with a rest study or not. The patients had undergone a gated stress MPS, using a Tc-99m sestamibi protocol. The gold standard used was the interpretations made by three experienced nuclear medicine specialists on the basis of all available clinical and image information. Results: In the subgroup of 57 patients regarded as having normal stress-rest MPS by the experts, the trainees suggested to have a rest study done significantly less (6.6 less rest studies), but with wide variations, from 24 (14-42) to 18 (8-23), after the advice from the DSS. The "specificity" (only to ask for a rest study when necessary) increased from 57% without the advice to 69% with the advice ($p<0.005$). The "sensitivity" (to ask for a rest study if it must be performed) for the 9 physicians was high and unchanged after DSS advice (without the advice 94% and with the advice 95%). Conclusion: This study shows that the decision support system may reduce the use of unnecessary rest MPS studies if less experienced nuclear medicine physicians have to make the decision.

P207

The dependence of the Transient Ischemic Dilatation ratio on the heart rate during Myocardial Perfusion Scintigraphy

B. J. van der Veen, N. Kuiperij, M. P. M. Stokkel; Leiden University Medical Centre, Leiden, NETHERLANDS.

Background: Transient Ischemic Dilatation (TID) is regarded a serious finding that may indicate severe and transient coronary artery disease, even in patients with seemingly normal perfusion patterns. Nonetheless, several case-studies indicate that the TID is influenced by variations in heart rate (HR). This study was initiated to evaluate the relation between TID and the heart rate during acquisition. **Method:** 299 consecutive patients referred for exercise or adenosine MPS acquisitions were included. Hemodynamic data and HR responses were measured during stress induction. Post-stress and rest acquisitions were acquired with a triple-head SPECT camera system using ECG gating. The MPS data was automatically analyzed to generate global (ejection fraction, volumes, heart rate) and regional (perfusion scores) functional parameters. The difference between the heart rate during rest and post-stress acquisition is denoted as Δ HR. **Results:** Significant differences were found in hemodynamic response after stress, functional parameters and TID values between the adenosine and exercise stressed populations. The TID was highly correlated with the ejection fraction (PCC -0.30, $p<0.001$) and summed difference score (PCC -0.35, $p<0.001$) in the exercise stressed population. No such correlations were found between the functional MSP parameters and the TID in the adenosine stressed population. Both populations showed a strong negative relation between the Δ HR and the TID (adenosine: -0.64, $p<0.001$; exercise: -0.54, $p<0.001$). **Conclusion:** The TID is dependent on the heart rate during acquisition. These results may have important implications for patients with heart rate variability and arrhythmias.

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Quantitative Assessment of supine and Semi-upright Left ventricular Function with a Dedicated Cardiac Camera

S. Ben-Haim¹, D. Shiti², J. B. Bomanji¹, S. Hain¹, E. M. Prvulovich¹, A. M. Groves¹, I. Kayani¹, Y. Toren², P. J. Ell¹; ¹University College London Hospitals NHS Foundation Trust, London, UNITED KINGDOM, ²Spectrum-Dynamics, Caesarea, ISRAEL.

Aim: D-SPECT (Spectrum-Dynamics, Caesarea, Israel) is a novel solid-state cardiac camera with improved sensitivity and improved image resolution and has been shown to provide visual and quantitative measures of myocardial perfusion and function comparable to conventional SPECT in up to one seventh the acquisition time. Images can be acquired either supine or in the semi-upright position. We compared left ventricular (LV) volumes and function obtained from ^{99mTc}-sestamibi rest myocardial perfusion SPECT (MPS) in the supine and semi-upright positions. **Materials and Methods:** Thirty-eight patients (F=28, age 64.05±12.48yrs) underwent one-day stress-rest ^{99mTc}-sestamibi gated MPS. Rest images were acquired in the supine and semi-upright position within 13.05±7.59 min. Images were quantitatively analyzed using a modified version of QGS (Cedars Sinai, LA, CA) accounting for the high resolution of the camera and were also assessed visually to detect regional wall motion abnormalities (WMA). **Results:** Supine and semi-upright LV end-diastolic and end-systolic volumes (EDV and ESV) and LV ejection fraction (EF) were 88.34±39.49 vs. 84.78±42.18 (p=0.008), 40.08±34.55 vs. 39.56±36.5 (p=0.672) and 60.56±17.11 vs. 59.45±16.61 (p=0.3), respectively. There was an excellent agreement between EDV, ESV and EF in the supine and semi upright positions (EDV 89.5%, ESV 92.1% and EF 89.5% using Bland-Altman (BA) analysis with $\alpha=0.05$). Significant differences in supine and semi-upright EDV were found only in females (77.15±30.06 vs. 71.67±31.15 p<0.001, for males: 118.7±47.21 vs. 120.2±49.04 p=0.55, respectively). The 3 outliers of BA EDV analysis were in women with low LV volumes. In 8 cases there were EF differences >5%: 2 with irregular heart rhythm, 2 with large attenuation artifacts, 3 with bowel loops overlapping the LV in the supine position and in one case with severe LV dysfunction. Eight patients had WMA, which were identical on supine and semi-upright imaging. **Conclusion:** LV volumes and function and LV wall motion remain fairly consistent between supine and semi-upright imaging using a dedicated cardiac camera. Irregular heart rhythm, attenuation artifacts, bowel overlapping the LV and severe LV dysfunction may interfere with volume and function measurements. In addition, there may be an underestimation of EDV in the semi-upright position in women with low LV volumes; however, more data is needed for statistical analysis.

P19 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Cardiovascular: Protocols in nuclear cardiology

P209

An investigation for the effect of time intervals between Tc-99m MIBI injection and image acquisition on heart-mediastinum count ratio and washout rate.

A. Okizaki¹, Y. Urano², N. Ibuchi², Y. Sasagawa², M. Nakayama¹, M. Odashima¹, Y. Kusano¹, K. Watanabe¹, K. Shiba¹, T. Aburano¹; ¹Asahikawa Medical College, Asahikawa, JAPAN, ²Rumoi City Hospital, Rumoi, JAPAN.

Aim The myocardial washout rate (WO) and heart-to mediastinum ratio (H/M) of Tc-99m sestamibi (MIBI) has been reported to be useful for evaluation of myocardial damage in heart diseases. WO and H/M are calculated from the uptake in the heart and mediastinum. The uptake of Tc-99m MIBI is relatively unstable immediately after the injection. We hypothesized that it may take some time for stabilization of H/M and WO. The purpose of this study was to investigate the stability of early H/M and WO in several variations of time interval between the radiotracer injection and early scanning (TI). **Materials & methods** Fifty-four patients with various heart diseases were studied. After an injection of Tc-99m MIBI (720MBq), the dynamic planar imaging was performed on a dual-headed digital gamma camera system for 24 minutes. ROIs were drawn over the whole heart and mediastinum to obtain the early H/M. Ten of 3-minute TI data (from 3-6 to 21-24) were extracted from the continuously collected data. Finally, 540 of early H/M and WO data were analyzed. Three hours after the injection, delayed image was acquired to calculate delayed H/M and WO. Time decay correction was performed with the Tc-99m half-life. Tukey's multiple comparison test was performed to estimate whether there was a significant difference of early H/M and WO in each TI or not. Degrees of variation were compared using coefficients of variation. **Results** The results were summarized in the tables. The early H/M and WO gradually increased with TI (Table 1). The H/M in small TI (3-6) was significantly smaller than in the others (p < 0.05). However, there was no significant difference of WO in each TI. The coefficients of variation of early H/M were stable, but those of WO were gradually decreased with TI (Table 2). **Conclusion** The H/M and WO gradually increased with TI. To estimate early H/M, scanning time might have to be 5 minutes or more after the radiotracer injection. Furthermore, the coefficients of variation of WO were gradually decreased with TI. Sufficient time interval between the radiotracer injection and early scanning might be useful for evaluation of H/M and WO.

Table1: Early H/M and WO (Average +/- Standard deviation)

TI	3-6	5-8	7-10	9-12	11-14	13-16	15-18	17-20	19-22	21-24
Early H/M	2.04 +/- 0.31*	2.21 +/- 0.38	2.28 +/- 0.41	2.32 +/- 0.42	2.35 +/- 0.43	2.37 +/- 0.44	2.40 +/- 0.45	2.42 +/- 0.45	2.43 +/- 0.45	2.44 +/- 0.45
WO	10.1 +/- 19.3	14.8 +/- 17.4	15.5 +/- 17.0	16.0 +/- 16.4	16.1 +/- 16.0	16.4 +/- 15.5	16.7 +/- 15.2	16.6 +/- 14.9	16.6 +/- 14.7	16.8 +/- 14.4

(*p<0.05)

Table2: coefficients of variation (%)

TI	3-6	5-8	7-10	9-12	11-14	13-16	15-18	17-20	19-22	21-24
Early H/M	15.2	17.2	18.0	18.1	18.3	18.6	18.8	18.6	18.5	18.4
WO	191.1	117.6	109.7	102.5	99.4	94.5	91.0	89.8	88.6	85.7

P210

The Impact of Caffeine On Results of Gated Myocardial Perfusion SPECT Study Using Dipyridamole: Still Debatable Issue

O. Yaylali¹, S. Kirac¹, Y. T. Yaylali¹, M. Serteser², D. Yuksel¹, B. Akdag¹; ¹Pamukkale University Medical Faculty, Denizli, TURKEY, ²Acibadem Labmed Clinic, İstanbul, TURKEY.

AIM: Dipyridamole is being widely used for vasodilatation stress test during gated myocardial perfusion SPECT imaging (GMPS). It enables to detect diminished coronary flow, but, this effect may disappear by caffeine ingestion. Therefore, caffeine is recommended to stop at least 24 hours prior to dipyridamole testing. The purpose of this research was to examine the impact of caffeine on the heart rate, blood pressure and dipyridamole GMPS findings. **MATERIAL&METHOD:** GMPS with standard dipyridamole stress test (DST) was used to assess myocardial perfusion defects and LVEF values in 20 patients, who had coronary angiography (CAG) showing >50% stenosis in at least one vessel, with known or high likelihood of coronary artery disease before (baseline) and after one cup of coffee ingestion (caffeine) following dipyridamole infusion. Both dipyridamole MPS procedures were completed within one week. All patients were asked for their daily caffeine consumption and asked to discontinue caffeine 24 h prior to the test. ECHO, heart rate, diastolic and systolic blood pressures were recorded baseline and caffeine during DST. Serum caffeine levels were measured by HPLC before and one h after coffee ingestion. GMPS images and gated analyses were assessed visually and quantitatively. **RESULTS:** Our study consisted of 14 men and 6 women (mean age ± SE; 56 ± 2 years). The mean serum caffeine levels were <1 mg/L and 5.4 ± 0.3 mg/L at baseline and 1 h after caffeine ingestion, respectively (p<0.05). The mean heart rate was increased by 16 % after dipyridamole infusion in patients without caffeine, but no any significant change was noted after caffeine intake (p>0.05). The blood pressures were decreased significantly after dipyridamole infusion with and without caffeine (p<0.05). The ratio of perfusion defects (90% on LAD territory in baseline GMPS images was significantly higher than that of caffeine (60% GMPS (p<0.05), and also, than the stenotic lesions in LAD arteries (55%) on CAG (Table 1). The LVEF by dipyridamole GMPS was 65 ± 4% at baseline and 60 ± 3% after caffeine (p<0.05). The baseline dipyridamole ECHO LVEF was (56 ± 2%) significantly lower than gated LVEF result (65 ± 4%) . **CONCLUSION:** We think that even one cup coffee may attenuate the results of dipyridamole GMPS imaging and patients should have been refrained from taking beverages containing caffeine one day before the dipyridamole test to avoid false negative GMPS result. Table 1. The number of myocard perfusion defects and the stenosis in coronary angiography

Arteries	Baseline GMPS		Caffeine GMPS		CAG*	
	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal
LAD	2	18	8	12	9	11
RCA	9	11	11	9	14	6
LCX	8	12	13	7	14	6

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Different results of stress myocardial perfusion gated SPECT in patients with coronary artery disease in comparison to various stress test level.

P. Maj; Nuclear Medicine Department. Medical University, Lublin, POLAND.

The aim of this study was to assess relation between different stress test achievements in patients with coronary artery disease (CAD) and results of myocardial rest/stress perfusion gated SPECT (GSPECT). **Materials and Method.** myocardial perfusion scintigraphy (MPS) was performed in 132 patients (F/M; 71/61 mean age 58.5 ± 10.5 years). High risk patients were referred for MPS with suspicion of CAD, chest pain or positive exercise electrocardiogram test. All patients underwent 2-days protocol (stress/rest) GSPECT MPS after 740 MBq of ^{99mTc} MIBI injection. All stress/rest images were visually analyzed for the presence, severity and reversibility of perfusion and wall motion abnormalities. For estimation of perfusion defects a 4-point scale system was used (1 - normal, 2 - moderate, 3 - severe reduction, 4 - absent perfusion). Patients were divided into 3 groups. Group A patients who reached predictive heart rate PHR (n= 84), group B - patients who did not achieve PHR, with symptoms of stress ischemia (n=19) and group C - patients did not achieve PHR, with fatigue during stress test (n 29). In these 3 groups there were separated subgroups of patients with not visible, moderate and severe stress defects in MPS in comparison to rest study. **Results.** The most frequent symptom in our group was chest pain - 54 cases (40.9%). It was typical in 33,4% and atypical in 7,5% patients. 37/132 patients (28%) had a documented myocardial infarction. Patients from group B were significantly younger (55.4 ±10.4 years) than in group A (60 ± 9.8 years, p<0.04). In group B there were statistically more male (14 of 19 [73,7%]) in comparison to group A (32 of 84 [38%], p<0.005). More severe stress defects than in rest MPS study were observed in significantly greater number of patients from group B (9 of 19 [47,4%]) than in group A (18 of 84 [21,4%] p<0.03) and group C (4 of 29 [13,8%] p<0.02). There were not significant differences in the number of patients with similar rest/stress perfusion defects in group A (29 of 84 [34,5%] and C (11 of 29 [37,9%]), versus B (5 of 19 [26,3%]), p>0.05). **Conclusions.** Results of stress test in patients from group B despite not achieving PHR were related with stress perfusion defects in MPS. In group A despite achieving PHR result of stress test showed weak relation with stress perfusion defects in MPS.

P212**Evaluation of TI-201 SPET scan in one-day stress-redistribution-reinjection protocol**

M. Lacic¹, S. E. M. Clarke², M. M. Lacic¹; ¹Polyclinic "Dr. Lacic", Zagreb, CROATIA, ²Department of Nuclear Medicine, Guy's Hospital, London, UNITED KINGDOM.

Aim: The aim of this study was to compare quantitatively and qualitatively TI-201 myocardial uptake during one-day stress-redistribution-reinjection TI-201 SPET protocol. **Methods:** Seventy patients (16 female and 54 male), aged from 31 to 77 years (mean 59,8 years), with high probability of coronary artery disease were included in this study. Stress, delayed and reinjection SPET scans were obtained using a 180-degree circular orbit in a step and shoot mode from left-posterior oblique to right-anterior oblique angle. Quantitative analysis was performed using commercially available software with Emory normal data files. **Results:** Qualitative interpretation of TI-201 SPET scans described 80 defects and quantitative analysis detected 86 defects. Eight bull's-eye defects were not observed on qualitative TI-201 SPET scan analysis and two defects observed on qualitative TI-201 SPET scan analysis did not appear on polar maps. An experience observer described 28 (35%) reversible, 9 (11%) irreversible and 43(54%) partly fixed partly reversible defects. Quantitative analysis revealed 42 (49%) irreversible defects, of which 28 (69%) improved or normalized after reinjection. Three fixed defects did not change following reinjection. Quantitative analysis showed that 41 (48%) defects were partially reversible on redistribution scans and in 25 (61%) of these 41 defects further improvement or normalization was observed after reinjection. In 11 (26%) fixed and 12 (29%) partially reversible defects quantitative analysis showed differential uptake (washout) following reinjection. Three defects were observed only on reinjection polar maps. Redistribution scan was diagnostic in 14% of defects. Good correlation ($r = 0.80$) for detection of defects or disease between quantitative and qualitative TI-201 SPET scan analysis was obtained. **Conclusion:** We concluded that quantitative analysis is a useful supplement to qualitative TI-201 SPET scan interpretation, especially for detection of differential uptake after reinjection and for precise evaluation of dynamic changes in particular defects during a one-day stress-redistribution-reinjection TI-201 SPET scan protocol.

P213**The assessment of association of dipyridamole side effects with hemodynamic parameters, ECG and scintigraphy outcomes**

H. Javadi¹, M. Shariati¹, M. Mogharrabi¹, I. Neshandar Asli², A. Hooman², S. Jallalat¹, **M. Assadi**³; ¹Department of Nuclear Medicine, 5th Azar Hospital, Golestan University of Medical Science, Gorgan, IRAN, ISLAMIC REPUBLIC OF, ²Department of Nuclear Medicine, Taleghani Hospital, Shahid Beheshti University of Medical Science, Tehran, IRAN, ISLAMIC REPUBLIC OF, ³Bushehr research center for Nuclear Medicine, The Persian Gulf Biomedical Sciences Institute, Bushehr University of Medical Sciences, Bushehr, IRAN, ISLAMIC REPUBLIC OF.

Aim: Dipyridamole has extensively been administered to simulate physical activity in cardiovascular assessment. The aim of this study was to assess the association of dipyridamole side effects with hemodynamic oscillations, scanning results and ECG findings. **Materials & Methods:** Overlay, 590 cases referred to nuclear medicine center for myocardial perfusion imaging were evaluated for the adverse effects of dipyridamole concurrent with low level of exercise. Before and during dipyridamole infusion, the patients' vital symptoms, electrocardiogram, hear rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were monitored; all patients underwent stress/rest 99mTc-sestamibi GSPECT using a 2-day protocol. **Results:** Eighty-eight patients (14.9%) showed at least one sort of undesired symptom during dipyridamole infusion; abnormal ECG and scan was observed in 32.3% and 48.6% of cases, respectively. There were significant differences between pre and post-infusion HR, pre-infusion SBP and post-infusion DBP among patients with or without untoward symptoms; whereas no significant difference was observed in any of the hemodynamic parameters between patients with normal and abnormal ECG or myocardial perfusion imaging. **Conclusion:** This study demonstrated a correlation between hemodynamic variables and patients' undesired symptoms but not with either imaging findings or ECG.

P214**Prone imaging results in cost-effective usage of radiopharmaceutical by obviating the necessity of rest study in Tc-99m MIBI myocardial perfusion scintigraphy**

E. Ceylan Gunay, A. Erdogan; Mersin University Faculty of Medicine Department of Nuclear Medicine, Mersin, TURKEY.

Aim: In myocardial perfusion SPECT studies, inferior wall attenuation produced by subdiaphragmatic structures may result in reduction of the specificity of the test. It is widely accepted that prone imaging minimizes the diagnostic impact of the attenuation. The aim of this retrospective study is to validate the impact of prone imaging on necessity of a rest perfusion study with a final goal of cost-effective radiopharmaceutical usage. **Material and methods:** The data of 82 patients who had examined both by supine and additional prone imaging were retrospectively evaluated. All of the patients were male, aged between 37 and 86 (median age:58). Patients were referred for suspected coronary artery disease with no history of myocardial infarction. All patients underwent Tc-99m MIBI myocardial perfusion SPECT in supine position after exercise or pharmacological stress with dipyridamole. The adjusted dose was 740 MBq. Prone images were taken right after the immediate visual evaluation of supine study. The need of prone study was decided by reduced perfusion of inferior wall. The acquisition time per projection was 25 sec for each. The final evaluation of reconstructed images of supine and prone studies were done both by visually and quantitatively. Rest myocardial SPECT images were taken in another day if needed. Rest study was omitted in patients with complete normalization of uptake in prone images. **Results:** Prone images obviated the conduct of a rest perfusion study in 68 of 82 patients (83 %). In those patients, absence of perfusion defects was observed in prone study. Diaphragma attenuation of inferior wall was proven by the aid of prone imaging without

additional radiopharmaceutical administration for a rest study. Fourteen of 82 patients (17 %) underwent rest perfusion study since the abnormality in inferior wall was not completely disappeared, and myocardial ischemia was detected in half of them. **Conclusion:** Adding prone imaging to post-stress Tc-99m MIBI myocardial perfusion study does not only reduce inferior wall attenuation but also reduces the need for rest test particularly in low or intermediate risk patients, thus seems to be both useful and cost-effective.

P215**Normal 18F-FDG PET/CT images with heparin loading method; is it homogenous?**

M. Morooka¹, K. Kubota¹, R. Minamimoto¹, K. Ito², Y. Miyata³, O. Okazaki¹, T. Mitsumoto¹, T. Sato¹, K. Fujita¹, T. Nohira¹; ¹National Center for Global Health and Medicine, Shinjuku, Tokyo, JAPAN, ²Saitama International Medical Center, Saitama, JAPAN, ³Medicheck Imaging Center, Minami-Koiwai, Tokyo, JAPAN.

Background and purpose: ¹⁸F-FDG PET has been sometimes used to detect inflammation, but it is hard to distinguish between inflammatory heart disease and normal, because glucose is the second main source of heart metabolism. It is known that ¹⁸F-FDG PET with heparin loading method is useful to detect the disease of cardiac sarcoidosis, however there are few reports about the ¹⁸F-FDG PET imaging in normal heart. **Methods:** ten normal volunteers and 1 patient with heart sarcoidosis underwent ¹⁸F-FDG PET with heparin injection. The %uptake of each area was mechanically measured in 17 segments and all average SUV in 17 segments were mechanically calculated by placing region of interest on the apex. **Results:** The normal ¹⁸F-FDG PET with heparin loading images showed increased uptake mainly in the base-mid septal and lateral area. There is a small difference among individual. The patient with sarcoidosis has focal increased uptake near the apex, and it was diagnosed as sarcoidosis by heart biopsy. **Conclusion:** ¹⁸F-FDG with heparin injection uptake is not homogenous in the heart, and elevated mainly in the base-mid. We report it for the first time (of our knowledge), and the knowledge of this pattern may be useful for detecting which increased uptake is abnormal or not.

P216**A comparison of oral glucose and GIK infusion with F18 FDG PET study in evaluation of myocardial viability**

H. Kaya¹, T. Ansal Balci¹, H. Komek², B. Kızılkcan Bellur¹, G. Bellur³; ¹Dicle University, Diyarbakir, TURKEY, ²Diyarbakir state hospital, Diyarbakir, TURKEY, ³veni vidi hospital, Diyarbakir, TURKEY.

Aim: Myocardial hibernation is impaired resting left ventricular function due to chronically reduced coronary blood flow that can be restored by revascularization.. We aimed in this study to compare oral glucose (OG) F-18 FDG PET with glucose-insulin-potassium (GIK) infusion F-18 FDG PET studies according to myocardial viability assessment and optimally image quality. **Material and methods:** The study was conducted among 40 (32 female, 8 male , mean age 62.1) retrospectively selected patients who have history of myocardial infarction, segmental wall motion abnormality on echocardiography and perfusion defect on myocardial perfusion scintigraphy. All 40 patients underwent PET imaging with OG F-18 FDG and one week later with GIK infusion F-18 FDG. For the analysis, 26 segment scoring system was used. A visual semi-quantitative analysis was carried out according to the following score indicating radioactive uptake: 0 = normal, 1= slight reduction of uptake, 2=moderate reduction of uptake, 3=severe reduction of uptake, 4 = absent of radioactive uptake. The scores obtained by GIK infusion F-18 FDG PET were compared to those obtained by OG F-18 FDG PET. **Results:** When the OG and GIK infusion F-18 FDG PET studies are compared, segmental uptake score difference which is changing between 1 and 14 has been determined. In OG and GIK infusion F-18 FDG PET studies in 10 patients there was normal metabolic activity in all segments and segmental uptake score (SUS) was low (SUS values 3.5 in OG, 2.5 in GIK infusion, $p=0.043$). [Unable to Display Character: İ] In both studies the SUS was high in 24 patients (SUS median values 19 in OG , 16.5 in GIK infusion, $p=0.069$). For the left 6 patients , in the study of OG F-18 FDG PET, there was no FDG uptake (ametabolism). But in the PET imaging after GIK infusion the SUS was significantly declined (SUS median values 24.5 in OG, 15.5 in GIK infusion, $p=0.041$). We found that the image quality in PET imaging with GIK infusion is clearly superior to OG administration. Average left ventricular SUVmax/liver SUVmax values was used for quantitative evaluation of myocardial F-18 FDG uptake. Left ventricular SUVmax/liver SUVmax values were significantly higher in GIK infusion F-18 FDG PET study than OG (GIK infusion 7.03 ± 2.53 , OG 5.02 ± 1.67 $P<0,001$) As a result in the assessment of myocardial viability and for the getting an optimal image quality GIK infusion F-18 FDG PET method is superior to OG F-18 FDG PET method.

P217**The optimization of quality of cardiac 18F-FDG PET imaging**

E. M. Nifontov¹, D. V. Ryzhkova², L. A. Tyutin³; ¹Pavlov State Medical University, St.-Petersburg, RUSSIAN FEDERATION, ²Russian Research Centre of Radiology and Surgical Technology, St.-Petersburg, RUSSIAN FEDERATION, ³Russian Research Center of Radiology and Surgical Technology, St.-Petersburg, RUSSIAN FEDERATION.

The purpose: in order to improve image quality of cardiac [18F]-FDG PET three different protocols were compared. **Methods:** 95 patients underwent static [18F]-FDG PET scanning using 3 different protocols: the standard protocol, consisting of 50 mg oral glucose loading (38 patients), the trimetazidin protocol, consisting of 2-week pretreatment with trimetazidin before [18F]-FDG PET to increase of myocardial glucose consumption (19 patients) and the hyperinsulinemic euglycemic clamp protocol (38 patients). To compare image quality we assessed myocardial [18F]-FDG uptake by calculating myocardium-to-blood-pool activity ratio (M/B ratio) between the different imaging protocols. Images were considered good, adequate, or poor when M/B ratio were over 2, 1.5-2, or less than 1.5, respectively. **Results:** The poor image quality was observed in 28.9% patients who underwent the standard protocol and 10.5% patients who underwent the trimetazidin protocol. In case of the standard protocol [18F]-FDG PET image quality was inadequate in patients with obesity and diabetes mellitus because of poor uptake of [18F]-FDG. The trimetazidin protocol yielded good image quality and higher rates of [18F]-FDG

uptake in patients with diabetes mellitus without obesity. We didn't observed poor image quality among patients with diabetes mellitus and obesity during the hyperinsulinemic euglycemic clamp protocol. Conclusion: In patients with diabetes mellitus and normal body mass index (less than 25) should expect good image quality if they received trimetazidine during two weeks before [18F]-FDG PET imaging. The hyperinsulinemic euglycemic clamp is a priority for patients with diabetes mellitus and body mass index over 25.

P218

Using myocardial kinetics of Iodine-123 beta-methyl iodophenyl pentadecanoic acid (BMIPP) for cardiac metabolism evaluation

Y. B. Lishmanov, L. N. Maslov, S. M. Minin, V. I. Chernov; Institute of Cardiology, Tomsk, RUSSIAN FEDERATION.

The aim experimental researches of functional suitability of 123I-BMIPP for myocardial fatty acid metabolism evaluation. Materials and methods: the solution 123I-BMIPP for injections with the following characteristics was exposed to research: volumetric activity not less than 18 MBq/ml, pH 5-8, period of validity 48 hours from the moment of preparation. Dynamics distribution of 123I-BMIPP was investigated on white rats-male with mass of 250-300, to which through a femoral vein was injected 123I-BMIPP in a dose of 2,5 mBq/kg, then they were killed by groups (of 5) on different terms of research. The radiometry of internal organs was made in 5, 15, 30, 60, 120, 180, 360 minutes after 123I-BMIPP injection. Distribution of 123I-BMIPP in heart was realised on unbreedy rabbits - male with mass of 3,1-3,5 kg. Results: after intravenous introduction in 1 ml of a blood of rats the contents 123I-BMIPP on the 5 minutes did not exceed 1,2 %. Since the first minutes after an injection of a preparation the high accumulation of 123I-BMIPP in a myocardium and liver was marked. The maximal accumulation of a preparation in the heart was observed on the 5 minutes of experiment 5,7 % and to 30 minutes was 5,1 %. In a liver on the 5 minutes the high contents of a preparation - 7,9 % from the entered dose was also marked. The index of myocardium/liver on the 5 minute was 1:1,3. On the 5 minutes of research there were 2,3 % 123I-BMIPP in lungs from the entered dose remained almost constant during an hour. The index myocardium/lungs on the 5 minutes was 2,5:1. Maximum of accumulation of radiopharmaceutical in kidneys and thin intestine was defined on the 30 minutes, thick intestine on the 360 minutes from the beginning of research. Visually the quality of the heart's picture of rabbits at a scintigraphy with 123I-BMIPP was quite acceptable since the 10 mines of observation. Thus optimum time for record of scintigrams was 30 minutes of research. Conclusion: biological behaviour of 123I-BMIPP is characterized by powerful accumulation radiopharmaceutical in heart (on the data of experiment on rats). The qualitative scintigramm of the rabbit heart was received.

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Myocardial SUV of C-11-Acetate in normal heart

I. Szilvasi¹, A. Radacs¹, M. Moravszki¹, D. Kiss¹, G. Toth², Z. Lengyel²,¹Semmelweis University Department of Nuclear Medicine, Budapest, HUNGARY, ²Pozitron Ltd., Budapest, HUNGARY.

Aim: C-11-acetate (C-A) PET has been used for imaging of prostate and some other types of cancer and for non-invasive evaluation of myocardial oxidative metabolism. Analysis of uptake and washout of C-A by using kinetic models informs on myocardial blood flow and oxygen consumption. Dynamic A-C PET/CT is useful in cardiology but the technique is complicated. Static parameters of various dynamic processes are used for functional evaluation in nuclear medicine. In our study we measured myocardial SUV of C-A on a static image taken at 20 minutes after injection in patients without cardiac disease. Patients and Methods: Myocardial uptake of C-A was evaluated in patients with prostate cancer referred to PET/CT. 20 consecutive patients without known cardiac disease, cardiac medication or diabetes (mean age: 63.5 ± 11.4 years) were enrolled in the study. After physical rest and 6 hours fasting 3.7-9.25 MBq/kg of C-A were injected. C-A was produced using our cyclotron and synthesis procedure approved by national authorities. Standard whole-body PET/CT (Siemens Biograph TruePoint HD, low dose non-enhanced CT) was performed from the skullbase to mid-thigh (6-7 bed positions with 3 minutes data acquisition). Imaging of the thorax started at 19-21 minutes after injection. After reconstruction (OSEM with 8 subsets/4 iterations) short and long axis slices of the heart were displayed. SUV_{mean} values of C-A in manually selected myocardial, pulmonary, hepatic regions were calculated with Osirix 3.7.1. free DICOM viewer. Right ventricle, anterior, inferior, septal, and lateral walls of the left ventricle were separately analyzed with ROIs drawn on the midventricular slices. Results: The heart was well visualized in all patients. Activity distribution was homogenous in each patient. No significant differences were found between SUV_{mean} of the anterior, inferior, lateral and septal wall (3.42±0.25, 3.69±0.24, 3.52±0.22, 3.97±0.28). Good correlations were found between the SUV_{mean} of the different walls (r= 0.74 - 0.86). SUV_{mean} of the right ventricle (2.09±0.32) was significantly lower than that of the left ventricular regions (p<0.01 for all) with no correlation to them. The liver had a mean SUV_{mean} of 5.47±0.89. Conclusion: myocardial SUV of C-A at 20 minutes after injection is an easy to get parameter. We have established normal values of the left and right ventricle. They seem to be statistically reliable. Clinical usefulness of these parameters need further studies in patients with various cardiac diseases.

P20 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Cardiovascular: Evaluation of intervention by nuclear cardiology

P220

Myocardial perfusion reserve and contractile pattern after beta-blocker therapy in patients with idiopathic dilated cardiomyopathy

R. H. J. A. Slart, R. A. Tio, P. A. van der Vleuten, T. P. Willems, D. D. Lubbers, D. van Veldhuisen, R. A. J. O. Dierckx; University Medical Center Groningen, Groningen, NETHERLANDS.

Background In Idiopathic Dilated Cardiomyopathy (IDC) an imbalance between myocardial oxygen consumption and supply has been postulated. The ensuing subclinical myocardial ischemia may contribute to progressive deterioration of LV function. β -blocker is the therapy of choice in these patients. However not all patients respond to the same extent. The aim of this study was to elucidate whether differences between responders and non-responders can be identified with respect to regional myocardial perfusion reserve (MPR) and contractile performance. **Methods** Patients with newly diagnosed IDC underwent Positron Emission Tomography (PET) scanning using both ¹³N-ammonia as a perfusion tracer (baseline and dipyridamol stress), and ¹⁸F-fluoro-deoxyglucose as a metabolism tracer, and a dobutamine stress MRI. MRI and PET were repeated 6 months after maximal β -blocker therapy. MPR (assessed by PET) as well as wall motion score (WMS, assessed by MRI) were evaluated in a 17 segment-model. Functional response to β -blocker therapy was assigned as a stable or improved LVEF or diminished LVEF. **Results** Sixteen patients were included (age 47.9 ± 11.5 years; 12 males, LVEF 28.6 ± 8.4%). Seven patients showed improved LVEF (9.7 ± 3.1%), and 9 patients did not show improved LVEF (-3.4 ± 3.9%). MPR improved significantly in responders (1.56 ± 0.23 to 1.93 ± 0.49, p=0.049), and MPR decreased in non responders, however not significantly (1.98 ± 0.70 to 1.61 ± 0.28, p=0.064), but was significantly different between both groups (p=0.017) after β -blocker therapy. A significant correlation was found between change in perfusion reserve and change in LVEF: a decrease in perfusion reserve was associated with a decrease in LVEF and vice versa. Summed rest score of wall motion in responders improved from 26 to 21 (p=0.022) whereas in non responders no change was observed from 26 to 25 (p=ns). Summed stress score of wall motion in responders improved from 23 to 21 (p=0.027) whereas in non responders no change was observed from 27 to 26 (p=ns). **Conclusion** In IDC patients global as well as regional improvement after initiation of β -blocker treatment is accompanied by an improvement in regional perfusion parameters. On the other hand in IDC patients with further left ventricular functional deterioration after initiation of β -blocker therapy this is accompanied by a decrease in perfusion reserve.

P221

Evaluation of FDG uPET imaging in atherosclerotic plaques after CEA: focus on resolution improvement

M. M. Masteling, R. A. Tio, H. H. Boersma, U. J. Tietge, J. de Boer, R. A. J. O. Dierckx, C. J. A. M. Zeebregts, R. H. J. A. Slart; University Medical Center Groningen, Groningen, NETHERLANDS.

Introduction: Currently, imaging techniques are available to assess atherosclerotic vascular disease in the carotid artery. Hence, the selection of patients for proper medical treatment, including so-called 'best medical treatment'; endovascular carotid artery stenting (CAS) and surgical carotid endarterectomy (CEA) is possible. However, there is a need to refine risk estimates. The majority of patients with clinical events cannot be selected using present imaging techniques. Clinical FDG PET camera's show restrictions with respect to resolution in relation to plaque uptake. Therefore, we used ex vivo carotid arteries of patients to evaluate the feasibility of FDG uPET for the ex-vivo assessment of plaque vulnerability. **Methodology:** In this study, 17 patients with planned CEA were included. The removed carotid plaque was incubated using ca.100 MBq FDG (60 min, r.t.) and subsequently imaged with uPET. CT was used to assess calcifications in the plaque. The plaque's macrophages were evaluated semi-quantitatively using immunohistochemistry. Macrophage activity was correlated to FDG uptake in the same area. Furthermore, calcifications in the plaque were correlated to FDG-uptake. **Results:** We showed a heterogeneous distribution and variable intensity of FDG uptake within the plaque. A positive correlation between the amount of macrophages and FDG uptake (r= 0.68, p< 0.01) was found. Moreover, FDG uptake showed a trend towards positive correlation of FDG uptake and symptoms in patients. Furthermore, a negative correlation was found between the amount of calcifications and FDG uptake (r= -0.84, p < 0.01). **Conclusion:** FDG uptake using uPET/CT in ex vivo carotid plaques showed a positive correlation with the amount of macrophages, as well as a trend towards positive correlation between patient symptomatology and FDG uptake.

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Comparison of F-18-FDG PET/CT and Transesophageal Echocardiography for Quantitative Evaluation of Plaque with Pitavastatine Treatment in Thoracic Aorta

N. KAKO¹, T. Watanabe², M. Ota¹, T. Noda¹, K. Ono¹, S. Watanabe¹, S. Minatoguchi², M. Kanematsu², H. Hoshi²; ¹Gifu Prefectural General Medical Center, Gifu, JAPAN, ²Gifu University, Gifu, JAPAN.

[Aim]: It has been known that the plaque of coronary arteries regressed by statine therapy, but an invasive IVR examination is necessary for the quantitative evaluation. We examined the usefulness of F-18-FDG PET/CT and transesophageal echocardiography (TEE) as less invasive examination for evaluation of plaque with Pitavastatine treatment in thoracic aorta. We examined the usefulness of F-18-FDG PET/CT and transesophageal echocardiography (TEE) as less invasive examination for evaluation of plaque with Pitavastatine treatment in thoracic aorta. [Material and methods]: 8 consecutive patients with hyperlipidemia but not treated were enrolled in the period of study, and imaged using F-18-FDG PET/CT and TEE. In PET/CT, we detect the highest two part of FDG accumulation in thoracic aorta and measured the maximum standardized uptake value (SUV_{max}). A week after PET/CT study, intima media thickness (IMT) was measured by TEE at the same location of FDG accumulation on PET/CT. After 24 weeks of Pitavastatine therapy, the same examinations were performed again at the same lesion. Changes in the IMT between baseline and follow up were also evaluated. [Results]: IMT decreased in 15 of 16 sites by the therapy, and reduced significantly (1.65±2.88 to 1.38±2.45, p=0.009). IMT varies much between individuals, there were no correlation between IMT itself and SUV_{max}. But the decrease in the IMT was well correlated with SUV_{max} (r=0.698). [Conclusion]: An effect of Pitavastatine treatment was able to evaluate quantitatively by using FDG PET/CT as well as TEE. PET/CT has advantage to TEE because it is more simple to evaluate and less invasive to examine.

P223**Changes in myocardial perfusion, viability and function after myocardial engraftment of autologous CD34+ cells administered transcoronary**

M. Kostkiewicz, W. Szot, P. Musialek, P. Banys, A. Lesniak-Sobelga; Dept of Nuclear Cardiology, Jagiellonian University, Krakow, POLAND.

Background; Coronary heart disease has a strong influence on life expectancy as well as quality of life. After infarction, one can distinguish ischemic and scar zone in the muscle. There are previous reports concerning a possibility of a conversion of the injected stem cells into cardiomyocytes in the border zone of the infarct. The aim of this study was to evaluate heart viability before stem cell therapy and the results on the myocardial perfusion of this therapy. **Material and methods.** 67 patients, 3-7 days after acute MI were included in the study. In all patients Gated SPECT was performed prior (1 to 5 days before therapy) and 12 months after revascularization. Additionally in all patients labeling of implanted cells with HMPAO was performed to enable evaluation of the heart uptake. Whole-body followed SPECT scan to assess evaluation of regional uptake and the amount of total cell count. **Results.** In the impaired segments, improvement in both perfusion and ejection fraction was observed in the 3-month follow-up. Mean isotope uptake of the implanted stem cells measured as a percentage of total activity was $5.6\% \pm 2.1$. In 14 patients the enhanced activity of the implanted cells was observed in the border zone of the infarct. In 8 patients the activity of the stem cells was homogenic in all infarcted segments and in 3 patients the activity of the isotope uptake was very low (<3% of the whole activity of implanted cells). **Conclusions;** Our results support the hypothesis that implantation of stem cells in the revascularized regions of the myocardial infarction has positive influence on the heart as measured by improvement of both viability and function.

P224**Does 6-months Exercise Training in Patients with Acute Myocardial Infarction Undergoing Percutaneous Coronary Intervention Improve Ventricular Remodeling and Autonomic Tone? : A Myocardial Perfusion Study.**

S. Fukuzawa, J. Sugioka, A. Ikeda, S. Okino, J. Maekawa, S. Ichikawa, T. Uchiyama, N. Kamioka, M. Inagaki; Funabashi Municipal Medical Center, Chiba, JAPAN.

Background: It has been widely shown that exercise-based cardiac rehabilitation in patients with acute myocardial infarction (AMI) and percutaneous coronary intervention (PCI) has several beneficial effects on cardiovascular functional capacity, quality of life. Moreover, it has been reported that exercise training is associated with a prevention of ventricular remodeling and an improvement in heart rate recovery (HRR) after exercise. **Objectives:** The aim of this study was to evaluate the effects of a 6-month supervised exercise program for patients with AMI and PCI in terms of left ventricular geometrical size and systolic function and HRR. **Methods:** 42 patients with acute anterior myocardial infarction who had undergone percutaneous coronary intervention. The exercise group (n = 22) followed a 6-month supervised exercise program, while the control group (n = 20) received routine pharmacological therapy and lifestyle education. The 2 groups were similar with regard to age, extent of coronary artery disease, brain natriuretic peptide, and pharmacological therapy. All patients underwent a cycle exercise myocardial perfusion single photon emission computed tomography (SPECT) at baseline and after 6 months. HRR was obtained from the subtraction of heart rate in the first minute of recovery after exercise testing from maximal heart rate during exercise. Myocardial perfusion SPECT was semi-quantitatively analyzed using a 17-segment left ventricular model. Left ventricular volume and ejection fraction was automatically calculated using quantitative gated SPECT software. **Results:** 2 patients in the exercise group did not complete the programmed. At 6 months follow-up, an improvement was seen in the exercise group compared with the control group regarding heart rate recovery (p < 0.05), left ventricular end-diastolic volume (p < 0.05) and left ventricular ejection fraction (p < 0.05). **Conclusion:** Six months exercise training in patients with acute myocardial infarction and percutaneous coronary intervention with mild ventricular systolic dysfunction could prevent ventricular remodeling to a certain extent, and favorable modulating sympatho-vagal balance evidenced by HRR may be an important mechanism.

P225**FDG uptake in synthetic aortic vascular graft on FDG-PET/CT**

M. Ishibashi, T. Ishimori, S. Nakashita, I. Ikeda, M. Yabuta, A. Sakata, A. Kawamura, T. Yamada, T. Nobashi, K. Nishimatsu, Y. Watanabe; Kurashiki Central Hospital, Kurashiki, JAPAN.

The aim: Graft infection is a serious complication to vascular surgery. FDG-PET is useful for visualizing inflammation or infection and is expected for the early detection of the graft infection. However, FDG-accumulation in the graft without infection is also often seen. This study was performed to assess FDG activity in synthetic aortic graft during FDG-PET/CT scan in patients without graft infection. **Materials and Methods:** A total of 10805 patients between February 2006 and March 2010 underwent whole-body FDG-PET/CT exam for the evaluation of malignancy or medical checkup. We obtained 47 FDG-PET/CT scans in 26 patients with synthetic aortic graft. Of the 26 patients (21 men and 5 women; age range, 56-85 years old), 25 patients experienced open surgery and one patient had undergone the endovascular technique (EVAR). On the basis of biochemical and clinical data, no patient had graft infection at the time of investigation. The maximum standardized uptake value (SUVmax) of each patient's graft was compared with biochemical data. **Results:** High FDG uptake adjacent to the aortic graft was found in all patients. The median SUVmax was 3.97 (range, 1.90 to 5.98). There was no significant correlation between SUV max and C-reactive protein or the number of white blood cell, suggesting FDG uptake was independent from systemic inflammation. **Conclusion:** Increased FDG uptake in the aortic vascular grafts was found in vast majority of patients without graft infection. It should be noted that increased FDG uptake in the vascular graft has a risk of misdiagnosis as graft infection.

P21 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Cardiovascular: Improvement of diagnosis by nuclear cardiology**P226****Cardiac resynchronization therapy: searching for optimal functional characterization impacting on clinical selection and patients' management**

F. Bandera¹, P. A. Erba², U. Conti³, M. Sollini², E. Soldati³, R. Boni², G. Zucchelli⁴, M. Bongiorno⁵, G. Mariani². ¹Division of Cardiology, University of Pisa Medical School, PISA, ITALY, ²Nuclear Medicine, University of Pisa Medical School, PISA, ITALY, ³Division of Cardiology, AOUP, PISA, ITALY, ⁴division of Cardiology, AOUP, PISA, ITALY, ⁵Division of Cardiology, AOUP, PISA, ITALY.

Cardiac resynchronization therapy (CRT) is currently indicated to reduce mortality and to improve symptoms in NYHA class III-IV patients with EF <30% and widened QRS. In this study we evaluated functional parameters with potential prognostic significance (sympathetic denervation, myocardial viability, LV mechanical dyssynchrony) both before and after CRT. Within an IRB-approved study protocol, since May 2009 all patients scheduled for CRT have been considered as possible candidates. After signing the informed consent, 14 patients (10 idiopathic dilative, 4 post-ischemic, 7 NYHA II and 7 NYHA III) underwent clinical, laboratory, functional and diagnostic (scintigraphy and echocardiography) evaluation before CRT, then again 6 months after CRT. Early (15 min) and late (180 min) planar and SPECT 123I-MIBG images were acquired to obtain the heart-to-mediastinum (H/M) ratios and the wash-out (WO) rates. Myocardial viability and LV mechanical dyssynchrony were evaluated by baseline 99mTc-Tetrofosmin myocardial perfusion 16-frames G-SPECT (MPI) after administration of nitrate and subsequent phase analysis of LV mechanical activation. Results of this latter analysis were compared with a complete standard echocardiographic evaluation of LV. The Table shows the main clinical, echocardiographic and scintigraphic results of the patients enrolled. LV enlargement and systolic function depression was concordantly detected by both echocardiography and G-SPECT. In 4 patients MPI identified relevant perfusion defects in the LV region. At baseline, mechanical dyssynchrony was present in 55%-64% of the cases, depending on the specific echocardiographic parameter considered. Phase analysis detected abnormal parameters in nearly all patients; the use of both standard deviation and bandwidth allowed to grade the severity of mechanical dyssynchrony (mild in 6/14, moderate in 3/14, severe in 5/14). In the 5 patients who have now completed post-CRT evaluation, a typical pattern characterized by reduced dispersion of the LV mechanical activation time-distribution was present in cases of clinical and echocardiographic (volume) response. 123I-MIBG images showed moderate-to-severe cardiac denervation rate (H/M ranging from 1.26 to 1.92) in all subjects, irrespective of clinical, echocardiographic and dyssynchrony parameters. MPI and 123I-MIBG scintigraphy allowed a comprehensive evaluation of the functional profile in patients candidate to CRT. A simple 16-frame post-nitrate G-SPECT MPI allowed the identification of relevant perfusion defects near to the site of LV stimulation, an important and treatable cause of CRT failure. Post-processing phase analysis can detect and grade mechanical dyssynchrony at baseline as well as the CRT-induced mechanical effects. Adrenergic cardiac denervation was present in all patients, consistent with the potential prognostic role of this functional parameters.

Main results

Echocardiographic	
LV end diastolic volume (ml)	242 (190-281)
LV EF	27 (18-35)
Left atrium volume	105 (70-207)
Gated SPECT	
LV end diastolic volume (ml)	250 (160-424)
LV EF	33 (15-38)
PSS	22 (9-30)
123I MIBG	
Early H/M ratio	1.51 (1.26-1.92)
Late H/M ratio	1.45 (1.24-1.81)
WO ratio	0.34 (0.10-0.42)
ECG QRS duration(ms)	160 (130-200)
Peak phase	135 (84-273)
Bandwidth	131 (44-229)
Skewness	1.99 (1.46-3.81)
Kurtosis	4.04 (1.7-15.4)

P227**Washout of Tc-99m Tetrofosmin on Delayed Myocardial Perfusion Imaging in Patients with Acute Myocardial Infarction after Coronary Revascularization**

D. Kim, C. Kim, S. Park, S. Jung, W. Kim; Wonkwang University School of Medicine, Iksan, Jeollabuk-do, KOREA, REPUBLIC OF.

Objective: Several investigators have been reported that delayed myocardial perfusion imaging with Tc-99m tetrofosmin (TF) shows a washout phenomenon. Present study was performed to investigate the incidence of the washout of TF (WTF) in patients with AMI after reperfusion therapy; in addition, we aimed to elucidate clinical implication of washout to indicate viable myocardium. **Methods:** A total sixty-seven consecutive patients who received successful reperfusion therapy with AMI were prospectively included. The myocardial perfusion imaging was performed twice; at 40 min for early imaging and at 180 min for delayed imaging. In semi-quantitative analysis, WTF was defined as an increase of ≥ 4 in the sum of all segmental perfusion scores in delayed images. **Results:** The WTF was observed in 34 patients (51%). The improvements of rest and stress perfusion scores, LV wall motion scores, and ejection fraction were more significant in patients with WTF than in patients without WTF. **Conclusions:** This study

demonstrates that WTF was frequently observed in patients with AMI after coronary revascularization. Also the tendency that the improvements of perfusion and function were more significant in patients with WTF than in patients without WTF, was observed. Table 1. Interval days between coronary revascularization and M-SPECT according to the presence and absence of washout of tetrofosmin ($p=0.026$)

Interval days	Washout of tetrofosmin		The incidence of WTF (%)
	Present (n=34)	Absent (n=33)	
1	9	7	12.5
2	1	12	42.9
3	3	7	30.0
4	11	4	73.3
5	7	3	70.0
6	1	0	100.0
7	2	0	100.0

WTF; washout of tetrofosmin. Table 2. The improvements of rest and stress perfusion scores, LV wall motion scores, and ejection fraction according to the presence and absence of washout of tetrofosmin

	Washout of tetrofosmin		p value
	Present (n=22)	Absent (n=11)	
Rest perfusion scores	3.1 ± 4.2	2.7 ± 6.0	.496 (NS)
Stress perfusion scores	4.2 ± 6.0	2.6 ± 7.3	.822 (NS)
LV wall motion scores	5.4 ± 9.8	3.6 ± 4.7	.501 (NS)
Ejection fraction (%)	+1.9 ± 8.5	-0.3 ± 6.1	.404 (NS)

NS = not significant. Table of Contents

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Comparison of Gated Myocardial Perfusion SPECT with 64-slice CT for Diagnostic Accuracy and Functional Relevance in Patients with Moderate to High risk of Coronary Artery Disease

S. Yoo¹, H. Song¹, J. Kim¹, A. Chong¹, J. Oh¹, J. Ha¹, Y. Kim², Y. Ahn³, M. Jeong³; ¹The Department of Nuclear Medicine of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF, ²The Department of Radiology of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF, ³The Heart Center of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF.

Purpose: To evaluate diagnostic accuracy of gated myocardial perfusion SPECT (G-SPECT) and computed tomography angiography (CTA), and to evaluate CTA in detection of functionally relevant coronary artery stenoses (CAS) in patients with moderate to high risk of coronary artery disease (CAD). MATERIALS AND METHODS: Thirty patients (mean age 62 ± 14 years) with known or suspected CAD underwent G-SPECT, CTA and CAG within 1 month. CAD risk was calculated by normogram. Total 90 coronary arteries in 30 patients were analyzed. Abnormal findings were defined as reversible or fixed defect on G-SPECT. Stenosis with luminal narrowing of ≥ 50% were defined as significant on CTA and CAG. CTA was compared with G-SPECT with respect to the detection of functionally relevant CAS. RESULTS: The sensitivity, specificity, and negative and positive predictive values were 83.7%, 63.8%, 67.9%, 81.1% with G-SPECT, and 74.4%, 55.3%, 60.4%, 70.3% with CTA respectively ($p=0.424$). The kappa index, represented the agreement of G-SPECT and CTA with CAG is 0.471 on G-SPECT ($p<0.001$) and 0.294 on CTA ($p<0.004$). Sensitivity, specificity, negative and positive predictive values of CTA in detecting any perfusion defects on G-SPECT were 68%, 54%, 54% and 68%, respectively. Those of CTA in detecting reversible perfusion defects on G-SPECT were 54%, 43%, 58% and 40% respectively. CONCLUSION: This preliminary data shows that G-SPECT has a higher accuracy than CTA, which failed to predict the functional relevance of CAS in patients with moderate to high risk of CAD.

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Optimized risk stratification of the patients with suspicion of CAD and normal perfusion scan by calcium scoring with SPECT-CT

G. Agu¹, A. Julardzija¹, D. Haoula², P. Knoll¹, M. Rodrigues¹, K. Huber², S. Mirzaei¹; ¹Institute of Nuclear Medicine with PET-Center, Wilhelminenspital, Vienna, AUSTRIA, ²3rd Dept Internal Med, Cardiology and Emergency Med, Wilhelminenspital, Vienna, AUSTRIA.

Aim: Stress myocardial perfusion imaging is used for clinical management of patients with suspected coronary artery disease (CAD). The aim of this study was to evaluate the additional role of measurement of calcium score in these patients with a normal perfusion scan. Patients and methods: In a prospective study we measured the calcium score of the patients (12 m, 14 f, mean age 57 (m) and 64 (f)) with suspicion of CAD and a normal perfusion scan. In all patients a pharmacological stress perfusion scintigraphy was performed. Both the myocardial perfusion scintigraphy (180° SPECT, 6°/frame, 25°/frame, LEHR collimator) and calcium scoring were performed on a T6 Symbia gamma camera (Siemens, Knoxville, USA). Tomographic reconstruction (OSEM 3D) was performed using a low dose CT scan for attenuation correction. Results: 10/12 of the male patients (83%) and 8/14 of the female patients (57%) had an Agatston score of > 10. There were 6 cases (3m, 3f) with a calcium score of > 400 and 3 cases (2m, 1f) with a calcium score > 1000 (1m, 2f). Conclusion: As increased calcium scores are known predictors of worse clinical outcome, calcium scoring in addition to stress perfusion scintigraphy on a one-day basis with a SPECT-CT device might improve risk stratification especially in patients with negative stress testing. Whether these combined diagnostic measures represent an

optimized and convenient method for early identification of patients at risk has to be further evaluated.

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Management of ischemic heart failure in elderly patients candidate to revascularization: a FDG-PET/CT based selection strategy. Preliminary results of a single institution experience.

A. Belletti¹, G. Conte², C. Cidda¹, M. Scarlattei¹, G. Baldari¹, D. Ardisino², L. Ruffini¹; ¹Nuclear Medicine Department, Azienda Ospedaliero-Universitaria, Parma, ITALY, ²Cardiology Unit, Azienda Ospedaliero-Universitaria, Parma, ITALY.

The elderly population is increasing and with it morbidity, hospitalizations, costs and mortality due to heart failure (HF). Patients with HF and left ventricular (LV) dysfunction might benefit from revascularization but not without risk. F-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging has long been regarded as the most sensitive method for the detection of viable myocardium recovering after revascularization. Integrated positron emission tomography/computed tomography (PET/CT) scanners provide challenges and solutions for the attenuation correction problem. **Aim of the study** was to evaluate the role of cardiac metabolic imaging with integrated PET/CT in characterizing risk profile of elderly patients with ischemic heart failure candidate to revascularization. **Methods.** From April 2009 to March 2010 we enrolled 20 consecutive patients (mean age 74±8 yrs, 18 M, 1F), with advanced heart failure and LV dysfunction (NYHA II-IV, mean ejection fraction 28±6%). Cardiac metabolic imaging was performed with 18F-FDG triggered PET/CT. FDG uptake was scored using a 5-point scale in each segment in a 17 segments LV model. For each patient, a summed viability score (SVS) was calculated (a SVS ≥ 20 was considered representative of preserved viability). Left ventricular function and clinical conditions were followed-up at 3, 6 and 12 months after PET evaluation. **Results.** Of the enrolled patients, 10 were submitted to PTCA/stenting or CABG, 6 to ICD/BIV implantation (2 for primary prevention before revascularization), 1 to intensive medical therapy, 1 dropped out. The last 2 patients are under evaluation. FDG-PET/CT showed viability in all the revascularized patients (mean score 26,4±1.6); at follow-up (3 and 6 months for all the patients, 12 months for 5 of them) LV function was improved (EF mean value 36.9%) and major adverse cardiac events were not registered in all revascularized patients; they are asymptomatic until now. In 6 pts the mean viability score was 17.3: of them, 1 was initiated to intensive medical therapy, 4 received ICD/BIV placement and 1 dropped out. At 3, 6 and 12 months left ventricular function was unchanged or worsened and 4 pts had new hospitalizations. **Conclusion.** In our study, patients with myocardial viability detected by FDG-PET/CT showed LV function improvement after revascularization and good clinical outcomes. The results suggest that cardiac metabolic imaging may assist decision making in elderly patients with advanced heart failure. Outcome may be benefited using 18F-FDG PET/CT in an experienced center with ready access to PET technology and integration with imaging, heart failure, and revascularization teams.

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Relationship between 123I-BMIPP Myocardial Scintigraphy and NT-proBNP in Patients with Acute Coronary Syndrome

H. Takase¹, Y. Dohi², T. Toriyama¹, T. Okado¹, A. Hagikura¹, M. Sasaki¹, H. Ishikawa¹, Y. Kume¹, G. Kimura²; ¹Enshu Hospital, Hamamatsu, JAPAN, ²Nagoya City University Graduate School of Medical Sciences, Nagoya, JAPAN.

Aim: Summed score of 123I-BMIPP myocardial scintigraphy or mismatch score obtained from dual single-photon emission computed tomography (SPECT) with 123I-BMIPP and 201TlCl reflects severity and prognosis of patients with acute coronary syndrome (ACS). On the other hand, sustained elevation of natriuretic peptide after acute myocardial infarction (AMI) predicts poor prognosis of patients with AMI. Thus, we investigated the relationship between these scores obtained from scintigrams and N-terminal pro B-type natriuretic peptide (NT-proBNP) in patients with ACS. **Materials and Methods:** Consecutive 47 patients (male=36, mean age=68 year-old) with ACS who underwent successful percutaneous coronary intervention (PCI) were enrolled. Non-stress dual SPECT with 123I-BMIPP and 201TlCl were performed within 4 days after PCI. SPECT imaging was evaluated and graded in 17 segments using a five-point scale (0=normal, 4=absence), and summed scores of 123I-BMIPP and 201TlCl and mismatch score (123I-BMIPP summed score - 201TlCl summed score) were obtained. NT-proBNP was measured at 12 hours and 7 days after PCI. Results: Summed score of 123I-BMIPP was positively correlated with NT-proBNP levels obtained at both 12 hours ($r=0.478$, $p=0.0007$) and 7 days ($r=0.522$, $p=0.0002$) and maximum creatine kinase (CK) levels ($r=0.467$, $p=0.0009$), and inversely correlated with ejection fraction ($r=-0.536$, $p=0.0001$), while this score was not different in patients with ($n=9$) and without increase in NT-proBNP levels ($n=38$) during the study period. On the other hand, maximum CK ($r=0.530$, $p=0.0001$) and ejection fraction ($r=-0.391$, $p=0.0066$) showed significant correlations with mismatch score of dual SPECT with 123I-BMIPP and 201TlCl. In multivariable regression analysis, summed score of 123I-BMIPP was associated with NT-proBNP levels measured at 12 hours, but not 7 days, and mismatch score was associated with maximum CK levels. Conclusion: Summed score of 123I-BMIPP, but not mismatch score of dual SPECT with 123I-BMIPP and 201TlCl, was associated with NT-proBNP levels. Since summed score was associated with NT-proBNP measured at 12 hours, it may reflect hemodynamic condition in acute phase in patients with ACS.

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The relation between quantitative parameters derived with ¹²³I-MIBG and post-adenosine Myocardial Perfusion Scintigraphy

B. J. van der Veen, A. J. Scholten, M. P. M. Stokkel; Leiden University Medical Centre, Leiden, NETHERLANDS.

Background: Myocardial perfusion scintigraphy (MPS) and ¹²³I-MIBG scintigraphy are used for visualizing and quantifying perfusion and innervation in various heart diseases. The relation between ¹²³I-MIBG and MPS parameters is assessed in other studies, however, these studies primarily included MPS acquisitions performed with exercise-stress protocols. The goal of this study is to assess the relation between quantitative parameters derived with ¹²³I-MIBG and post-

adenosine MPS. **Method:** 150 patients referred for both MPS and MIBG acquisitions were included. All patients underwent adenosine induced stress as part of the 2-day stress/rest MPS protocol. Gated SPECT MPS acquisitions were used to determine the left ventricular ejection fraction (LVEF) and systolic volume (ESV). Anterior planar MIBG acquisitions were used to determine Heart-to-Mediastinum (HM) ratio and Washout rate (WOR). Information with respect to cardiac risk factors, medical history and cardiac innervation was gathered. **Results:** Correlations between HM ratios and WORs ranged from -0.114 to -0.719 ($p < 0.001$). Delayed HM ratio showed best correlation with WORs (mean PCC -0.645). Correlation between delayed HM ratio and post-Adenosine LVEF or ESV were respectively 0.614 and -0.614 ($p < 0.001$); correlation with the WORs ranged from -0.361 to -0.483 ($p < 0.001$) for LVEF and from 0.383 to 0.520 ($p < 0.001$) for ESV. Multivariate analysis provided WOR, post-stress LVEF and the presence of abnormal perfusion as major indicator of delayed HM ratio, and, ESV, LVEF decrease, delayed HM ratio and history of cardiomyopathy as important indicators of post-stress LVEF. **Conclusion:** Quantitative parameters of ^{123}I -MIBG and post-adenosine MPS acquisitions are related. The indicators of abnormal LVEF were found to be comparable to the factors associated with an abnormal delayed HM ratio.

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Evaluation of metabolic activity of aortic abdominal aneurysm in patients candidate to surgery

S. Morbelli¹, C. Marini², M. Massollo¹, E. Pomposelli¹, C. Augeri¹, G. Spinella³, B. Pane³, D. Camellino⁴, L. Opezzì¹, M. A. Cimmino⁴, D. Palombo³, G. Sambucetti⁵; ¹Nuclear Medicine, San Martino Hospital, Genoa, ITALY, ²NR Institute of Biomedicine and Molecular Physiology, Milan, ITALY, ³Unit of Vascular and Endovascular Surgery, San Martino Hospital, Genoa, ITALY, ⁴Rheumatology, Dept Int Medicine, University of Genoa, Genoa, ITALY, ⁵Nuclear Medicine, University of Genoa, Genoa, ITALY.

The role of ^{18}F -FDG-PET imaging is under active investigation as possible additional tool to predict the rupture of abdominal aortic aneurysm (AAA). AIM: to verify the presence of elevated FDG uptake in AAA among patients candidates to surgery according to morphologic criteria. **METHODS:** The study included 43 patients (age: 72 ± 7 years) candidates to surgery for AAA diameter range (4.5-5.5 cm) and 44 age-matched controls (mean age: 72 ± 6). Both groups underwent simultaneous FDG-PET and Angio-CT imaging from the skull base to the femoral neck using a PET/CT scanner (Hirez, Siemens). After OSEM reconstruction and CT-based attenuation correction images were visually inspected and quantitatively analysed, placing volumetric regions of interest (VROIs) on the anatomic Angio-CT slices to identify the four aortic segments: subclavian arteries, common carotid arteries, iliac arteries, the liver and the left ventricular chamber. In all patients with AAA, an additional VROI was drawn over the aneurismatic arterial walls. FDG uptake was quantified by calculating the mean standardized uptake value (SUV) within each VROI and expressed as the ratio between each VROI mean SUV value and blood-pool VROI mean SUV values. Total calcium load (ACL) was estimated in the same arterial segments grading calcium density according to a semi-quantitative 5 point scale based on percent calcification of the arterial ring documented in the transaxial views. **RESULTS:** No patient showed an increased focal uptake in the aneurismatic arterial wall (mean SUV 0.7 ± 0.2). Similarly, average SUV of aneurismatic wall was lower with respect to both adjacent control region of the same patient and the same arterial segment of control subjects (mean SUV 0.9, $p < 0.01$ and 0.8 ± 0.3 , 0.003 respectively). Arterial wall metabolism was similar in all aortic segments and in the subclavian arteries in the two groups, while both common carotid arteries and in iliac branches displayed a significantly higher SUV in the AAA patients compared to controls ($p < 0.02$ and 0.05 respectively). A significant inverse correlation was present between ACL and SUV at the level of both iliac arteries and abdominal aorta metabolic activity ($p < 0.05$) in AAA patients but not in control subjects. **Conclusions:** In this population of candidates to AAA surgery, the incidence of increased focal uptake of FDG in aneurismatic aortic wall is extremely low. Inverse correlation between ACL and metabolism might identify the reduced cell density in the arterial segment as the possible explanation of this finding.

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Detection of left ventricular dyssynchrony and prediction of functional recovery after revascularization by using quantification of segmental function by solving the Poisson equation and gated myocardial perfusion SPECT

T. Niimi¹, H. Maeda², M. Nanasato³, M. Sugimoto¹; ¹Department of Radiological Technology, Nagoya Daini Red Cross Hospital, Nagoya, JAPAN, ²Department of Radiological Technology, Nagoya University School of Health Sciences, Nagoya, JAPAN, ³Department of Cardiology, Nagoya Daini Red Cross Hospital, Nagoya, JAPAN.

Purpose: Nowadays, electrocardiographically (ECG)-gated myocardial perfusion SPECT with quantitative gated SPECT (QGS) is routinely employed to assess global and regional left ventricular (LV) functions. Global LV function is measured on the basis of the ejection fraction (EF), which is an important index for the prognosis of coronary artery disease (CAD). However, the information obtained using QGS, such as wall motion, wall thickening, and results of phase analysis, is not sufficient for the evaluation of local ischemic myocardial injury (regional LV function). Cardiac function is estimated on the basis of the wall motion (calculated from the centripetal motion of the inner surface of the cardiac walls) rather than myocardial contraction; hence, the information obtained using QGS is inadequate for the evaluation of local ischemic myocardial injury, which first manifests as abnormal contractions rather than alterations in the wall motion. In this study, we evaluated the degree of functional recovery after revascularization in patients with known CAD by using the quantification of segmental function by solving the Poisson equation (QSFP) by which synchronization of myocardial contraction with the cardiac wall motion along with EF can be measured. **Methods and Materials:** We assessed 10 patients with recent myocardial infarction and old myocardial infarction by using resting ECG-gated ^{99m}Tc -methoxyisobutylisonitrite (MIBI) SPECT for QSFP, which was performed for all the patients before and after revascularization. To differentiate abnormal regional contractions of the cardiac wall, synchronous contraction index (SCI) was introduced and defined as the temporal correlation coefficients between the LV volume and myocardial contraction. The cardiac wall was divided

into 17 segments according to American Heart Association (AHA) criteria, and the SCIs for each segment were obtained. Regional contractions in the cardiac wall were evaluated in a total of 1700 segments. **Results:** Before revascularization, global SCI (average of the SCIs of the 17 segments) was 61.3% but improved to 76.5% after revascularization (likewise, EF was improved from 37.4% to 43.7%). The regional SCIs for all the patients before and after revascularization were improved to 0%-59.6% (average, 16%). LV dysfunction owing to CAD could be detected using the regional SCIs, and the areas of LV dysfunction could be clearly delineated using QSFP; further, by using the SCIs, the cause of decrease in the EF was revealed. **Conclusion:** The SCI calculated using the QSFP is a novel index of cardiac function. Along with EF, it may prove useful for the prediction of functional recovery after revascularization.

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Role of SPECT and Angiographic Vessel score in quantification the extent and severity of coronary artery disease

I. Kotsalou¹, P. Xaplanteris², I. Karfis¹, J. Karydas², A. Zoumboulidis¹, K. Lazaridis², N. Dimakopoulos¹; ¹NIMTS Hospital, Nuclear Medicine Dept., Athens, GREECE, ²NIMTS Hospital, Cardiology Department, Athens, GREECE.

AIM : Coronary angiography is accepted as the gold standard method of coronary artery disease detection. Angiographic Vessel Score (AVS) is a quantification tool, expressing the number of vessels with a significant stenosis (50% or greater reduction in lumen diameter) with range from 0 to 4, depending on the number of vessels involved. In this study we compared AVS with the SPECT Vessel Score (SVS) based on SPECT myocardial perfusion imaging: coronary artery territories and Semiquantitative Scoring System (Five-Point Model). **METHODS - MATERIALS :** We reviewed the diagnostic studies of 41 individuals (m/f:32/9) with typical or atypical angina, but no history of coronary artery disease, who underwent stress (treadmill (n:35), adenosine (n:6)) ^{99m}Tc -tetrofosmin myocardial perfusion testing and were later subjected to coronary angiography. Semiquantitative visual interpretation was performed using the 20-segment model and a summed stress score was obtained by adding the scores of 20 segments from the stress tetrofosmin images (<4 normal; 4-8 mildly abnormal; 9-13 moderately abnormal and >13 severely abnormal). Moreover SPECT Vessel Score (SVS) was calculated using the known estimated perfusion territory model, whereas Angiographic Vessel Score (AVS) was also measured. Both Scores express the number of vessels involved. **RESULTS :** Positive Coronary angiography studies (n: 31) grouped by AVS, indicated 26% 1-vessel disease, 29% 2-vessel disease and 45% 3-vessel disease and Pathologic Perfusion Images (SVS) 38,7%, 38,7% and 22,6% respectively. 32,3 % of Angiographically proven Coronary Deficient individuals (n:10/31) were subjected to percutaneous coronary intervention (PCI) whereas 32,3% (n:10/31) were referred to bypass (CABG). Comparing scintigraphic and angiographic study, the achieved concordance of the two methods in coronary disease detection was 75,6% and respective discordance 24,4% was attributed to false-positive SPECT and false-negative angiographic studies. Non parametric Wilcoxon matched analysis showed no significant difference between the two Scores. **CONCLUSIONS :** Quantification of vessels involved by AVS during Angiography and SPECT Vessel Score is very important for coronary artery disease risk stratification and further follow up of these patients.

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The incidence of "reverse redistribution" phenomenon seen at the septal area during TI-201 myocardial scintigraphy in patients with LBBB and its clinical significance

A. Doumas¹, I. Iakovou¹, T. Christoforidis¹, D. Boundas², D. Lopresti¹, S. Georga¹, V. Nikos¹, N. Karatzas¹; ¹Papageorgiou Hospital, 3rd Department of Nuclear Medicine Aristotle University of Thessaloniki, Thessaloniki, GREECE, ²"Hippokrates" Nucl. Med. Laboratory, Thessaloniki, GREECE.

AIM. The reverse redistribution phenomenon is seen in 5-9% of all TI201 myocardial exams, performed in our department. In almost 10% of these patients, angiographically proven stenosis was found, at the vessel responsible for the perfusion of this area. It is well known that in patients with left bundle branch block (LBBB), false positive for ischemia scintigraphic result may be obtained at the area of inter ventricular septum, especially after treadmill test. For this reason, pharmacologic intervention is preferred. We tried to investigate if the phenomenon of reverse redistribution is more often seen in patients with LBBB and if this represents ischemia in a greater frequency than in patients without abnormal conductivity. **METHODS:** We retrospectively studied 85 patients with LBBB, who were undergone both myocardial TI-201 scintigraphy and coronary angiography in meantime of a month. The above patients were compared with an equal number of individuals with normal conductivity, served as control. The reverse redistribution phenomenon was estimated both qualitatively and quantitatively, using the Emory toolbox bull's-eye technique. **RESULTS:** The reverse redistribution phenomenon at the area of interventricular septum was seen in 12 out of 85 (14%) patients with LBBB and in 6 out of 85 (7%) control patients. The above difference was statistically significant ($p < 0.001$). Among these patients angiographically proven coronary artery disease (stenosis >50%) at left anterior descending artery (LAD) was seen in 2 patients (16,6%) with LBBB and only in 1 patient (16,6%) of the control group, finding without statistical significance ($p > 0.05$). **CONCLUSION:** We conclude that reverse redistribution phenomenon is more often seen in patients with LBBB, most probably due to coronary flow reserve alterations caused by the paradoxical movement of the septum. This phenomenon is not connected to a greater extend in the presence of coronary artery disease.

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The relationship between gated myocardial perfusion SPECT findings and heart rate recovery after exercise test

M. E. Erkan, M. Yıldırım, A. N. Korkmaz, M. Aşık, A. S. Doğan; Medical School of Duzce University, Duzce, TURKEY.

Aim: Abnormal heart rate recovery after exercise test, is a simple available parameter, that reflects autonomic nervous system disfunction. GATED myocardial perfusion SPECT is used in the

diagnosis and prognosis of coronary artery disease. In this study we compared heart rate recovery with myocardial perfusion scintigraphy findings. Thus, we aimed to determine the role of heart rate recovery on diagnosis of coronary artery disease and prognosis. **Methods:** Patients ($n = 50$, 27 female 23 men) who underwent exercise technetium-99m sestamibi GATED myocardial perfusion SPECT were enrolled in this cross-sectional study. Exercise treadmill testing was performed according to a symptom-limited Bruce's protocol. HRR was obtained from the subtraction of heart rate at the first minute after exercise treadmill testing from maximal heart rate during exercise. Myocardial perfusion SPECT was semi-quantitatively analyzed using a 20-segment left ventricular model. Left ventricular quantitative parameters were automatically calculated using quantitative GATED SPECT software. **Results:** Multiple linear regression revealed strong independent negative association between heart rate recovery and myocardial defect severity on stress images ($\beta = -0.957$; $SE = 0.650$; $p = 0.043$). Age was also an independent predictor of heart rate recovery with negative association ($\beta = -0.473$; $SE = 0.250$; $p = 0.022$). Correlation coefficient (R) and R square (R^2) of the model were 0.604, and 0.365 respectively. **Conclusion:** On stress protocol, myocardial damage is more severe in patients who have decreased heart rate recovery. Since the severity of myocardial damage on stress is a strong predictor of cardiac events and prognosis, heart rate recovery was also have prognostic value on future cardiac events.

P238

Assessment of Septal Perfusion with ECG-gated Myocardial Perfusion Scintigraphy in LBBB Patients

K. Nikoletic¹, S. Lucic¹, A. Peter¹, J. Stojiljkovic², J. Kmezc-Grujin², M. Stefanovic², A. Jovelic², S. Tadic²: ¹Institute of Oncology of Vojvodina, Sremska Kamenica, SERBIA, ²Institute of cardiovascular disease of Vojvodina, Sremska Kamenica, SERBIA.

Aim of the study: In patients with LBBB abnormal septal perfusion can frequently be found on myocardial perfusion images even without the presence of coronary artery disease (CAD). Aim of this study was to assess and compare septal perfusion in LBBB patients on non-gated and ECG-gated myocardial perfusion scintigraphy (MPS) images. **Materials and methods:** Forty-eight patients (19 man, 29 women; aged 37-67; mean 56.12 \pm 3) with LBBB on ECG and with probability of CAD were included in the study (January 2006 to October 2009). Two-day stress/rest protocol ECG-gated MPS with ^{99m}Tc-MIBI was performed starting with stress dipyridamole study followed by rest study the next day. Images were interpreted for septal perfusion (group 1: normal septal perfusion, group 2: reversible septal hypoperfusion and group 3: irreversible septal defect). ECG-gated MPS images were evaluated for septal wall motion and septal thickening on end-diastolic and end-systolic images. All patients undergo coronarography within six months after MPS. The results of MPS of septal wall and coronarography findings of LAD were compared. Stenosis of 75% on coronarography was concerned to be significant. **Results:** On non-gated images septal perfusion was normal in 11 (23%) patients (group 1), 21 (44%) had reversible septal hypoperfusion (group 2) and 16 (33%) were interpreted as irreversible septal defect (group 3). Out of 21 patients with reversible septal hypoperfusion (group 2), 15 (71%) had normal findings on ECG-gated images (normal septal wall motion and septal thickening). The remaining six patients (29%) from the same group had positive CAD findings showing true reversible hypoperfusion. Out of 16 patients with irreversible septal defect (group 3), 12 (75%) had normal findings on ECG-gated MPS. **Conclusion:** ECG-gated MPS is useful diagnostic procedure for the evaluation of septal perfusion, septal wall motion and septal thickening allowing better differentiation between true and false septal perfusion defect in LBBB patients.

P239

ECG-GATED-SPECT imaging in detection of viable myocardium.

S. Schiavariello¹, A. Fé¹, L. Mussolin¹, L. Martino¹, F. Costantino², M. Elijiato², G. Paternó², P. Grieco²: ¹Nuclear Medicine San Carlo Hospital, Potenza, ITALY, ²UTIC San Carlo Hospital, Potenza, ITALY.

In this work we have studied 15 patients with recent (4weeks) myocardial infarction affected by left ventricular dysfunction, ejection fraction (EF) <40%; all patients were candidates to myocardial revascularization. We have compared ECO-Stress-Dobutamine, ECG-Gated SPECT Perfusion stress/rest and Nitrate-ECG-Gated SPECT for identification of viable myocardium. All patients have been subjected to myocardial revascularization and the left ventricular ejection fraction (LVEF) has been valued after 1 month with echocardiography. **ECO-Stress-Dobutamine:** injection 5 mcg/kg/min for 3' min, increase each 3' min at 10, 20, 30, 40 mcg/kg/min + Atropine. The examination evaluates the inotrope reserve after administration of catecholamine, by improving wall motion with low dose and reduction wall motion with high dose (biphasic response). **ECG-Gated SPECT-Perfusion stress/rest:** two days protocol, radiopharmaceutical ^{99m}Tc-Tetrofosmin, 600-900 MBq/study. Stress-Test: dynamic exercise (treadmill stress) or pharmacological stress (Adenosine or Dipyridamole + low-level exercise or Dobutamine+ Atropine). **Nitrate ECG-Gated SPECT:** study executed after administration of sublingual nitroglycerine, usually at dose of 400-800 mcg, tracer injection after 10' min, images acquisition after 30' min. After reconstruction and reorientation of the Gated-SPECT projection data sets, fully automated algorithms may be used to quantify LVEF, LV EDV and ESV. The algorithms available for LVEF is GATED SPECT (QGS). **Results:** ECO-STRESS-Dobutamine examination identified positive response for myocardium viability in 7 of 15 patients. Echocardiography examination one month after revascularization show improvement of FE in 4 patients. **ECG-Gated SPECT-Perfusion stress/rest** identified 5 of 15 patients with reversible defect; 3 of these 5 patients shown positive response with Nitrate ECG-Gated SPECT examination. Echocardiography examination one month after revascularization show improvement of FE in 4 patients. **Nitrate ECG-Gated SPECT** identified 8 of 15 patients with significant tracer uptake improvement (segments considered viable if activity exceeded 50% maximum activity peak). Echocardiography examination one month after revascularization show improvement of FE in 6 patients. **Conclusion:** Nitrate ECG-Gated SPECT examination is the more accurate method for assessment of myocardial viability.

P240

Early gated myocardial perfusion SPECT detects stunned

myocardium in patients with ischaemic heart disease

M. Tóth, M. Moravszki, K. Buga, I. Szilvási; State Health Centre, Budapest, HUNGARY.

Aim: ECG-gated myocardial perfusion SPECT (GSPECT) gives simultaneous information on myocardial perfusion and global/regional left-ventricular (LV) function. Ergometric stress can provoke myocardial stunning. We studied the usefulness of early GSPECT (15-G: 15-minutes after exercise) compared to the standard GSPECT (60-G: 60-minutes after exercise) in detecting exercise-induced reversible LV dysfunction in patients with ischemic heart disease (IHD). **Patients and Methods:** 37 patients (mean age 58+9 year) with angiographic evidence of IHD were enrolled in the study. 21 had decreased (50%) LV ejection fraction (EF) at rest by echocardiography (US). We performed 15-G, 60-G and resting GSPECT. Standard two-days Tc-99m acquisition protocol was used (dual-head camera, 180° circular rotation, 8 frame/cycle gating). LV-EF, segmental wall-motion and systolic wall-thickening of the three studies were compared using quantitative (QPS/QGS) program. Functional parameters were related to perfusion data. **Results:** From 16 patients with normal LV-EF by US EF decreased in 5 patients by 60-G and in 7 patients by 15-G. In all of them decrease was more pronounced by 15-G (in 3 patients more than 5%). Mean decrease of EF value by 15-G was 2.4 %, statistically non-significant. From 21 patients with low LV-EF by US EF decreased in 14 by 60-G and in 16 by 15-G. Decrease was more pronounced by 15-G in 12 patients. Mean decrease of EF value was 4.9% by 60-G ($p < 0.05$) and 6.0% by 15-G ($p < 0.01$). A week correlation ($r = 0.38$) was found between decrease of EF and myocardial ischaemia (summed difference score of perfusion). **Conclusions:** 15-G is useful in detecting exercise-provoked LV-dysfunction. Transient decreasing of LV-EF is more frequently found by 15-G than by 60-G. Early gated myocardial perfusion SPECT is indicated routinely because it can detect myocardial stunning in patients with low and with normal resting EF as well. Supported by the IAEA (RP:14676).

P241

Nitrate-enhanced Tc-99m MIBI gated SPECT for evaluating viable myocardium and left ventricular functions in patients with coronary artery disease

Ö. Ömür¹, A. Akgun¹, Z. Ozcan¹, A. Yanarates¹, T. Calkavur², O. Yavuzgil³, H. Ozkılıç¹: ¹Ege University Medical Faculty, Department of Nuclear Medicine, Izmir, TURKEY, ²Ege University Medical Faculty, Department of Cardiovascular Surgery, Izmir, TURKEY, ³Ege University Medical Faculty, Department of Cardiology, Izmir, TURKEY.

AIM: Foreseeing the revascularization results in order to separate the viable myocardium from the infarct tissue is very important in the coronary artery disease and the determination of the treatment approach. In this study, we aimed to research the place of Tc-99m MIBI Gated SPECT used with the sublingual nitrate application in the viability diagnosis. **METHOD:** 50 patients diagnosed with a coronary artery disease (11 female, 39 male; mean age: 61.7+8.3) were included in the study. All subjects were evaluated with rest-nitrate Tc-99m MIBI Gated SPECT, echocardiography and angiography. In 50 patients, myocardial perfusion and functional parameters such as wall motion, thickening and ejection fraction of the left ventricle were examined in both visual and quantitative methods. Five segments myocardial model was used. Findings were compared with the echocardiography and angiography data on a segment basis. **FINDINGS:** While normal perfusion was determined in 165 of the 250 segments, there were reversible perfusion defect in 44 of them and irreversible perfusion defect in the remaining 41. If >50 coronary artery narrowness is accepted as significant stenosis, in 59 of the 85 segments in total in which perfusion defect was detected, we have detected a significant narrowness in the feeding coronary artery. In the myocardial perfusion scintigraphy (MPS) there were not any significant coronary artery stenosis in 105 of the 165 segments with no perfusion defect. When the findings of the Gated SPECT and echocardiography findings were compared, no statistically significant difference was found between the average Ejection Fraction (EF) value (43.8+29.5) calculated with the QPS/QGS programme and the value obtained from the echocardiographic data (46.3+29.5). In the subjects with irreversible perfusion defects in MPS, average EF (36.2) was lower than the general group average (43.8). LV functional data obtained with GATED SPECT and echocardiography were found compatible in 219 of the 250 segments. When the wall movement and thickness scores calculated with the QGS/QPS programme in MPS were examined, LV functional scores were notably lower in the segments with a detected irreversible defect in MPS. Wall movement score was the lowest segment septum, in the other segments there was a statistically significant correlation between the visual findings and the wall movement scores. **CONCLUSION:** We have concluded that Rest-Nitrate Tc-99m MIBI Gated SPECT is a reliable method in the viable myocardium research which gives the advantage to evaluate perfusion and LV functions.

P242

99mTc-Tetrofosmine SPECT in Diagnostics of Stress Induced Cardiomyopathy

V. Y. Sukhov¹, S. A. Bondarev², A. N. Yalimov², K. L. Zaplatnikov³: ¹Military Medical Academy, St.Petersburg, RUSSIAN FEDERATION, ²Pediatric Medical Academy, St.Petersburg, RUSSIAN FEDERATION, ³Clinic of Nuclear Medicine, Nurnberg, GERMANY.

Objective. Stress cardiomyopathy (SCMP) is complex pathophysiological process often meet in young people, consequent upon several interrelated causes. It thoroughly studied by physiologists and cardiologists, but up to day there are no diagnostic criteria and algorithm for its detection. Purpose of the study was to implement in cases of SCMP gated SPECT - widely used clinical method of different heart diseases diagnostics. **Material and Methods.** 77 male patients with SCMP (main group) and 52 healthy volunteers (controls) 33.4±9.0 y.o. underwent standard clinical investigation, Bruce protocol ETT, EchoCG, rest/stress gated SPECT and psychological testing for assessment of emotionality and personality (Lusher and Spielberg tests). The entry criteria for patients of the main group were as follows: (1)fatigue, atrial and ventricular arrhythmia, (2)diastolic dysfunction of LV, (3)negative ETT results, (4)no evidence of inflammatory heart disease, (5)presence of psychological tension and anxiety, (6)no coronary pathology. SPECT studies were performed twice in patients of main group: before and after metabolic treatment followed by "Bulls eye" polarmaps (17 sectors) plotting for assessment of

difference in tracer uptake. **Results.** Diffuse non-uniformity and partial decrease of uptake in >6 non-adjacent sectors were detected in all patients. In 76.1% of patients relatively higher uptake (>70%) within these sectors was noted during stress ($p<0.001$), that is probably an effect of increased transport and mitochondrial activity due to sympathetic regulation. It's typical for primary cardiomyopathy/myocardial hypertrophy as well as for stress cardiomyopathy. In some cases (23.9%) regional uptake decreased at stress without angina, with negative ETT and normal coronal arteries. While comparing regions of impaired repolarization and decreased tracer uptake at rest in 12 patients, 92% of them were considered match ($di=0.615-0.998$), 8% - mismatch ($di=0.002-0.385$). Though sensitivity in detecting of impaired repolarization by ECG and decreased tracer uptake regions by SPECT were 17.6% vs 83.0%. Moreover, number of sectors with <70% uptake and EchoCG signs of cardiac conjunctive tissue display in 19 patients were almost equal and significant ($p=0.004$, Spearman coefficient of 0.2) indicating of strong correlation between cardiomyocyte dystrophy, ECG abnormalities and decrease of tracer uptake. Repeated SPECT after treatment showed increase of tracer uptake in 353 previously altered sectors up to >70%. **Conclusion.** Rest/stress gated SPECT with ^{99m}Tc -tetrafosmin as the non-specific marker can characterize cardiomyocyte transmembrane transport and synthetic mitochondrial activity in cases of suspected myocardial metabolic injury. Therefore, this method is feasible and highly informative for diagnostics of SCMP and also for treatment monitoring during follow-up.

P22 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Cardiovascular: Cardiovascular disease and comorbidities

P243

Value of myocardial perfusion scintigraphy as a pre-transplant screening test for the assessment of coronary disease in diabetic patients.

R. Macedo¹, A. Ferrer-Antunes¹, M. Ferreira², C. Baptista³, M. Cunha¹, A. Moreira¹, G. Costa¹, J. Pedrosa Lima¹; ¹Servico de Medicina Nuclear. Hospitais da Universidade de Coimbra, Coimbra, PORTUGAL, ²Servico de Cardiologia. Hospitais da Universidade de Coimbra, Coimbra, PORTUGAL, ³Servico de Endocrinologia. Hospitais da Universidade de Coimbra, Coimbra, PORTUGAL.

Aim: In diabetic patients with terminal renal insufficiency, silent coronary disease is an important cause of morbidity and mortality after renal transplantation. Myocardial Perfusion Scintigraphy (MPS) may be used as a pre-transplant screening test for coronary heart disease. The aim of this study was to evaluate the incidence of occult coronary disease, detected by MPS, in an asymptomatic diabetic population, referred for renal transplant in our hospital, during a one year period. **Material and Methods:** MPS performed in the 41 diabetic patients (24 males and 17 females; mean age 58±9 years) candidates for renal transplantation during 2008, were retrospectively reviewed. A one day stress/rest standard protocol has been used after i.v. administration of ^{99m}Tc -Tetrafosmin. Thirty seven patients underwent pharmacologic stress with adenosine and 4 underwent treadmill stress test (Bruce protocol). Stress and rest studies were analyzed by two nuclear medicine physicians. Each study has been classified according to the perfusion pattern: normal (no perfusion defects in both studies), ischemia (reversible perfusion defect) and necrosis (fixed perfusion defects). **Results:** Of the 41 diabetic patients, 20 (48.8%) had normal MPS results. In 21 patients (51.2%) MPS was abnormal, showing reversible perfusions defects in 17 cases (81%) and fixed defects in 4 patients (19%). **Conclusions:** Our results showed a high incidence of asymptomatic coronary disease (51.2%) in a diabetic population, and support the inclusion of MPS in the pre-transplant work-up of those patients.

P244

Prognostic criteria for screening Diabetics type 2 with Myocardial Perfusion SPECT Studies

I. Kotsalou¹, A. Kotsalos², C. Kotsalos², N. Zakopoulos³, M. Dimopoulos³; ¹NIMTS Hospital, Nuclear Medicine Dept., Athens, GREECE, ²NIMTS Hospital, Cardiothoracic Surgery Dept., Athens, GREECE, ³University of Athens, Internal Therapy Dept., Alexandra Hospital, Athens, GREECE.

AIM: Diabetes Mellitus is widely considered as a Coronary Artery Disease risk equivalent, because of the high incidence of coronary ischemia and high cardiovascular mortality rates of this population. This study aims to stress the need of early detection of CAD via Myocardial Perfusion Scan in diabetic population to prevent acute cardiovascular events. **MATERIALS -METHODS:** In this retrospective study we included 96 diabetics type 2 (mean age 62 years, male/female: 75/21) with DM duration 1-15 years (64% Group 1) and 16-25years (36%Group 2), which were either asymptomatic (43%- Group A) or had typical (28% Group B) or nonspecific anginal (29%- Group C) symptoms. 37 out of 96 diabetics had also history of Hypertension (38,5%- Group D), 20 were smokers (20,8% Group E), 26 (27% Group F) had hyperlipidemia, 32 (33,3% Group G) were overweight, whereas 46 (48%-Group H) had no additional risk factors, but Diabetes. All patients were subjected to a stress-rest ^{99m}Tc -tetrafosmin myocardial perfusion SPECT study and images were interpreted as fixed perfusion defects, reversible ischemia findings and normal perfusion studies. **RESULTS:** Using the 20-segment scoring model for SPECT analysis we found that 73% of perfusion studies (Group A) were positive for CAD (scar and/or ischemia) and 47%, 48% for Group B and Group C respectively. Finally, incidence of ischemia was not statistically significant different in variable duration of DM. Significant perfusion abnormalities were found in 37 (74%) out of the 50 diabetics with more than two cardiovascular risk factors, and in 33 (71%) out of 46 diabetics (Group H). On the other hand, there were totally 26 (27%) normal myocardial perfusion SPECT studies. **CONCLUSIONS:** Coronary Artery Disease (CAD) is a common complication of Diabetes Mellitus type 2 and very often lacks diagnosis, due to silent ischemia. Research data suggest that 41% of abnormal MPI results come from asymptomatic diabetics with ≥ 2 risk factors (RF). Therefore diabetics with more than 2 coronary RF, even asymptomatic, should preventively undergo MPI SPECT studies to estimate their specific cardiovascular risk profile, which is proved

to be heavy. The high incidence of ischemia findings in our study, may be explained by the long diabetic history and the heavy cardiovascular profile of our patients.

P245

Influence Of Sex And Cardiovascular Risk Profile In The Results And Pronostic Value Of Myocardial Perfusion SPECT.

M. Garrido Pumar, V. Pubul, S. Argibay, A. B. Ciobotaru, M. Pombo, P. Arce, R. Vidal, C. Peña, A. Sánchez-Salmón, J. Cortés, A. Ruibal; Complejo Hospitalario Universitario de Santiago de Compostela., Santiago de Compostela, SPAIN.

OBJECTIVES: The aim of this study is to evaluate the influence of both sex and cardiovascular risk profile in the results of myocardial perfusion SPECT, as well as the prognostic value of the SPECT in the following outcome. **METHODS:** Between 2003 to 2009, 3870 patients (61% men and 38% women) with suspicion of Cardiovascular disease (CVD) were submitted to the realization of a myocardial perfusion SPECT in our department. We selected 976 (448 men and 528 women) consecutive patients who underwent a two-day protocol stress/rest myocardial SPECT with diagnostic purposes. Cardiovascular risk profile data included age, smoking, diabetes mellitus (DM), hypertension (HT), dyslipemia (DL) and obesity. We defined high cardiovascular risk profile (HCRP), as the presence of three or more simultaneous risk factors. In the posterior follow-up, we considered as events the presence of acute coronary syndrome, revascularization surgery, development of cardiac insufficiency or death from heart failure twelve months after the SPECT. **RESULTS:** Men were older ($62,7\pm 12,2$ vs $64,2\pm 10,3$; $p=0,038$) and presented more cases of smoking. Men had a higher proportion of positive SPECTs than women (35% vs 17%; $p<0,001$). Positive results in the SPECT in men showed significant relation with age ($66,5\pm 10,3$ vs $60,6\pm 12,6$; $p<0,001$), HT (75.5% vs 61.2%; $p=0,002$), DM (38% vs 21%; $p<0,001$), DL (67% vs 53%; $p=0,05$) and HCRP (77% vs 53%; $p<0,001$). Women with positive SPECT were related to age ($66,4\pm 9,9$ vs $66,3\pm 10,3$; $p=0,024$), obesity (55% vs 42%; $p=0,023$) and HCRP (73% vs 61%; $p=0,026$), and they showed no relation with smoking, HT, DM or DL. In the twelve-month follow-up, 53 men and 37 women presented cardiovascular events. Positive SPECT results were related to a higher number of events in both men (31% Events in SPECT-positive men vs 2% Events in SPECT-negative men; $p<0,001$) and women (30% Events in SPECT-positive women vs 2% Events in SPECT-negative women; $p<0,001$). **CONCLUSIONS:** At this time, the number of men who were submitted to perform a Gated-SPECT is significantly greater than women. This fact may be indicative of difficulties in the diagnostic suspicion of CVD that may lead to a less intensive management in women. In our results, cardiovascular risk factors in men are more related to a positive result in the SPECT than in women, with the exception of age and obesity. The myocardial perfusion SPECT showed similar results in the prediction of events in men and women.

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Impact of cardiovascular risk factors and pharmacological treatment in myocardial perfusion scintigraphy interpretation for female gender

A. Mendoza Paulini, A. Mariana Monguia, C. Paniagua Correa, S. I. Vasquez Tineo, M. A. Balsa Breton, M. P. Garcia Alonso, L. Castillejos Rodriguez, A. Ortega Valle, F. J. Penin Gonzalez, C. Pey Illera; Hospital Universitario De Getafe. Medicina Nuclear, Gatafe (madrid), SPAIN.

OBJECTIVE: To asses the cardiovascular risk factors and pharmacological treatment that may influence the discrepancy between findings from anatomical and functional tests that evaluate coronary flow. **MATERIAL AND METHODS:** 63 medical reports from women who underwent myocardial perfusion scintigraphy (MPS) with ^{99m}Tc (MIBI) and an invasive coronary angiography (ICA) were evaluated. The mean age was 65 ± 12 years, 58% concerned atypical pain, 78% suffered high blood pressure (HTA), 60% was affected by diabetes mellitus (DM) and 47% had dyslipidemia (DLP), as major risk factors; 49% of them were treated with Aspirin, 41% with angiotensin-converting enzyme inhibitors (ACEI), 38% received beta-blockers and 33% nitroglycerin. **RESULT:** 73% of MIBI and 63% of ICA studies showed pathological findings. Results were concordant regarding the presence or absence of pathology in 40 cases in which HTA, DLP and DM were associates with ICA pathological findings mostly, the most affected field was located on anterior descending artery territory, with serious injury in 80% and three-vessel disease in 53%. Patients with MIBI pathological findings and unaltered ICA (12 cases) were 83% hypertensive women, as the only significant cardiovascular risk factor, 67% showed typical pain, 50% were treated with ACEI and 33% with beta-blockers. In 63% MIBI demonstrates involvement at anterior descending artery territory. Regarding patients with negative MIBI and pathological findings on ICA (11 cases) 90% were affected by HTA, 70% DL, treated with ACEI 40% and 40% taking aspirin. ICA showed severe injury of at least one vessel. **CONCLUSION:** The disagreement by MIBI positive and negative ICA is further associated with hypertensive patients and the left anterior descending territory, whereas patients with non-pathological MIBI and anatomical changes associated DLP, were under antiplatelet therapy and presented multivessel disease was in one third of cases.

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Ischemic cardiopathy in asymptomatic diabetic patients evaluated with gated-SPECT myocardial perfusion

F. Gomez-Camirero¹, R. Ruanos¹, M. Diego², P. Tamayo¹, A. Martin De Arriba¹, D. Garcia¹, A. S. Rosero¹, J. R. Garcia Talavera¹; ¹Nuclear Medicine, University Hospital of Salamanca, SPAIN, ²Cardiology, University Hospital of Salamanca, SPAIN.

Aim: to evaluate the incidence of myocardial ischemia in asymptomatic diabetic patients after a gated myocardial perfusion spect. **Methods:** during the period 2001-2009, a total of 463 diabetic patients were sent to our department for a diagnostic stress-rest gSpect myocardial perfusion. We selected 104 cases (22.5%) asymptomatic and without known ischemic cardiopathy. A one day stress-rest gSpect protocol was done in all patients. Ischemia criteria was: moderate when SDS was from 4 to 8 points, severe if SDS greater than 8 points. **Results:** among the 104 patients considered (60men, 44women, mean age 66,92y), cardiovascular risk factors were 74 arterial hypertension, hypercholesterolemia in 30 cases, and obesity in 19 cases. Pharmacological

dipyridamole stress occurred in 58% patients. Results from the cardiac stress test and gated-spect myocardial perfusion images are shown in the following chart:

Results GatedSpect Cardiac Stress Test	ISCHEMIA moderate/severe	NECROSIS	NECROSIS+ISCHEMIA	NORMAL
Clinically - ECG -	8 (7,7%) 4 (3,8%)	5 (4,8%)	3 (2,9%)	43 (41,3%)
Clinically - ECG NOT VALORABLE	3 (2,9%) 0 (0%)	3 (2,9%)	2 (1,9%)	12 (11,5%)
Clinically - ECG +	2 (1,9%) 2 (1,9%)	1 (1%)	1 (1%)	10 (9,6%)
Clinically +	3 (2,9%) 2 (1,9%)	0 (0%)	2 (1,9%)	0 (0%)
TOTAL	16 (15,4%) 8 (7,7%)	9 (8,7%)	8 (7,7%)	65 (63%)

We found no statistical differences in the type of stress applied (treadmill or dipyridamole) ($p > 0.05$). 37% patients showed scintigraphic ischemic signs, even 16% with associated necrosis. Stress test was clinically positive in 6,7% patients, and electrically positive in an additional 5,8%. gSpect perfusion images detected an extra 24,5% that stress test alone would have infradiagnosed. **Conclusion:** Up to 35-40% asymptomatic diabetic patients present ischemic cardiopathy estimated by a gated myocardial perfusion spect. This technique allows a better diagnosis in this population with high incidence of silent ischemic, avoiding the infradiagnosis resulted from a non-isotopic stress conventional test.

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Risk stratification by cardiac gated SPECT combined with coronary artery calcium score in patients with diabetes mellitus and/or renal failure

I. Metelkova¹, M. Kaminek¹, M. Budikova¹, E. Buriankova¹, R. Formanek¹, L. Henzlova¹, M. Myslivecek¹, P. Koranda¹, E. Sovova², R. Metelka³, ¹Department of Nuclear Medicine, University Hospital, Olomouc, CZECH REPUBLIC, ²Department of Internal Medicine I, University Hospital, Olomouc, CZECH REPUBLIC, ³Department of Internal Medicine III, University Hospital, Olomouc, CZECH REPUBLIC.

Aim: Schepis T et al. (J Nucl Med 2007;48:1424-30) described added value of severe abnormal coronary artery calcium (CAC) score (≥ 709) as an adjunct to cardiac gated SPECT for evaluation of coronary artery disease (CAD) in an intermediate-risk population. The aim of this study was to expand this observation to population of patients with diabetes mellitus (DM) and/or renal failure. **Methods:** The study group consisted of 67 patients who were referred for stress gated myocardial perfusion SPECT and CAC score because of suspected CAD. Characteristics of study population: 40 men, mean age 59 ± 12 years, DM ($n = 45$), renal failure ($n = 39$), DM and renal failure simultaneously ($n = 28$). Perfusion summed stress and difference scores (SSS, SDS), the left ventricle ejection fraction (LVEF) and end-diastolic/end-systolic volumes (EDV/ESV) were automatically calculated using 4D-MPSPECT software. The hard cardiac event was defined as sudden cardiac death or myocardial infarction (MI); angina or other symptoms requiring coronary revascularization were also calculated. **Results:** During the average period of 18 ± 10 months, we registered 8 cardiac deaths, 4 nonfatal MI, and 7 patients underwent revascularization. In the subgroup of 19 patients with cardiac events, the observed parameters were significantly worse concerning perfusion (SSS 9 ± 11 vs. 2 ± 3 and SDS 6 ± 9 vs. 1 ± 2 , $P < 0.05$), the left ventricle function (stress LVEF $53 \pm 13\%$ vs. $59 \pm 13\%$, rest LVEF $55 \pm 14\%$ vs. 59 ± 12 , stress EDV/ESV $144 \text{ ml}/71 \text{ ml}$ vs. $128/59 \text{ ml}$, $P < 0.05$), and CAC score (1965 ± 1772 vs. 387 ± 740 , $P < 0.05$) in comparison with patients without cardiac event. In patients without a reversible perfusion abnormality (SDS < 2), we observed lower annual hard event rate (8% vs. 19.6%, $P < 0.05$) and revascularization procedures (4% vs. 19.6%, $P < 0.05$) in comparison with patients with SDS ≥ 2 . In patients with or without reversible defects, we registered significantly higher annual hard event rate in the setting of post-stress worsening of the LVEF $> 5\%$ and/or severe CAC score ≥ 709 (23.8% vs. 1.9% in patients with $\text{SDS} < 2$, and 26.7% vs. 9.5% in patients with SDS ≥ 2 , $P < 0.05$). **Conclusion:** The findings of highly elevated CAC score as well as the post-stress left ventricle stunning enable further risk stratification in patients with or without reversible perfusion abnormalities.

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Extramyocardial findings on myocardial perfusion scintigraphy in patients with end stage liver disease

A. Aktas, A. Cinar, G. Yaman, T. Bahceci; Baskent University, Ankara, TURKEY.

Objectives: End stage liver disease is known to be associated with systemic and cardiovascular complications. The increased incidence of coronary artery disease in cirrhosis makes careful preoperative risk assessment imperative. In this retrospective study, we present extramyocardial findings detected on myocardial perfusion scintigraphy in patients with end stage liver failure. **Methods:** This study included 108 patients with end-stage liver disease undergoing preoperative evaluation for liver transplantation. Myocardial perfusion imaging was performed using Tc-99m sestamibi. Stress test was either performed with oral dipyridamole or treadmill exercise. Rest images were acquired 3 hours after stress imaging. In addition to routine evaluation of left ventricular myocardial perfusion and function, raw data and reconstructed images were inspected for the presence of right ventricular dilatation/hypertrophy, ascites and other extramyocardial abnormalities. **Results:** Nine patients (8%) had hydrothorax in the form of lateral thoracic hypoactivity. Hydrothorax was on the right side in 8 and on the left side in one patient. Right ventricular dilatation/hypertrophy was observed in 23% of patients. Out of 108 patients, 41 (38%) had mild to moderate skeletal uptake. On reconstructed images, sternal uptake was superimposed with right ventricular activity in several patients. This necessitated the reevaluation of raw data in all patients for the presence of skeletal uptake. **Conclusion:** In previous studies, mild diffuse skeletal sestamibi uptake was reported in patients with renal failure and also in several normocalcemic patients. The results of our study indicate that this finding is also frequent in patients with end stage liver failure. Since the incidence of both right ventricular hypertrophy/dilatation and skeletal uptake is relatively high in this patient group, evaluation of raw data for the presence of sternal uptake is important in order to avoid false-

positive interpretation of right ventricular activity. Also, hydrothorax can easily be detected by evaluating raw data.

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Efficacy of ivabradine on myocardial perfusion and clinical evidences in patients with combination of cardiovascular and chronic obstructive pulmonary diseases.

S. M. Minin, A. A. Garganeeva, S. M. Bagreeva, V. I. Chernov, Y. B. Lishmanov; Institute of Cardiology, Tomsk, RUSSIAN FEDERATION.

Aim: Studying the effect if-channels inhibitor - ivabradine on myocardial perfusion in patients with combination of coronary heart diseases (CHD) and chronic obstructive pulmonary disease (COPD). **Materials and methods:** The study involved 20 patients (M/F: 11/9, mean age: $52,3 \pm 1.12$ years). Eleven patients had stable angina and 9 patients had CHD mixed with COPD. The results evaluated are 12-weeks therapy with if-canals inhibitor - Ivabradine (Koraksan, Servier, France) with the average dose of $5,2 \pm 0,7$ mg/day. All patients were studied before and after Ivabradine administration general medical examination, spirometry, veloergometric and 6-minutes walk test. A myocardial perfusion with 99mTc-MIBI was performed at adenosine administration before (baseline) and 12-weeks after therapy. **Results:** As the results of the Ivabradine therapy the reduction of coronary insufficiency clinical implications were noticed - the decrease of episodes and heart stroke disappearance in some cases (3 patients). The number of angina patients with II and III class reduced and the number of patients with I degree and without angina episodes increased statistically-valid ($p < 0,05$) in both groups. The reliable average increase of physical tolerance in both groups is $18,4 \pm 5,3\%$ according to veloergometric tests and $14,8 \pm 6,2\%$ according to 6-minutes walk test. 12-weeks Ivabradine therapy has expressed antiangiogenic efficiency caused by reliable decrease of heart attacks (to 15,7%; $p < 0,001$) and daily requirement of nitroglycerine decreased to 16,0%; $p < 0,05$. Study showed that mean baseline summed perfusion stress score decreased from $7,38$ to $3,2$ ($p < 0,001$). It is important fact that patients of group with CHD mixed with bronchopulmonary abnormality had not inappropriate effects at the time when Ivabradin therapy was held neither according to clinical evidences nor according to spirometry examination. **Conclusion:** The if-canals inhibitor Ivabradine therapy has a positive effect on myocardial perfusion, clinical evidences of coronary insufficiency and physical tolerance in patients with CHD mixed with stable angina of II-III class, also in patients with CHD mixed with COPD. At the time when the therapy was held there were not any mixed bronchopulmonary abnormality deterioration.

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The comparison of $99\text{mTc-HMPAO-WBC-SPECT}$ results with immunologic findings in patients with suspicious myocarditis

S. I. Sazonova, I. Y. Proskokova, A. M. Gusakova, Y. B. Lishmanov; Institute of Cardiology, Tomsk, RUSSIAN FEDERATION.

Aim: to compare 99mTc-HMPAO-WBC myocardium SPECT results with levels of serum anti-heart antibodies, interleukines (IL)-1 β , -10, -8, tumor necrosis factor- α in patient with myocarditis. **Materials & methods:** We examined 64 patients (34 males and 30 females) with mean age $34,3 \pm 5,2$ with suspected myocarditis. All patients underwent SPECT with 99mTc-HMPAO-WBC at 18 hours post injection, following by SPECT with 99mTc-MIBI at the rest condition. Both images were then combined to define more exactly the localization of 99mTc-HMPAO-WBC uptake in the heart and to exclude ventricles blood pool. Accumulation of 99mTc-HMPAO-WBC was accepted as pathological when focus/background ratio exceeded 1,4. In the same time, a serum of these patients was analyzed and levels of anti-heart antibodies («immuGlo™» IMMCO Diagnostics Inc.), IL-1 β , -10, -8, tumor necrosis factor- α («Biosource») were determined. All patients were then divided into two groups: 1 - with presence of pathological accumulation of 99mTc-HMPAO-WBC in the heart area, 2 - without any accumulation. Statistical distinctions of laboratory-immunologic findings between groups were calculated by Mann-Whitney U-test. **Results:** The pathological accumulation (variable localization) of 99mTc-HMPAO-WBC in the heart was found at 23, perfusion defects at 52 patients (average size - $10,3 \pm 3,57\%$ (max -16%)). Anti-heart antibodies titre in the 1 group was ($110,6 \pm 69,6$) and statistically exceed the same ($63,9 \pm 40,6$) in the 2 group ($p < 0,05$). Levels of IL-10, -8 and tumor necrosis factor- α didn't differ. However, level of time y ation (nidal,t IL-1 β in patients with pathological accumulation of 99mTc-HMPAO-WBC ($149,8 \pm 214,4$ pg/ml) was significantly higher then in group without any accumulation ($35,6 \pm 16,3$ pg/ml) ($p < 0,001$). **Conclusion:** results of our study have showed that myocardial imaging with 99mTc-HMPAO-WBC combined with perfusion scintigraphy probably has lack of sensitivity in myocarditis diagnostics. In the same time, the interconnections between pathological accumulation of 99mTc-HMPAO-WBC in the heart and anti-heart antibodies titre (specific for myocarditis) as well as IL-1 β level (specific for inflammation) was showed. That can be the indirect sign of rather high specificity of mentioned above radionuclide method. Further studies comparing results of scintigraphy with histological findings are necessary for accurate calculation of diagnostic accuracy of 99mTc-HMPAO-WBC in myocarditis diagnostics.

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Cardiac involvement in transthyretin familial amyloid polyneuropathy - comparison between 99mTc-DPD SPECT and magnetic resonance imaging

F. Minutoli¹, M. Gaeta², G. Di Bella³, C. Crisafulli¹, G. Murè¹, V. Militano¹, M. Brancati¹, R. Di Leo⁴, A. Mazzeo⁴, S. Baldari¹; ¹Nuclear Medicine Unit, Messina, ITALY, ²Department of Radiological Sciences, Messina, ITALY, ³Clinical and Experimental Department of Medicine and Pharmacology, Messina, ITALY, ⁴Department of Neurosciences, Messina, ITALY.

Aim: to compare cardiac 99mTc-DPD SPECT findings with cardiac delayed contrast enhancement (CE) MR imaging findings in a group of patients with transthyretin (TTR) familial amyloid polyneuropathy (FAP). **Materials and methods:** Sixteen patients with TTR-FAP underwent 99mTc-DPD SPECT and cardiac-MR examination. Four patients suffered from peripheral polyneuropathy; 3 from carpal tunnel syndrome; one complained of symptoms and signs of heart failure (NYHA

III); 8 patients were asymptomatic with positive family history for FAP. SPECT images were obtained three hours after the intravenous injection of 740 MBq of ^{99m}Tc -DPD by using a dual-headed gamma camera. CE MR images were obtained by a 2D gradient echo inversion recovery sequence, within 4–20 min after bolus injection of 0.2 mmol/kg of gadobutrol. Presence of left ventricle (LV) radiotracer accumulation and CE were analysed for SPECT and MRI respectively; moreover, their extension was determined on a 16 segments model for both techniques. **Results:** ^{99m}Tc -DPD SPECT demonstrated no abnormal radiotracer accumulation in 10 patients (FAP non-cardiac group) and cardiac accumulation in 6 patients (FAP cardiac group). In all patients of FAP cardiac group, radiotracer uptake was also seen in extra-cardiac soft tissues (particularly skeletal muscle and/or splanchnic organs). FAP cardiac group included the 4 patients with peripheral neuropathy, 1 with carpal tunnel syndrome and the only one with heart failure. A complete correspondence between extension of ^{99m}Tc -DPD accumulation and CE was found in three patients; in three other patients the extension of cardiac radiotracer accumulation was larger than CE at MRI. **Conclusion:** ^{99m}Tc -DPD SPECT and CE-MR imaging show a similar sensitivity in revealing cardiac amyloidosis on a patient based analysis; however, in a segment by segment analysis, LV involvement as evaluated by CE-MRI is underestimated.

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An Investigation of the Relationship Between Cardiac Accumulation of Tc-99m-PYP scintigraphy and amyloidotic pathologies.

M. Matsushita, M. Momose, S. Yanagisawa, T. Matsushita, H. Matsushita, H. Tokoro, D. Komatsu, M. Kadoya; Shinshu University School of Medicine, Matsumoto, JAPAN.

Aim We assessed the differences in uptake and the accumulation of technetium-99m pyrophosphate (Tc-PYP) accumulation in the heart for several types of transthyretin amyloidosis such as familial amyloidotic polyneuropathy (FAP) and senile transthyretin amyloidosis from other amyloidoses by the scintigraphy analysis. **Materials and methods** We performed Tc-PYP scintigraphy on 31 patients (23 men and 8 women, mean age:63 years) for FAP, 26 patients (12 men and 14 women, mean age:60 years) for immunoglobulin light-chain amyloidosis and immunoglobulin heavy-chain amyloidosis (AL/AH amyloidosis), 9 patients (7 men and 2 women, mean age: 72 years) for senile transthyretin amyloidosis, and a patient (a woman, age :63 years) for reactive amyloid A amyloidosis. All of them showed an abnormal level in the ultrasound cardiogram. 740MBq of Tc-PYP was dosed intravenously. The thoracic planar scans and the myocardial single photon emission computed tomography (SPECT) were obtained in three or four hours later after the administration. The images were graded from 0 to 4, according to the level of radioisotope uptake in myocardium; 0 = no uptake in the region of the heart, 1 = a faint uptake equal to the blood pool or chest wall, 2 = a definite but weak uptake but less than the ribs, 3 = a moderate uptake in the myocardium equal to the ribs but less than the sternum, 4 = a intense uptake equal to or greater than the sternum. We considered that 2 and above indicates a positive result. **Results** The different cardiac accumulations were observed in many FAP and senile transthyretin patients. The positive rate was 63%(26/41)in FAP and 50%(6/12)in senile transthyretin amyloidosis. The AL/AH amyloidosis and reactive amyloid A amyloidosis patients did not show the cardiac accumulation. **Conclusion** We implicate that there is a difference in the uptake between the types of transthyretin amyloidosis (FAP and senile transthyretin amyloidosis) from other amyloidoses by the uptakes of Tc-PYP scintigraphy.

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Myocardial scintigraphy in the diagnosis and follow-up of inflammatory diseases in children

E. Swiatek-Rawa, L. Ziolkowska, M. Biernatowicz, A. Kaminska, W. Kawalec, A. Turska - Kmiec, A. Boruc, M. Raszek; The Children's Memorial Health Institute, Warsaw, POLAND.

Objective: Clinical and noninvasive diagnosis of myocarditis (myo) is difficult. The aim of study was to investigate whether scintigraphy with ^{99m}Tc AGA is useful for diagnosis and follow-up in children with myo. **Methods:** From 2005 to 2009, 11 children, mean age 13 ± 3.8 yrs presenting with symptoms of myo were evaluated at the time of initial presentation and 6, 12 and 24 months after the first study. In all pts heart scintigraphy with ^{99m}Tc AGA (Cisbio Scintimun Granulocyte) was performed, dose 12MBq/kg body mass intravenously. Scintigraphic images recorded 4 hours after tracer administration, the AP projection. The image covers the entire chest region. The study was performed by Siemens gamma camera, using a high resolution collimator, the matrix of 128×128 . Images were recorded at 1 million counts (about 4 minutes). Estimation of antigenulocyte antibodies uptake was performed by calculation of the heart-to-lung ratio (HLR). For semi-quantitative calculation of the HLR outlines three areas of interest (ROI) of each lung and heart. HLR is the ratio of the number of counts above the heart to the average of both lungs. HLR value above 1.50 was used as a positive result. Control group consisted of 10 children without cardiovascular disease underwent scintigraphy with ^{99m}Tc AGA due to suspicion of enterocolitis (HLR 1.06-1.50). **Results:** In 10 (91%) pts positive antigenulocyte uptake was observed (mean HLR 1.96; range 1.51 to 3.2). In follow-up scintigraphy after 6 months positive uptake was observed in 9 (82%) pts, the mean HLR was 1.97 (range 1.51 to 2.9). The scintigraphy after 12 months indicated positive uptake in 8 (73%) pts, mean HLR 1.88 (range 1.51 to 3.0). The scintigraphy after 24 months was positive only in 4 (36%) pts, mean HLR 2.03 (range 1.7 to 2.4). **Conclusion:** (1) Scintigraphy with ^{99m}Tc -Anti-Granulocyte antibody is a useful, noninvasive method for diagnosis and follow-up in children with myocarditis. (2) The control scintigraphy performed in follow-up after 6, 12, 24 months enable to evaluate resolved or persistent myocarditis. (3) Scintigraphy with ^{99m}Tc AGA seems to be a useful diagnostic method in children with suspected myocarditis, but further studies are needed to establish its sensitivity and specificity.

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Effects of chemotherapy on global and regional FDG myocardial uptake

A. Bruno, B. Zangheri, I. Vilardi, G. Del Gatto, L. Calabrese, P. Romano, D. Alberti, A. Lepre; IRCCS MultiMedica, Sesto San Giovanni - Milano, ITALY.

Aim: Aim of the study is to evaluate global and regional myocardial FDG uptake in non-diabetic cancer subjects without heart disease, before and after chemotherapy. **Materials & Methods:** Analysis of myocardial uptake has been performed on 18 patients (6 M, 12 F, mean age 50.2) who underwent 2 high resolution PET/CT studies each in fasting condition; the first PET for staging, while the second one at least 3 weeks after chemotherapy. Maximum Standardized Uptake Value (SUVm) has been calculated by drawing ROIs on septal (S), anterior (A), lateral (L) and inferior (I) wall, considering one short axis slice including the global ventricular volume. A further ROI has been drawn on the liver in each PET scan in order to normalise myocardial uptake to the liver activity. **Results:** A global and segmental difference in myocardial uptake, with no variation in liver activity, is found between the first and second study: in 14/18 cases normalized SUVm (nSUVm) is on average >75% in the second acquisition, in 1/18 nSUVm remains constant and in 3/18 nSUVm decreases on average by 33% (see table). Nevertheless in the first scan, SUVm in S, A and I walls is on average 90% of that in L wall and these proportions do not significantly change in the second scans. In the first PET scan, uptake is homogeneous in 8/18 patients; this pattern is confirmed in 5/8 in the second scan while 3 patients show uptake defects (1S, 1L and 1I). Ten/18 show uptake defects (1S, 4A, 1L and 5I): in the second scan 5/10 confirm the same defects (2A and 3I), 3 show no defects and 2 show defects in different positions (1S, 1A and 1I). Nevertheless such small defects do not change the global evaluation of myocardial uptake. **Conclusions:** Our preliminary data confirm the inhomogeneous myocardial FDG distribution. Furthermore chemotherapy may influence an increase of global myocardial glucose metabolism, although the uptake ratio (SUVm) among ventricular walls has not significantly changed.

		Liver (SUVm)	Septum (nSUVm)	Anterior (nSUVm)	Lateral (nSUVm)	Inferior (nSUVm)
Increasing cases	First PET scan	2.2 ± 0.6	2.1 ± 1.1	2.2 ± 1.1	2.6 ± 1.6	2.2 ± 1.2
	Second PET scan	2.2 ± 0.4	3.7 ± 1.9	3.9 ± 2.1	4.3 ± 2.2	3.9 ± 2.1
Decreasing cases	First PET scan	2.1 ± 0.5	2.9 ± 0.3	3.5 ± 0.6	3.5 ± 0.6	3.0 ± 0.4
	Second PET scan	2.2 ± 0.2	1.9 ± 0.8	2.4 ± 1.3	2.4 ± 1.3	2.0 ± 0.8

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Myocardial perfusion alterations observed several months after radiotherapy are related to the cellular damage.

I. Dogan¹, O. Sezen², B. Sonmez¹, A. Y. Zengin², E. Yenilmez³, E. Yulug³, I. Abidin⁴, Z. Bahat²; ¹Department of Nuclear Medicine, Karadeniz Technical University, Faculty of Medicine, Trabzon, TURKEY, ²Department of Radiation Oncology, Karadeniz Technical University, Faculty of Medicine, Trabzon, TURKEY, ³Department of Histology and Embryology, Karadeniz Technical University, Faculty of Medicine, Trabzon, TURKEY, ⁴Department of Biophysics, Karadeniz Technical University, Faculty of Medicine, Trabzon, TURKEY.

Aim: Myocardial perfusion scintigraphy (MPS) is one of the widely used tools to follow the development of radiation-induced heart disease (RIHD). But the clinical significance of MPS defects and the pathological mechanism have not been fully understood. We have investigated the biodistribution alterations related to perfusion defects following radiotherapy (RT) and have shown the coexisting morphologic changes. **Methods:** A single cardiac 20 Gy radiation dose was used to induce long-term cardiac defects. A total of 18 rats were used (12 rats received irradiation and six rats served as the controls) Biodistribution and histological evaluations were performed 120 days and 180 days after irradiation (early chronic and chronic phases, respectively). ^{99m}Tc -MIBI (20 MBq/0.2ml) was injected into the rats' tail vein. One hour following the injection, the animals were sacrificed. After portions of the hearts were allocated for cytologic investigations, samples of the myocardium were separated and then weighed. The radioactivity in each sample was counted. The percent of radioactivity (%ID/g) was calculated. The DNA fragmentation and apoptosis were assayed by TUNEL method. Myocardial cell degeneration, myocardial fibrosis and vascular damage were noted and semi-quantitatively scored for each heart to determine the degree of myocardial damage. The capillary endothelial and myocardial cells were ultrastructurally evaluated by transmission electron microscopy. **Results:** Six months after the treatment, a significant drop in the myocardial uptake was observed ($P<0.01$, compared to control). The apoptosis was detected within the first four months after the radiation treatment and stayed elevated until the end of the observation period ($P<0.01$, compared to control for both). Also, the myocardial degeneration, perivascular and interstitial fibrosis were visible in the heart at the end of six and four months ($P<0.005$, compared to control for both). The severity and extent of the myocardial injury has become more evident at the end of six month ($P<0.05$, between irradiation groups). At the ultrastructural level, prominent changes were observed in the capillary endothelial and myocardial cells. **Conclusion:** Our findings suggest that the reduced rest myocardial perfusion, occurring months after the radiation, indicates serious tissue damage characterized by myocardial degeneration and fibrosis. The irradiated patients with a perfusion defect on the MPS should be handled carefully examined for RIHD. **Keywords:** Radiotherapy, radiation-induced heart disease, cardiac damage, myocardial perfusion scintigraphy, technetium-99m sestamibi

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Pulmonary uptake of myocardial perfusion imaging agents in patients with end stage liver disease: A sign of hepatopulmonary syndrome ?

A. Aktas, G. Yaman, T. Bahceci, A. Cinar, A. Genocglu; Baskent University, Ankara, TURKEY.

Objectives: Pulmonary radionuclide uptake on myocardial perfusion scintigraphy (MPS) is generally observed in patients with multivessel coronary artery disease. Pulmonary hypertension

and hepatopulmonary syndrome constitute the two most common pulmonary complications of cirrhosis. However, the incidence of coronary artery disease in patients with end-stage liver disease is low. The aim of this study was to investigate scintigraphic and echocardiographic findings in cirrhotic patients with pulmonary uptake on MPS. **Methods:** This study included 188 patients with end-stage liver disease undergoing preoperative evaluation for liver transplantation. Gated MPS was performed using Tc-99m sestamibi (n=108) or thallium-201 (n=80). Raw data was evaluated for the presence of ascites and pulmonary radionuclide uptake. Ascites was graded from 1 to 3 according to the degree of lateral abdominal hypoactivity and the presence of diaphragmatic elevation. Reconstructed images were evaluated for the presence of ischemia/fixated hypoperfusion, left ventricular dilatation and right ventricular dilatation/hypertrophy. The presence of pulmonary hypertension and left atrial dilatation was based on echocardiography findings. **Results:** Among 188 patients, 172 (91%) had normal MPS. None of the patients with pulmonary hypertension (n=11) had pulmonary radionuclide uptake. Pulmonary uptake of perfusion imaging agents was detected on stress images in 44 patients (23%; 16 with sestamibi and 28 with thallium). These patients had normal myocardial perfusion. Lung uptake correlated with right ventricular hypertrophy/dilatation (p<0.05). Statistically significant correlation existed between right ventricular hypertrophy/dilatation and ascites (p<0.05). **Conclusion:** Hepatopulmonary syndrome is characterised with pulmonary dilatation and its final diagnosis is based on contrast echocardiography or lung perfusion scintigraphy. Association of hepatopulmonary syndrome with either right ventricular dysfunction or left atrial dilatation was reported. In this study, the existence of pulmonary radionuclide uptake with normal myocardial perfusion in patients with end stage liver disease was considered to be due to hepatopulmonary syndrome.

P23 — Sunday, October 10, 2010, 16:00 — 16:30, Hall Z

Cardiovascular: Ventricular function by 4-D imaging

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Body Surface Area (BSA) is inappropriate for indexing cardiac volumes : a radionuclide ventriculography (RVN) data analysis

G. Arsos¹, E. Moravidis², C. Sachpekidis¹, I. Tschelidhis¹, G. Sakagiannis¹, A. Svoukas¹, A. Iakovidou¹, V. Sidi³, E. Papakonstantinou³, ¹Dept of Nuclear Medicine, Aristotle University Medical School, Hippokraton Hospital, Thessaloniki, GREECE, ²Dept of Nuclear Medicine, Aristotle University Medical School, AHEPA University Hospital, Thessaloniki, GREECE, ³Dept of Pediatric Oncology, Hippokraton Hospital, Thessaloniki, GREECE.

Aim: The common practice to normalize cardiac volumes by indexing them to BSA, stems from the erroneous belief that BSA is an adequate estimate of the metabolically active body mass (MABM). Lean body mass (LBM), a more direct MABM estimate than BSA, can be easily assessed by bioimpedance analysis (BIA). By definition, appropriate indexing must remove the correlation between the indexed and the indexing variable. The aim of the present study was to test the efficiency of indexing cardiac volumes (assessed by RVN), by BSA or LBM. **Methods:** Sixty-one children and young adults with intact cardiac function, aged 11.6±4.3 years with body weight 18 - 120 kg and body mass index 14.0-34.0 m/kg² were included. Patients were referred for RVN before starting potentially cardiotoxic chemotherapy for neoplastic disease or as pediatric neoplasia long term survivors. Ejection fraction (EF) was assessed by standard means, left ventricular end diastolic and end systolic volumes (EDV and ESV respectively) were calculated using a previously validated count ratio-based method (Massardo T et al. 1995) and stroke volume (SV) as their difference. All patients were submitted to impedance measurement using a Bodystat 1500 MDD (UK) body composition analyzer, through two pairs of self-adhesive spot electrodes placed on the dorsal surface of the right hand and foot and LBM was calculated using previously validated regression equations. BSA was derived using the DuBois and DuBois formula. Cardiac volume variables were normalized for both BSA (iS) and LBM (iL) by dividing them by BSA or LBM respectively. Association between variables was assessed by means of linear regression analysis (r, Pearson correlation coefficient). **Results:** EF was 63.0±5.4% and >50.0% in all cases. EDV, ESV and SV, all were strongly correlated with both BSA and LBM (r>0.77, p<0.001 in all cases). After indexing for BSA the indexed variables continued to correlate with BSA (r = 0.48, 0.42 and 0.48 for EDV, ESV and SV respectively, p<0.001 in all cases). On the contrary, no residual correlation could be shown after indexing for LBM (r = 0.01, 0.03 and 0.03 for EDV, ESV and SV respectively, p>0.80 in all cases). **Conclusion:** Despite its wide application, BSA has been shown inappropriate for indexing cardiac volumes and should be abandoned. LBM on the contrary, seems ideal as cardiac volume index leaving no appreciable residual correlation.

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Assessment of the coronary angioplasty with stenting effects on the left and right ventricular performance in patients with systolic and diastolic dysfunction using 4-D tomographic radionuclide ventriculography

V. B. Sergienko, N. V. Shashkova, A. A. Skvortzov, S. N. Tereschenko, L. E. Samoylenko; Russian Cardiology Research Center, Moscow, RUSSIAN FEDERATION.

Aim: To assess long-term outcome following percutaneous coronary intervention (PCI) with stenting in patients with ischemic LV systolic and diastolic dysfunction using 4-D tomographic radionuclide ventriculography (4-D TRVG). **Methods:** 20 pts with ischemic chronic heart failure (NYHA II-III) were underwent 4-D TRVG at baseline and at 1 year follow-up after successful elective PCI with stenting. Imaging studies were performed using gamma-camera 20 min after in vivo RBC labeling with 740 MBq 99mTc. End Systolic and Diastolic Volumes (ESV and EDV), Stroke Volume (SV), Ejection Fraction (EF) of Left and Right Ventricles (LV and RV) were assessed using AUTOSPECT/QGS protocol. According to left ventricular ejection fraction (EF) all the patients were divided into two groups: group 1 (EF 45%) - 10 pts (5 m/5f, mean age 62.6±2.7 yrs; mean symptoms duration 2.0±0.4 yrs). **Results:** Group 1 patients 1 year later after PCI with stenting demonstrated significant increase in LV SV (from 63[49; 66] to 71.5 [57; 78] ml), RV SV (from 45[32; 79] to 66 [52; 82] ml), LV EF (from 31[25; 43] to 39.5 [37; 44]%), RV EF (from 45[40; 61] to

59 [51; 66] %), LV PER (from 1.66[0.92; 1.8] to 2.0 [1.8; 2.3]), LV PFR (from 1.3[0.6; 1.6] to 1.5 [1.2; 2.2]), LV MFR/3 (from 0.8[0.4; 1.0] to 1.2 [0.9; 1.5]), RV MFR/3 (from 1.3[0.8; 1.6] to 1.8 [1.4; 1.9]), decrease in LV TTPF (from 186.5[141; 222] to 130 [111; 220]); (p<.05 for all variables). Group 2 patients demonstrated significant increase in RV EDV (from 111.5[87; 127] to 124 [104; 141] ml), LV SV (from 55.5[46; 58] to 59.5 [45; 74] ml), RV SV (from 53.5[47; 67] to 69 [52; 87] ml), RV MFR/3 (from 1.1[0.6; 1.6] to 1.7 [1.4; 2.1]), and decrease in RV TTPF (from 169[128; 384] to 120.5 [107; 138]); (p<.05 for all variables). Positive hemodynamics changes were associated with decrease in HF functional class, increase in distance during 6 minutes walking test, and improvement in health-related quality of life parameters. **Conclusion:** 4-D tomographic radionuclide ventriculography might be a useful tool for the assessment of the coronary intervention effects on ventricular performance. Coronary angioplasty with stenting in patients with CHF resulted in increase in EF and SV, improvement of parameters both systolic and diastolic function of left and right ventricles associated with the increase in physical tolerance, and improvement of functional class and quality of life.

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4-D Tomographic Radionuclide Ventriculography in the Assessment of the Endothelin-receptor Antagonist Treatment Effect on the Right Ventricle Performance in the Patients with Idiopathic Pulmonary Arterial Hypertension

L. E. Samoylenko, O. A. Arkhipova, N. M. Danilov, T. V. Martynyuk, V. B. Sergienko, I. E. Chazova; Russian Cardiology Research Center, Moscow, RUSSIAN FEDERATION.

Aim: to estimate treatment effect with endothelin-receptor antagonist bosentan on RV hemodynamic parameters using 4-D tomographic radionuclide ventriculography in the patients with IPAH. **Methods:** 16 pts (13 f/3 m, mean age 38.5±11.3 yrs) with IPAH (WHO FC II-III, mean disease duration 8±7.1 yrs) were enrolled and divided into two groups. 8 pts were assigned to receive bosentan 125 mg/day, and 8 were assigned to receive bosentan 250 mg/day. All the patients were underwent 4-D tomographic radionuclide ventriculography at baseline and after 12 weeks of therapy. Imaging studies were performed using gamma-camera 20 min after in vivo RBC labeling with 740 MBq 99mTc. ESV and EDV, SV, EF of Left and Right Ventricles (LV and RV) were assessed using AUTOSPECT/QGS protocol. Results are presented as a median and top and bottom quartile. Med [25 %–75 %]. **Results:** On bosentan 125 mg/d patients demonstrated decrease of EDV LV from 76.5 [70–88] to 75 ml [70.5–92], ESV LV from 28 [20–33] to 23 ml [19.5–27], ESV RV from 78 [60.5–152] to 67.5 ml [63–145] and increase SV LV from 51 [46.5–51] to 54 ml [46.5–65], EF LV from 68 % [61–70] to 70.5 % [67–73.5], EDV RV from 139 [115.5–190.5] to 149 ml [121–216], SV RV from 46 [41.5–74.5] to 55 ml [50.5–97.5]; p<0.05, EF LV from 38 % [29.5–52.5] to 44.5 % [35–60]; p<0.05. In the group on bosentan 250 mg/d there were increase in EDV LV from 57.5 [48.5–72] to 67.5 ml [63.5–113.5]; ESV LV from 15 [14.5–17.5] to 22 ml [18–40.5]; p<0.05; SV LV from 43 [35–50] to 48 ml [43–71.5]; SV RV from 59.5 [52.5–80.5] to 60.5 ml [53–82.5]; EF RV from 37 % [28–41] to 43.5 % [30–54.5], and decrease in EF LV from 74.5 % [66.5–77] to 67 % [63–71], EDV RV from 172.5 [144–221] to 170 ml [136–220.5], ESV RV from 111.5 [91.5–144.5] to 109 ml [66–122.5]. **Conclusions:** 4-D tomographic radionuclide ventriculography may be useful tool for the non-invasive assessment of the RV hemodynamics response to the treatment in patients with IPAH. The endothelin-receptor antagonist bosentan had a beneficial effect on RV hemodynamics in the patients with IPAH at a dose of 250 mg/d. In contrast, bosentan at a dose 125 mg/d failed to demonstrate significant positive hemodynamic effect on RV and could not prevent the progression of the RV chambers dilation with consequent alteration of LV function might be due to the reverse Bernheim phenomenon.

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Gated equilibrium radionuclide ventriculography with autologous red blood cells in the follow-up of breast cancer women treated with trastuzumab

L. Mena Bares¹, F. Martín Ordóñez¹, M. Muñoz Sánchez², J. Santiago Crespo², I. Jiménez Romero³; ¹Nuclear Medicine Department. Hospital Virgen de la Luz, Cuenca, SPAIN, ²Oncology Department. Hospital Virgen de la Luz, Cuenca, SPAIN, ³Radiopharmaceutical Unit REDPET Iberia, Cuenca, SPAIN.

Aim: The purpose of this study was to analyze the gated equilibrium radionuclide ventriculography (GERV) utility as a monitoring tool in the follow-up of women with breast cancer treated with trastuzumab. **Material and Methods:** 37 consecutive breast cancer patients treated with trastuzumab were included in the study (January 2004–March 2010). All patients underwent to a GERV with autologous red blood cells labeled with ^{99m}Tc by using in-vivo technique before oncology treatment and every three months until treatment was considered completed. The left ventricular ejection fraction (LVEF), regional and global wall motion and left ventricular systolic and diastolic function were analyzed. If LVEF decreased more than five points in absolute value was considered indicative of cardiotoxicity, although results were over 50% of LVEF. None of the patients appeared with cardiac symptoms of cardiotoxicity. **Results:** 146 studies were performed in 37 patients and a decrease in LVEF was observed in 27/37 patients (73%) (5–10 points in 26/146 studies and over 10 points in 7/146 studies). 7/27 patients presented two declines in LVEF during follow-up and all of these patients had the first decrease in LVEF after the first trastuzumab dose, 2/7 patients (29%) the first decline in LVEF was higher than 10 points. Were performed three or more studies in 19/27 patients, mean baseline LVEF before treatment was 59.5% (49–70%) and after treatment was 52.5% (45–66%). This difference is statistically significant. **Conclusions:** The gated equilibrium radionuclide ventriculography seem to be good tool in controlling the toxicity in breast cancer patients treated with trastuzumab. We recommended to perform a study every three months, because 26% of the patients analyzed showed a further decline in LVEF, that seems to be reversible in most cases. In our series there has been a high rate of cardiotoxicity (73%) resulting from treatment with trastuzumab.

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Radionuclide assessment of right ventricle function and mechanical intraventricular dyssynchrony in children with ventricular tachyarrhythmia

K. W. Zavadovskiy, A. A. Chernishov, V. V. Saushkin, Y. Y. B. Lishmanov; Institute of Cardiology, Tomsk, RUSSIAN FEDERATION.

Aim: to estimate the diagnostic possibilities of quantitative blood pool single photon emission computer tomography (QBS) in diagnostic of function and mechanical dyssynchrony in children with ventricular tachyarrhythmia (VT). **Materials and methods:** 70 children with VT were included in the investigation (average age 12±4 years). All patients underwent a standard clinical and instrumental investigation which included QBS with marked in vivo 99mTc-stannous pyrophosphate erythrocyte. The investigation was carried out on gamma camera Philips-Forte in tomographic ECG-synchronized mode. **Results:** All patients were divided into 2 groups according to the quantity of focuses of premature contraction according to QBS. The first group included 22 children with 1-2 areas of premature contraction, the second group - 48 patients with more than two similar areas. RV peak ejection rate, peak filling rate, mean filling rate for first third of cardiac cycle, RV ejection fraction was significantly more in the first group of patients. Interventricular and intraventricular dyssynchrony in the second group was significantly more. These alterations of right heart contractility are probably connected with the fact that the majority of focuses of ectopic activity were registered exactly in RV walls and ventricular septum. The areas of ectopic activity (according to ECG and electrophysiological study) coincided with positioning of focuses of early contraction (according to QBS) in 86% cases. **Conclusion:** The scintigraphic criterion of ectopic activity area is a focus of early contraction according to QBS. This method is less painful for children in comparison with electrophysiological study. Because of its noninvasiveness and simplicity of implementation QBS may be used for observation of children with VT for the purpose of arrhythmogenic myocardium dysfunction diagnostics.

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Comparison of myocardial perfusion gated SPECT and clinical symptoms in proper diagnosis of coronary artery disease.

P. Maj; Nuclear Medicine Department. Medical University, Lublin, POLAND.

The aim of this study was to assess relationship between stress/rest myocardial perfusion gated SPECT (GSPECT) and clinical symptoms of ischemia in patients with diagnosis of coronary artery disease (CAD). **Materials and Method.** Myocardial perfusion scintigraphy (MPS) was performed in 91 patients (M/F; 36/55 mean age 58,7 ± 10,23 years). High risk patients were referred for MPS with suspicion of CAD, increased chest pain or positive exercise electrocardiogram test. All patients underwent 2-days protocol (stress/rest) GSPECT MPS after 740 MBq of 99mTc MIBI injection. Stress/rest images were visually analyzed for the presence, severity and reversibility of perfusion and wall motion abnormalities. For estimation of perfusion defects a 4-point scale system was used (1 - normal, 2 - moderate, 3 - severe reduction, 4 - absent perfusion). Patients were divided into 4 groups. Group A suspicion of CAD, atypical chest pain (n=17); B high probability of CAD, chest pain (n=31); C stable CAD (n=32); D risk of instable CAD (n=11). In these 4 groups were separated subgroups of patients with not visible, moderate and severe stress defects in MPS in comparison to rest study. In 58/91 patients (63.7%) predictive heart rate (PHR) was reached; 13/91 (14.3 %) had positive stress test; 21/91 (23%) did not achieve PHR; 21/91 (23%) had documented myocardial infarction; 15/91 [16,5%] had cardiovascular intervention PCI. **Results.** There was not significant difference in age of group A, C and D p>0.05. Patients in group B were statistically younger (55,7±9,18 years) than C (63,6 ±9,92 years) p<0.02. Significantly less patients from group A and B had more severe stress defects than in rest MPS study (1/17 [5,9%]; 6/31 [19,3%] versus C (14/32 [43,7%] p<0.006; p<0.04 respectively). There was no significant difference in the number of patients with similar rest/stress perfusion defects between A, B, D and C group (8/17[47%]), 11/31[35,5%], 4/11 [36,4%] versus 6/32 [18,7%] p>0.05 and also in patients with moderate stress defects/normal rest MPS study in group A, B, D (4/17[23,5%], 7/31[22,6%], 4/11 [36,4%] versus C 6/32 [18,7%] % p>0.05). Statistically more patients in group B than C had non diagnostic stress test (10 [32,2%]; 3[9,4%] p<0.05). **Conclusion** In patients with stable ischemia (group C) significant relation was observed between symptoms and rest/stress MPS. In patients from group A (atypical chest pain) and B (chest pain) discrepancy between symptoms and rest/stress MPS was observed.

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Impact of Caffeine on The Quantitative and Semiquantitative Analyses of Dipyridamole Stress Myocardial Perfusion Gated SPECT study

O. Yaylali¹, Y. T. Yaylali¹, S. Kirac¹, M. Serteser², D. Yuksel¹, B. Akdag¹, I. Susam¹; ¹Pamukkale University Medical Faculty, Denizli, TURKEY, ²Acibadem Labmed Clinic, Istanbul, TURKEY.

OBJECTIVE: The dipyridamole stress gated myocardial perfusion SPECT imaging (GMPS) is a well-established diagnostic tool for patients with suspected or known coronary artery disease (CAD). Caffeine may attenuate the effect of dipyridamole during GMPS. Extent and severity of perfusion abnormalities in each segment during stress and rest can be semiquantitatively evaluated using summed stress score (SSS) and rest score (SRS). However, there are no sufficient data how caffeine effect semiquantitative segmental analysis of dipyridamole GMPS images. We aimed to examine the effect of caffeine on the results of dipyridamole GMPS. **MATERIAL&METHOD:** GMPS with standard dipyridamole stress test was used to assess myocardial perfusion defects and LVEF values in 25 patients (14 women, 11 men; mean age 57±2 yr) with known or high likelihood of CAD before (baseline) and after coffee ingestion (caffeine) following dipyridamole infusion. All patients were asked for their daily caffeine consumption and reported abstinence from caffeine 24 h prior to the test. Serum caffeine levels were measured by HPLC before and one h after coffee ingestion. Myocardial perfusion images and gated analyses were assessed visually and semiquantitatively. The SSS and SDS (scale of 0 to 3, where 0 is normal and 3 is absent perfusion) based on 20 segmental model were calculated. Semiquantitative analysis from polar map (CSQ Software Package, LA.) and quantitative analysis for LVEF calculation (by QGS software) were performed. **RESULTS:** Mean serum caffeine were <1 mg/L and 5.6±3 mg/L at baseline and at one hour after caffeine. The mean SSS (baseline: 12±2; caffeine: 11±1) and SDS (baseline: 3±1;

caffeine: 2±1) did not change with caffeine. Reverse defects were observed with baseline and caffeine GMPS at same ratio (35%). The number of abnormal myocardial segments was 10±1 at baseline and 9±1 after caffeine on polar maps. Mean LVEF obtained with GMPS did not change after caffeine (baseline 68±3%, caffeine 65±3%). Much more perfusion abnormalities (54%) were observed visually on baseline GMPS than that of caffeine images (40%) (Table 1). **CONCLUSION:** We suggest that caffeine should be discontinued before dipyridamole stress because it effects visual evaluation of GMPS, even though no any impact on quantitative and semiquantitative analyses. Table 1. MPS SPECT defects based on vascular territories

Arteries	The number of perfusion defects			
	Baseline GMPS		Caffeine GMPS	
	Normal	Abnormal	Normal	Abnormal
LAD	7	18	12	13
RCA	14	11	16	9
LCX	13	12	17	8

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Ventricular ejection fraction calculated by gated blood pool SPECT processing software: correlation with MUGA and first pass RNV

S. Santhosh, R. Senthil, R. Kashyap, A. Bhattacharya, B. R. Mittal; PGIMER, Chandigarh, INDIA.

Introduction: Patients with dilated cardiomyopathy (DCM) tend to suffer from right ventricular cardiomyopathy also. Isolated right sided cardiomyopathy is also a known entity. Since RVEF is an essential parameter in guiding the management of these patients, first pass radionuclide ventriculography (FPRNV) is usually performed to obtain RVEF. Given the practical difficulties like good bolus administration with FPRNV, GBPS automated software can be warranted. **Aim:** To find out the LVEF and RVEF in patients with cardiomyopathy using commercially available automated GBPS processing software. **Methods:** Patients (total=45; 31 males; mean age 51 ± 13 years) referred to our department for assessment cardiac function were prospectively included in the study. Nineteen patients had dilated cardiomyopathy (DCM), 11 were on chemotherapy for CML and 15 were post myocardial infarction follow up. In patients with DCM, First pass radionuclide ventriculography (FPRNV) and planar multigated radionuclide angiography (MUGA) were performed at rest after in-vivo labelling of RBCs. LVEF was also calculated by Echo in these patients. Only MUGA was performed in other patients. LVEF and RVEF were calculated by dual ROI method. Gated blood pool SPECT (GBPS) was performed immediately after MUGA and was processed using the fully automated QBS algorithm to calculate LVEF and RVEF. Spearman's coefficient (r) of correlation was calculated for the different sets of values. The level of statistical significance was set at < 5%. Bland-Altman plots were inspected to visually assess the association between measurements from different methods. **Results:** Head on comparison of the mean LVEF and RVEF values obtained by different techniques was done and shown in the table. In all patients, LVEF calculated by MUGA and QBS-SPECT showed very good correlation: (r=0.94), p < 0.0001. Bland-Altman plot showed overestimation for GBPS-LVEF values compared to MUGA. In patients with DCM, LVEF values calculated from GBPS showed very good correlation with MUGA (r=0.95) and echocardiography (r=0.90; all p<0.0001). RVEF values calculated by FPRNV and QBS-SPECT also showed good correlation (r=0.78; p=0.0009). Bland-Altman plot for RVEF values showed a tendency for an overestimation of higher RVEF values with GBPS. **Conclusion:** Our study showed a good correlation between MUGA and GBPS for LVEF measurement as well as FPRNV and GBPS for RVEF estimation. Bland-Altman showed good association between these techniques. Thus the automated QBS algorithm for LVEF and RVEF calculation using GBPS is feasible for clinical routine diagnostic in DCM patients.

Table showing head on comparison of the mean LVEF and RVEF values obtained by different techniques

	PLANAR	QBPS	ECHO
LVEF%			
DCM Patients, n=19	31±11	34±13	32±11
RVEF%			
DCM Patients, n=19	48±13	47±16	
LVEF%			
All Patients, n=45	37±17	42±19	

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WBR 16 Frames GATED Cardiac SPECT - Volumes And Phase Analysis Impact

H. Pena¹, G. Cantinho¹, P. Gomes², M. Pinheiro², M. Wilk³, Y. Srour³, F. Godinho¹; ¹Atomedical, SA & Instituto de Medicina Nuclear da Faculdade de Medicina de Lisboa, Lisboa, PORTUGAL, ²Atomedical, SA, Lisboa, PORTUGAL, ³UltraSPECT, Haifa, ISRAEL.

Introduction: WBR, as a recovery reconstruction gated SPECT (GSPECT) half time methodology, has shown very good results in the simultaneous evaluation of perfusion and systolic VE function, using the 8 frames/ cardiac cycle acquisition. LV systolic and diastolic function parameters obtained by Fourier analysis are important and sensitive for early identification of cardiac disease. More recently, was developed an automated method to extract amplitude and phase LV counts changes to quantify LV dyssynchrony (LVD), parameters that seems sensitive to select patients for cardiac resynchronization, with good correlation with other LVD markers. The parameters for systolic, diastolic and phase analysis are dependent on cardiac cycle and, in theory, on temporal resolution. Our aim was to compare all the parameters in WBR 8frames/cycle (8f) and 16 frames/cycle (16f) GSPECT studies. **Material and Methods:** 18 patients were sequentially submitted to an 8f-GSPECT (A) and a 16f-GSPECT (B), 11-13 s / view, 60 views. WBR algorithm was applied for tomographic processing. For quantification of the two sets of studies, Germano's QGS was used for LVEF, volumes, systolic and diastolic rates, motion and

thickening. For phase and amplitude analysis, Synchtool ECToolbox (E. Garcia) was used to obtain the peak phase (PP), SD, histogram (H) bandwidth (B), H skewness and H kurtosis. Mean, standard deviation, paired Student t test (p) and the correlation coefficient (r) were determined. Results: LVEF in B (76±7%) was higher than in A (71±8%) (p=0.004 and r=0.65), with a systematic higher EDV(105±29ml) in B (94±31ml in A) (p=0.0002 and r=0.95), values always in normal range. On the diastolic analysis, we only found differences on the peak ejection rate (p<0.01) We didn't find any differences on the peak filling rate, time to peak, motion and thickening scores. Synchronization analysis showed that PP and HB were statistically different: HB = 52±16° for B and 61±20° for A (p=0.04 and r=0.50) and PP = 140±19° for B and 129±20° for A (p=0.001 and r=0.79). The other parameters didn't show important differences (p<0.05), however with a lower correlation coefficient. Conclusions: We didn't find a good correlation in all the evaluated parameters, except for EDV (r=0.94). These random variations don't clarify nor corroborate the theoretical hypothesis that 16f-GSPECT is better than 8f-GSPECT acquisition. To our present knowledge, time consumption and patient discomfort in 16f-GSPECT seem not to be justified.

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Gated ¹³N-ammonia PET for the evaluation of left ventricular ejection fraction and volumes: comparison of 2 different software packages

S. Lazarenko¹, A. Serano², C. J. A. M. Zeebregts¹, R. A. Tio¹, A. Signore¹, A. T. M. Willemsen¹, R. A. J. O. Dierckx¹, R. H. J. A. Slart²; ¹University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS, ²University La Sapienza, Second Faculty of Medicine, Rome, ITALY.

The aim of this study was to compare left ventricular (LV) volumes and ejection fraction with gated ¹³N-ammonia PET using 2 different software packages. **Methods:** LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LV ejection fraction (LVEF) were calculated with QGS adapted to gated PET images (Cedars Sinai, Medical Center, Los Angeles, U.S.A.), and Corridor 4DM (University of Michigan, Ann Arbor, Michigan, USA) software programs in 35 patients suspected of cardiac syndrome X using gated ¹³N-ammonia PET. **Results:** Moderate to good correlations were observed between QGS, Corridor 4DM and QGP software for all parameters, with r values of 0.96 (LVEDV), 0.87 (LVESV) 0.85 (LVEF). With Corridor 4DM, there was an overestimation of LVEDV, LVESV, and underestimation of LVEF in comparison with QGS. **Conclusion:** There was a good correlation between QGS adapted to gated PET images and Corridor 4DM, however LV volumes were overestimated and LVEF was underestimated with Corridor 4DM in comparison with QGS.

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Evaluation of the different software programs for the left ventricular volume assessment by FDG PET validated by MRI.

S. V. Lazarenko¹, A. T. M. Willemsen¹, A. M. J. Paans¹, R. A. J. O. Dierckx², R. A. Tio¹, R. H. J. A. Slart²; ¹UMCG, Groningen, NETHERLANDS, ²UMCG, RuG, Groningen, NETHERLANDS.

Background: Assessment of left ventricular (LV) ejection fraction (LVEF) and LV volume are essential for the evaluation of prognosis in cardiac disease. LVEF and LV volumes can be measured with several imaging modalities, such as magnetic resonance imaging (MRI) or computed tomography (CT), however, these are relatively expensive and time consuming. In contrast, positron emission tomography (PET) for LVEF assessment is a fast and reliable technique. There are different programs for LV volumes determination, but the precision of the heart volume determination with these programs is not known. Aims: Validation of a new Cedars-Sinai's Quantitative PET (QPET) software modified for PET in comparison with the old version of the Cedars-Sinai's Quantitative Gated SPECT (QGS) software for the calculation of LV volumes measured with gated FDG PET using MRI as reference. **Methods:** Thirty eight cardiac patients underwent routine gated PET with a standard dose of 5 MBq per kg of the patient weight of ¹⁸FDG and an additional cardiac MRI as reference method. LV volumes of PET data were calculated by two different programs. **Results:** Both programs underestimated slightly the left ventricle volumes as compared to the MRI measured volumes. The difference (mean ± SD) of end-diastolic volume (EDV) between PET and MRI was 15 ± 25 ml for QGS (p<0.001) and 20 ± 32 ml for QPET (p<0.001). The correlation coefficients for EDV between PET and MRI were r = 0.90 for QGS (p<0.001) and r = 0.84 for QPET (p<0.001). The difference of end-systolic volume (ESV) between PET and MRI was 6 ± 17 ml for QGS (p=0.011), 10 ± 24 ml for QPET (p=0.052). The correlation coefficients for ESV between PET and MRI were r = 0.94 for QGS (p<0.001) and r = 0.92 for QPET (p<0.001). The difference of left ventricle ejection fraction (LVEF) between PET and MRI was 4 ± 6 % for QGS (p<0.001), 4 ± 7 % for QPET (p<0.001). The correlation coefficients for LVEF between PET programs and MRI were r = 0.86 for QGS (p<0.001) and r = 0.82 for QPET (p<0.001). **Conclusion:** Both programs correlated well with MRI, although LVV calculation showed some differences.

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Comparison of Cedars QGS and Michigan University Corridor4DM for determination PFR, TPFR and MFR3 from 16 frame Gated Myocardial Perfusion SPECT

M. Ayub¹, M. Iqbal¹, M. B. Imran², M. Azhar¹; ¹Punjab Institute of Cardiology, Lahore, PAKISTAN, ²King Khalid University Hospital, Riyadh, SAUDI ARABIA.

OBJECTIVES: To compare Cedars-Sinai QGS and Michigan University Corridor4DM algorithms for determination PFR, TPFR and MFR3 using 16 frames gated myocardial perfusion SPECT. To determine reproducibility of Cedars QGS and Michigan University Corridor 4DM for determination PFR, TPFR and MFR3 using 16 frames gated myocardial perfusion SPECT **METHODS:** Forty patients (28 males and 12 females) with age range 35-70 years (mean 58.85±8.82) referred for assessment of left ventricular perfusion and function were included in the study. All patients were injected 1100 MBq of freshly prepared ^{99m}Tc Sestamibi. One hour later, patients underwent gated myocardial perfusion SPECT on Siemens ecam* dual head

variable angle gamma camera using 16 frames per cardiac cycle. Data were reconstructed using filterback projection and re-orientated to generate short axis slices. Short axis slices were processed with QGS and Corridor 4DM for assessment of PFR, TPFR and MFR3 by two observers. Data from both observers were compared to determine inter-observer reproducibility of both methods. Observer1 PFR, TPFR and MFR3 values derived from QGS and Corridor4DM were compared and correlated. **RESULTS:** Peak filling rate determined with Cedars QGS program was not significantly different from that determined with Corridor 4DM (p= 0.564). Good correlation was found between QGS and 4DM measured PFR values (R²=0.6698). TPFR values determined with QGS program were not significantly different from those determined with Corridor 4DM program (p= 0.615). However, there was poor correlation between these two methods with R² value =0.0382. MFR/3 values determined with QGS were not statistically different from those derived from 4DM (p=0.587). However, there was poor correlation between these values R²= 0.0174. Cedars QGS algorithm was highly reproducible for determination of PFR, TPFR and MFR/3 with R² values of 0.9922, 0.9874 and 0.9932 respectively. PFR, TPFR and MFR/3 derived from Corridor 4DM were also highly reproducible with R² values of 0.7775, 0.8381 and 0.456 respectively. **CONCLUSIONS:** Both Cedars QGS and Michigan University Corridor 4DM programs are robust for determination of PFR, TPFR and MFR/3 diastolic function parameters. There is good correlation between QGS and 4DM derived PFR measurements. However, there is poor correlation between QGS and 4DM derived TPFR and MFR/3 values. **Key words:** PFR, TPFR, MFR3 Gated SPECT

P24 — Monday, October 11, 2010, 16:00 — 16:30, Hall Z

Neurosciences: Basic science & miscellaneous

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Validation of [¹¹C]-5-HTP for Measurement of Serotonin Synthesis in the Rat Brain, Using MicroPET

A. K. D. Visser, A. Van Waarde, N. Kuzhuppilly Ramakrishnan, A. A. Rybczynska, A. T. M. Willemsen, I. P. Kema, R. A. J. O. Dierckx; University Medical Center Groningen, Groningen, NETHERLANDS.

Aim The neurotransmitter serotonin (5-HT) is synthesized in serotonergic neurons. Serotonin synthesis occurs in two enzymatic steps: 1) metabolism of the amino acid tryptophan to 5-HTP by tryptophan hydroxylase (TPH) and 2) conversion of 5-HTP to 5-HT by aromatic amino acid decarboxylase (AADC). So far, no well-established tracer for measuring serotonin synthesis exists. We have examined if changes in serotonin synthesis in the rat brain can be measured by the tracer [¹¹C]-5-HTP and microPET. [¹¹C]-5-HTP is chemically identical to endogenous 5-HTP and thus a substrate for AADC. **Materials and methods** Radioactive metabolites in rodent plasma were measured and biodistribution studies were performed to assess uptake of the tracer in different organs. Since serotonin is formed in peripheral organs, peripheral AADC activity was inhibited with carbidopa to increase tracer delivery to the brain, and the dose-dependency of the carbidopa effect was examined. Both enzymes involved in 5-HT synthesis were inhibited (TPH with p-chlorophenylalanine [PCPA] and AADC with NSD 1015). Rats were depleted of the precursor tryptophan by providing them with a synthetic diet with low tryptophan content. The microPET data was analyzed with a two-tissue compartment model with irreversible tracer trapping or with graphical analysis (Patlak plot). **Results** Carbidopa increased the brain uptake of [¹¹C]-5-HTP most efficiently at a dose of 10 mg/kg. Therefore, all groups were treated with 10 mg/kg carbidopa. After 60 min there was still 70-80 % of parent tracer present in plasma of control and tryptophan depleted animals, indicating no need for metabolite correction. High uptake of the tracer in kidney and urine indicated renal clearing. There was a remarkably high uptake in the pancreas. Surprisingly, neither treatment with NSD 1015 nor dietary tryptophan depletion affected [¹¹C]-5-HTP trapping in rat brain. However, inhibition of TPH resulted in a decrease. **Conclusion** A possible explanation of our data is that after AADC inhibition, [¹¹C]-5-HTP rather than [¹¹C]-5-HT accumulated in brain and contributed to the radioactive signal. Tryptophan depletion may not have had any effect because of the minor decrease (~ 30%) in plasma levels of unbound tryptophan. Since [¹¹C]-5-HTP could detect changes in the activity of the rate-limiting enzyme TPH, HTP-microPET may provide an indication of serotonin synthesis rates. However, the effect of PCPA on [¹¹C]-5-HTP trapping is small whereas PCPA should have major effects on serotonin synthesis. This raises the question if [¹¹C]-5-HTP is sensitive enough to measure serotonin synthesis in the rat brain.

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In vivo evaluation of [¹⁸F]-FEAnGA for β-Glucuronidase activity in neuroinflammation

I. Farinha Antunes¹, J. Doorduyn¹, H. J. Haisma², P. H. Elsinga¹, R. A. J. O. Dierckx¹, E. F. J. De Vries¹; ¹University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS, ²University Center for Pharmacy, University of Groningen, Groningen, NETHERLANDS.

Aim: Activation of microglia cells is a hallmark of inflammatory, infectious and degenerative diseases of the CNS. Activated microglia cells can exert either neurotoxic or neurotrophic effects. However, which factors determine whether the response induced by activated microglia cells is detrimental or beneficial remains unclear. Several studies indicated that at the sites of neuroinflammation, there is an increase in release of β-glucuronidase by activated microglia cells into the extracellular space. β-glucuronidase is involved in the hydrolysis of glycosaminoglycans on the cell surface and the degradation of the extracellular matrix. Therefore, β-glucuronidase might be a biomarker for microglia cell induced neurodegeneration. In this study, we investigated whether the recently developed PET tracer [¹⁸F]-FEAnGA was able to detect β-glucuronidase release during neuroinflammation, in a rat model of herpes encephalitis. **Materials and methods:** Male Wistar rats were intranasally inoculated with HSV-1 (HSE) or PBS (control). At day 6 or 7 after inoculation, [¹⁸F]-FEAnGA micro-PET scans were acquired. Arterial blood sampling was performed to determine the input function for quantification by pharmacokinetic modeling. Logan graphical analysis of the plasma and tissue time-activity curves were used to calculate the [¹⁸F]-FEAnGA distribution volumes. Metabolite analysis was conducted in the arterial blood samples. **Results:** After administration of [¹⁸F]-FEAnGA, the whole brain area under the concentration versus time curve (AUC) was 2 times higher in HSV-1 infected rats than in control

rats. In addition, the data could be fitted well by Logan graphical analysis, but not by Patlak analysis, indicating that tracer uptake was reversible. The distribution volume (DV) of [18 F]-FEAnGA in the cerebral cortex, cerebellum and thalamus of HSV-infected rats was 2 times higher ($p < 0.05$) as compared to control rats. Metabolite analysis did not show any metabolites of [18 F]-FEAnGA in plasma throughout the 60 minutes scan period, indicating that [18 F]-FEAnGA is stable in blood in vivo. **Conclusion:** [18 F]-FEAnGA seems to be a suitable PET tracer for evaluation of β -glucuronidase activity in neuroinflammation. Whether [18 F]-FEAnGA PET is a suitable tool to discriminate the neurotropic from the neurotoxic response of activated microglia cells remains to be investigated.

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Hyposexual Desire Disorder (HSDD) women have less brain activation and de-activation than healthy women in response to visual sexual stimuli

H. K. Huynh¹, A. T. M. Willemsen¹, C. M. Beers¹, R. J. Lont¹, E. Laan², M. Jansen³, M. Sand⁴, R. A. J. O. Dierckx¹, W. C. M. Weijmar-Schultz¹, G. Holstege¹; ¹University Medical Center Groningen, Groningen, NETHERLANDS, ²Academic Medical Center Amsterdam, Amsterdam, NETHERLANDS, ³Boehringer Ingelheim bv, Alkmaar, NETHERLANDS, ⁴Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, UNITED STATES.

Background: Hyposexual Desire Disorder (HSDD) is a common complaint of 15-20% of all premenopausal women. HSDD is characterized by a lack of, or even complete absence of sexual fantasies and desire for sexual activities. HSDD produces significant distress for the women suffering from it, which is the reason that they often see their physician for a solution. Studies on brain activation and de-activation during sexual activities or watching erotic movies are scarce, especially in women. A recent study has shown that some differences may exist between the patterns of brain activation in healthy women and women suffering from HSDD while watching erotic movies. It brings up the question whether these differences in brain activity in HSDD patients compared to healthy volunteers cause the problem. **Aim:** To assess whether premenopausal women with and without HSDD differ in their patterns of brain activation and/or deactivation in response to visual sexual stimuli. **Materials & methods:** The brain (de-) activation of 12 premenopausal women with primary generalized, acquired HSDD and 12 premenopausal healthy volunteers (NHSD) were scanned using Positron Emission Tomography (PET) across three kinds of video stimuli: neutral, low sexual, and high sexual stimuli. The study included assessment of subjective sexual arousal. The PET data were analyzed using SPM in a factorial design, using a significance level of $p < 0.05$ (corrected for multiple comparisons). **Results:** The "sexual interest and desire inventory", the "female sexual distress scale", the "Beck depression inventory" and their subjective experience in watching the sexual stimuli demonstrated clear differences between HSDD and NHSD subjects. Moreover, the PET-results revealed great differences on the right and left side of the brain between HSDD and NHSD volunteers. On the right side NHSD subjects showed a stronger activation in the parietal and frontal cortex than HSDD volunteers comparing erotic with neutral movies. On the left side the NHSD subjects showed a strong deactivation in a large area, comprising the insula and the adjoining posterior temporal parietal and frontal lobes. HSDD volunteers did not show this de-activation, indicating that they remained at the same level of alertness as during watching neutral movies. **Conclusion:** The differences between HSDD and NHSD volunteers according to the various inventories and scales were confirmed by the PET-scan findings, which suggest that during visual sexual stimuli HSDD women, in contrast to NHSD women, remain at a relatively high level of alertness.

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First In-Human Data of Fluorine-18 Labelled Fluoromethyl-McN5652 for In-Vivo imaging of Brain Serotonin Transporters (SERT) with PET

S. Hesse¹, P. Brust², P. Mäding², J. Zessin², G. Becker¹, M. Patt¹, A. Seese¹, D. Sorger¹, B. Habermann¹, P. Meyer¹, J. Luthardt¹, A. Bresch¹, J. Steinbach¹, O. Sabri¹; ¹University of Leipzig, Department of Nuclear Medicine, Leipzig, GERMANY, ²Forschungszentrum Dresden-Rossendorf, Institute of Radiopharmacy, Dresden und Leipzig, GERMANY.

Aim: DASB is currently the most frequently applied highly selective radiotracer for visualisation and quantification of central SERT. Its use, however, is hampered by the short half-life of carbon-11, the moderate cortical test retest reliability, and the lack for quantifying endogenous serotonin. The aim of our study was to first apply in human the new highly SERT-selective fluorine-18 labelled fluoromethyl analogue of (+)-McN5652 ([18 F]FMe-McN). **Methods:** The synthesis of [18 F]FMe-McN was performed according to Zessin et al. with some modifications. Briefly, the demethylated (+)-McN5652 was reacted with bromo-[18 F]fluoromethane to yield [18 F]FMe-McN, which was purified by reversed-phase HPLC. For in vivo human studies, five healthy volunteers (2 female, age 39±10 years) underwent dynamic PET over 120 minutes after intravenous injection of a 90 s bolus of 298±57 MBq [18 F]FMe-McN and a static acquisition over 30 minutes 3 h p.i. PET data were coregistered with individual MRI data set using PMOD and VOI analysis was performed. Target-to-background-ratios (TB-R, cerebellum as background structure) were compared with those of a reference data set assessed by [11 C]DASB-PET in 21 healthy subjects (11 female, 38±8 years). **Results:** TB-R ([18 F]FMe-McN) displays no hemispheric differences. The values are for the frontal cortex (FC) 1.02±0.04 (right-hand side) and 1.01±0.03 (left), for the head of caudate region (caud) 1.46±0.16 (right) and 1.50±0.15 (left) and for the raphe region 2.04±0.11. Corresponding TB-R ([11 C]DASB) are 1.10±0.07 (FC right, ANOVA $p < 0.05$), 1.08±0.78 (FC left, 0.06), 2.14±0.21 (caud right, 0.02), 2.06±0.19 (caud left, 0.04) and 2.23±0.39 (raphe, 0.04). Visually, image quality of [11 C]DASB-PET is superior to [18 F]FMe-McN. **Conclusion:** Cerebral radiotracer uptake fits well with the known SERT distribution also in humans. Hence, [18 F]FMe-McN might be suitable for in vivo quantification of SERT. Despite a tendency to lower TB-R compared to [11 C]DASB, the lower standard deviation of [18 F]FMe-McN TB-R can be advantageous with regard to test-retest estimations in larger study cohorts. Also, labelling with fluorine-18 allows (1) later data acquisition times, which is useful for the investigation of the tracer kinetics in brain tissue (modelling), and (2) a widespread application within a satellite concept e.g. in multicenter trials. **References:** Zessin J, Eskola O, Brust P et al. Nucl Med Biol 2001; 28: 857-863.

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Development and evaluation of a digital atlas for PET neuroimaging in domestic cat (Felis catus).

S. Lancelot¹, N. Costes², L. Lemoine¹, L. Zimmer³; ¹Neuropharmacology Unit, CNRS/University of Lyon, Lyon, FRANCE, ²CERMEP - Imagerie du vivant, PET department, Lyon, Lyon, FRANCE, ³Neuropharmacology Unit, CNRS/University of Lyon, CERMEP - Imagerie du vivant, PET department, Lyon, FRANCE.

Aim: The purpose of this work is to create a digital atlas of the cat brain and an anatomical template for spatial normalization, anatomical identification, quantification and modelling of PET images. Cats are used to characterize the brain uptake of tracers in development in CERMEP (5-HT1A, 5-HT6, 5-HT7 agonists among others) and already validated tracers used in preclinical PET pharmacological research. However, there is no digital atlas or normalization template of the cat brain available and described in the scientific literature. The data processing of functional PET images requires a precise and reproducible delineation of cortical and sub-cortical structures, as well as non-emitting structures (white matter, ventricles, bone and tissues). This delineation is necessary for regional kinetics extraction, spill over and partial volume correction and spatial normalization of cat brain for parametric image analysis. **Material and methods:** The digital atlas has been created from a high-resolution (0.6 mm cubic) 3D T1 MRI of cat. On this anatomical image, a precise manual delineation of cortical and sub-cortical structures, white matter, ventricles, bone and scalp was conducted with reference to published cat brain atlas. This labelled MRI is our digital atlas. The same MRI was then used as the target for an automatic iterative procedure of template creation: each animal MRI (N = 6) was subjected to automatic brain extraction, co-registered to the target with rigid-body transformations and resampled. Co-registered MRIs were averaged. The average brain was then co-registered to the original brain target to compensate for misalignment bias. The resulting image constituted the first template, and was used as the target for the next iteration. Iterations continued until each parameter of the co-registration of the *i*th template to the original target was below 0.3 mm and 1 arc degree. The final template was tested for accuracy, robustness and reproducibility as follows: accuracy was assessed by visually inspecting the normalized brain on the template, with positioning inspection of the brain structures of the atlas projected on individual MRI with the reverse normalization transform. Robustness was tested by normalizing a new set of MRIs coming from others individuals to the template. **Conclusion:** This atlas will improve the methodology for image processing of an animal in terms of normalization, automated regional values extraction and modelling of functional PET acquisitions.

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Study on the biodistribution and imaging of 131 I-SAP in a mice model of AA-amyloidosis

R. Wang, H. Wei, C. Zhang, J. Zhang, P. Yan, L. Kang, M. Liu, F. Guo; Department of Nuclear Medicine, Peking University First Hospital, Beijing, CHINA.

[Abstract] **Objective** Serum amyloid P component (SAP) is a normal plasma protein and a universal non-fibrillar constituent of amyloid deposits. Radiolabelled serum amyloid P component scintigraphy is a non-invasive and quantitative method for imaging amyloid deposits in vivo, which produces diagnostic images in most patients with systemic amyloidosis, and can be used repeatedly to monitor the course of the disease. The purpose of this paper was to validate 131 I-SAP as a novel tracer in mice bearing amyloidosis and to evaluate its potential diagnostic value. **Method** Standard sample SAP was radiolabeled with 131 I by iodogen method. The labeling efficiency and radiochemical purity of 131 I-SAP were calculated, and its stability were determined. Amyloidotic KM mice model was produced by daily subcutaneous injection of 0.5ml 10% casein for 21 days. The control group was injected with Normal Saline. Both groups were injected with 200 μ l 131 I-SAP (7.4MBq) via tail vein and subjected to radiographic imaging at 1h, 3h, 6h, 24h, 48h, 72h respectively. 50 amyloidotic KM mice were divided into 5 groups and dissected at 1h, 3h, 6h, 24h, 48h respectively after intravenous injected with 131 I-SAP. The tissues of interest (the heart, lung, liver, spleen, renal, stomach, intestine, bladder, bone, muscle, vascular, brain and blood) were weighed, and their radioactivity was measured using a γ well counter. Radioactivity results were recorded as percentage injected activity per gram (%ID/g). **Results** The labeling efficiencies of 131 I-SAP reached 60% ~ 70%, and the radiochemical purity was above 90% even after 48 hours. There were marked radioactivity uptakes in the specific regions of liver, spleen and kidneys after 24h in the test group while there were mild uptakes in the control group. The results of biodistribution were consistent with the imagings. **Conclusion** 131 I-SAP is easy to be radiolabeled and stable in vivo and in vitro. It may be a novel tracer in the diagnosis of amyloidosis. **[Key words]** Amyloidosis; Serum amyloidosis P-component (SAP); Biodistribution; SPECT scintigraphy

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HSV-1 induced behavioural changes and microglia cell activation are inhibited by antipsychotics

J. Doorduyn, H. C. Klein, R. A. J. O. Dierckx, E. F. J. de Vries; University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS.

Aim: Schizophrenia is a chronic, severe and disabling brain disease, that is characterized by abnormal mental function and disturbed behaviour. Although the aetiology of schizophrenia is not exactly known, it is hypothesized that herpes viruses play a role in the aetiology. In line with this hypothesis, we investigated if the herpes simplex virus type-1 (HSV-1) could induce behavioural changes in rats and if these changes could be reduced by treatment with antipsychotics. In addition, it was investigated if HSV-1 induced neuroinflammation could be reduced by antipsychotic treatment. **Material and methods:** Rats were intranasally inoculated with 1×10^7 PFU of HSV-1 (HSE) or with PBS (CNTRL). Disease symptoms, which were ascribed to a disease score, were monitored daily. Open field behaviour was assessed on day -1 pre-inoculation, and on day 2 and 4 post-inoculation. The antipsychotics, clozapine (CLOZ) or risperidone (RISP) (or saline (SAL) as a control), were administered intraperitoneally once daily from day 0 to day 4 post-inoculation. [11 C]-(*R*)-PK11195 PET was used to study

neuroinflammation at day 5 post-inoculation. **Results:** In HSE-SAL rats, the first disease symptoms were seen on day 1 post-inoculation. CLOZ and RISP delayed the onset of disease symptoms. On day 4 post-inoculation, the disease score was lower in HSE-CLOZ rats (100%, $p=0.03$) and HSE-RISP rats (73%, $p<0.05$) than in HSE-SAL rats. Exploratory behaviour (time spent on exploration and rearing) was significantly increased in HSE-SAL rats ($p<0.05$), when compared to CNTRL-SAL. CLOZ and RISP decreased the time spent on rearing in HSE rats on day 4 post-inoculation (83%, $p=0.008$ and 45%, $p>0.05$, resp.), when compared to SAL. CLOZ and RISP did not affect behaviour of CNTRL rats. The uptake of [^{11}C]-(*R*)-PK11195 in HSE-SAL rats was 20–30% higher ($p<0.05$) in the bulbous olfactorius, frontal cortex, striatum, thalamus and brainstem, when compared to CNTRL-SAL rats. In HSE-CLOZ and HSE-RISP rats a lower uptake of [^{11}C]-(*R*)-PK11195 uptake was found in the bulbous olfactorius (23%, $p=0.012$ and 13%, $p>0.05$, resp.) and frontal cortex (21%, $p>0.05$ and 12%, $p>0.05$, resp.), in comparison with HSE-SAL rats. CLOZ and RISP did not affect [^{11}C]-(*R*)-PK11195 uptake in CNTRL rats. **Conclusion:** Disease symptoms, behavioural changes and neuroinflammation in response to HSV-1 infection were reduced by antipsychotic treatment. This suggests that the antipsychotic action in schizophrenia patients may in part be explained by reduction in viral infection and/or the presence of neuroinflammation, and warrants additional research.

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Study of Mechanisms for Acetyl-L-Carnitine Neuroprotective Action

L. Cunha¹, D. Damiani², C. Alves³, L. F. Metello¹, T. Summavielle⁴; ¹Nuclear Medicine Department of the High Institute for Allied Health Technologies of Porto, Polytechnic Institute of Porto (ESTSP.IPP), Vila Nova Gaia, PORTUGAL, ²Molecular Neurobiology, Neuroprotection Laboratory, Institute for Molecular and Cell Biology (IBMC), Porto, PORTUGAL, ³Nuclear Medicine Department of the High Institute for Allied Health Technologies of Porto, Polytechnic Institute of Porto (ESTSP.IPP) and Molecular Neurobiology, Neuroprotection Laboratory, Institute for Molecular and Cell Biology (IBMC), Porto, PORTUGAL, ⁴Molecular Neurobiology, Neuroprotection Laboratory, Institute for Molecular and Cell Biology (IBMC) and Functional Sciences Department, High Inst. for Allied Health Technologies of Porto, Polytechnic Inst. of Porto (ESTSP.IPP), Porto, Portugal.

Introduction: Acetyl-L-Carnitine (ALC) has been proposed to have beneficial effects in chronic neurodegenerative disorders caused by production of abnormal proteins, mitochondrial dysfunction and oxidative stress. Recently, our group demonstrated that pre-treatment with ALC confers effective neuroprotection against 3,4-methylenedioxymethamphetamine (MDMA)-induced neurotoxicity. These pre-clinical studies reinforce the beneficial potential of ALC as a neuroprotectant in neurodegenerative disorders. However, little is known about the molecular mechanisms underlying ALC action. **Material and Methods:** To study the molecular mechanisms involved in the neuroprotective features of ALC, we exposed PC12 cells, a cell line derived from rat adrenal pheochromocytoma, to methamphetamine (METH). The protective effect of ALC was assessed by treating cells with three concentrations of ALC (1.0; 0.1; and 0.01 mM), 30 min prior to the addition of METH (1 and 100 μM). 24h and 72h after METH treatment cell viability (MTT assay) and Dopamine (DA) and Epinephrine release (HPLC). Since some authors suggested that ALC contribute to enhanced efficiency of glucose utilization, 18F-FDG uptake assay will allow to verify this issue, as well as to validate the results from MTT assay and HPLC. Medium was replaced by serum-free medium 2h before 18F-FDG addition and incubated for 20 min with fresh medium, containing 37 kBq of 18F-FDG/mL. Cells were washed, trypsinized and centrifuged. The pellet was lysed by adding NaOH 10mmol/L. Aliquots from cell lysates as well as supernatant were assayed for radioactivity by gamma-counting. Phase-contrast microscopic analysis was also used. **Discussion:** Comparing to control, we observed a decrease in cell viability of 20% and 40%, 24h after the addition of 1 and 100 μM of METH, respectively. At 72h these figures were more pronounced (20% and 90%). Treating the cells with ALC before METH did not result in a protective effect at 24h, but at 72h cell viability was increased for intermediary concentrations of ALC when using 1 μM of METH. DA production was not significantly affected at 24h. Inversely, at 72h there was an increase in DA production. However, we observed a reduction in DA concentration when the higher concentrations of METH and ALC were used concomitantly. Similar results were obtained for Epinephrine. Microscopic analysis revealed that ALC may also reduce the METH-induced altered morphology of PC12 cells. **Conclusion:** As a whole, these preliminary results indicate that ALC might have a protective role that is dose and time-dependent.

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Semi-quantitative Method for Estimation of Rat CMRglucose Using F-18-FDG and Small Animal in vivo Imaging System

Y. Magata, M. Ogawa, H. Yamaguchi, Y. Ouchi; Hamamatsu University School of Medicine, Hamamatsu, JAPAN.

Introduction One of the merits of small animal in vivo imaging researches is non- or less-invasive and sequential data acquisition with a same individual. Such animal experiments are expected for pharmacological studies or pre-clinical studies for a new drug discovery. Not only an image but also quantitative estimation of imaging probe kinetics is necessary for evaluation of pharmacological effect of compounds. Quantitative estimation generally requires arterial blood sampling to draw a time-activity curve. This procedure induces invasive lesion and is not repeatable for small animals. In order to solve this conflict, semi-quantitative method is required. In this paper, we explored semi-quantitative method for CMRglucose and validated it. **Materials and Methods** 25 Male SD rats (250g) were used in this study. The rat was fasted for 12 hours before the PET scan. After anesthesia with several anesthetic agents, cannula was inserted into a femoral artery. The rat was placed in the prone position on the bed of small animal PET system (FLEX, Gamma Medica Idea, USA). Dynamic PET scan was performed after a bolus intravenous injection of 7.4 MBq [^{18}F]FDG for 45 min. Arterial blood sampling was carried out throughout the scanning period, and plasma was separated by centrifugation and counted by a γ -counter. Blood glucose concentration (BS) was measured at [^{18}F]FDG injection. The rats were sacrificed after PET scan and the brain was removed, weighed and counted by a γ -counter to calculate %dose/g. The regions of interest (ROIs) were placed on the coronal sections of serial PET images generated every 1 min. The rate constants (k₁, k₂, k₃, k₄) were estimated to calculate CMRglucose. We used

0.625 for LC. **Results and Discussion** SUV was calculated using the PET data obtained from 35–45 min post-injection of [^{18}F]FDG. Correlation between the SUV and CMRglucose was not shown. However, a good correlation was indicated with correction of the SUV by multiplication of individual BS value. It was indicated that this semi-quantitative parameter, SUVxBS, is available as an index of CMRglucose. This method is useful for estimation of sequential alteration of brain glucose metabolism in the same individual.

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Functional imaging of newly identified antibody induced encephalitis - early detection of rho-GTPase-activating protein 26 induced neuronal decay using 18F-FDG PET/CT.

C. C. A. v. Gall¹, J. Regula², J. Ludwig³, F. L. Giesel¹, C. Zechmann¹, A. Afshar-Oromieh¹, H. Meinck², U. Haberkorn¹; ¹Dept. of Nuclear Medicine, University of Heidelberg, Heidelberg, GERMANY, ²Dept. of Neurology, University of Heidelberg, Heidelberg, GERMANY, ³Dept. of Laboratory Medicine, University of Heidelberg, Heidelberg, GERMANY.

Abstract: Objectives: paraneoplastic encephalitis is often linked to antibody induced neuronal decay. We describe an early detection of cerebellar affection using 18F-FDG PET/CT while MRI and CT did not show significant changes at first. After time, specific cerebellar antibodies against rho-GTPase-activating protein 26 were identified and are suspected to be responsible for the symptoms. **Methodology:** sequential 18F-FDG (N=6) every 6 months were done for whole body staging presuming paraneoplastic cause. In addition, five brain scans were done separately according to our paraneoplastic standard protocol. PET scans were analyzed using ROI comparison. Clinical progress was monitored using Klockgether Ataxy score and neurological examination, chemistry and sophisticated analytics of potential antibody targets were performed. In addition, MRI and CT brain were performed. **Results:** Decrease of cerebellar metabolism correlated with progression of clinical symptoms while neither MRI nor CT were able to show intraaxial pathologies at first. Meanwhile, MRI demonstrates a corresponding cerebellar atrophy. Statistical analysis regarding SUV changes in the cerebellum, antibody titer and Klockgether ataxia score are ongoing. Initial results demonstrate a close relation with progress of cerebellar hypometabolism. Up to date, no cause of a potential paraneoplastic origin was found. **Conclusions:** First results give evidence of an association of early changes in 18F-FDG brain scan with newly identified antibody induced structural decay of the brain. In addition, 18F-FDG PET/CT was able to show early changes in cerebellar metabolism compared to morphological imaging modalities.

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Small animal PET imaging: Is strict standardization the key to more robust data?

M. I. Kehl, M. Honer, P. A. Schubiger, S. M. Ametamey; ETH Zürich, Zürich, SWITZERLAND.

Small animal PET imaging is a frequently used methodology to investigate the rodent brain in healthy and disease states. Non-invasive imaging methods like PET allow longitudinal follow-up studies, where animals can be used as their own controls. Such set-ups are considered to give more reliable results than the traditional control group approach. In this study, the inherent variability of FDG and fallypride brain uptake within and between individual animals was assessed using a fixed protocol. Moreover, experimental factors were elicited, which might essentially impact the outcome of rodent PET studies and therefore require strict standardization. Finally, the potential benefit of standardization over heterogenization was evaluated for an experimental setting with varying parameters regarding age, gender and cage occupancy. **Methods:** Animals underwent fixed protocols of repeated FDG or fallypride scans using the dedicated small-animal PET/CT scanner eXplore Vista. Each animal was measured three times with one week recovery phase between scans. SUVs determined by ROI analysis were compared between scans of the same animal (intra-subject variability) and scans of different individuals (inter-subject variability). Furthermore, several FDG scans were performed under variation of various experimental parameters, e.g. gender, age, cage occupancy, anaesthetic protocol, environmental temperature during uptake phase and 10% ethanol in tracer solution. Animals were sacrificed subsequent to the PET scan; organs were collected and measured by classical gamma counting. **Results:** No significant difference between inter- and intra-animal FDG/fallypride uptake variability was identified (COV=14±7% vs. 21±10% for FDG). Significant differences in fallypride and FDG brain uptake were found between scans of different test days, suggesting false positive effects. Biodistribution was robust in terms of experimental parameters; only anaesthetic protocols proved to significantly impact brain uptake (27% less uptake for animals anaesthetized over 60min vs. 40min). In contrast to heterogenization, standardization of groups produced substantially more false positive effects in FDG organ distribution (false positive rate: 9% vs. 6%). **Conclusion:** Repeated measurements on the same animal did not reduce data variability of FDG/fallypride brain uptake compared to measurements on different animals. Strict standardization of experimental parameters is not advisable, as it produces high numbers of idiosyncratic results with no external validity. Except for anaesthetic protocols, all investigated parameters did not impact brain uptake significantly. Controlled heterogenization of test groups with regard to gender, age, cage occupancy and laboratory climate is therefore recommended, as it decreases the generation of false positive results and thus increases external validity of study outcome.

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Voxel-Based Control Data Base for Statistical Brain SPECT Analysis using Generalized Extreme Studentized Deviate Many-Outlier Procedure

N. Shuke¹, A. Ando¹, T. Onishi¹, K. Yamamoto¹, T. Inagaki¹, S. Irie¹, K. Saito¹, K. Nishikawa², M. Kato-Azuma²; ¹Kushiro Kojinkai Memorial Hospital, Kushiro, Japan, ²Imaging Information Technology Center, Nihon Medi-Physics Co., Ltd., Tokyo, JAPAN.

Objective: Control data base is necessary to evaluate patients' SPECT data in statistical brain SPECT analysis. However, it would be difficult to obtain normal data base from substantial

number of normal volunteers. We have tried to generate voxel-based control data base from grossly normal patients' SPECT data using generalized extreme studentized deviate many-outlier (ESD) procedure (Rosner B, Technometrics 25, 165, 1983), which is a noble method to detect potential outliers. The objective of this study was to investigate the effect of ESD by applying it to clinical Tc-99m HMPAO SPECT data. Methods: Tc-99m HMPAO SPECT data from consecutive 522 patients with acute stroke (71±11 y old, M/F=293/229) were studied. By visual inspection, all SPECT data were classified into 4 groups by extent of CBF reduction on SPECT images: no reduction (G0, n=309), reduction in branches' territory (G1, n=120), one vascular territory (G2, n=81), and more than one vascular territory of main cerebral arteries (G3, n=12). From these data, standardized brain surface images normalized by global mean voxel count were generated using 3D-SSP. Voxel means and SDs of brain surface images were calculated with and without ESD procedure from G0 and expanded data sets of G0-1 (G0 and G1), G0-2 (G0-1 and G2), and G0-3 (G0-2 and G3). Voxel-based data base generated from G0 with ESD was assumed to be a control database, and was compared with those obtained from combined data sets, which was considered to include obvious outliers, to test whether outliers could be effectively excluded by ESD. Between G0 and combined data sets, number of voxels that had statistically different ($P < 0.05$) voxel mean or SD was counted and expressed as fraction (%) of the total voxel numbers (n=15964) in the brain surface image. Results: Without ESD, mean voxel SDs of G0, G0-1, G0-2, and G0-3 were 0.153, 0.161, 0.176, and 0.179. With ESD, corresponding mean voxel SDs were reduced to 0.146, 0.152, 0.160, and 0.161. Between G0 and combined data sets (G0-1, G0-2, G0-3), the fractions of the voxels that had statistically different ($P < 0.05$) voxel means and SDs were 0.4 - 12.1% and 38.5 - 81.6% without ESD. With ESD, corresponding fractions were reduced to 0.06 - 6.2% and 4.4 - 44.1%, indicating that ESD procedure could effectively exclude outliers on a voxel-by-voxel basis. Conclusion: ESD procedure could be useful to generate voxel-based control data base from clinically available grossly normal SPECT data sets.

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Methylphenidate and binding of iodine-123-IBZM to the rat D2 receptor - Assessment of the dose-response-relationship

S. Nikolaus¹, M. Beu¹, C. Antke¹, K. Kley², A. Wirrwar¹, H. W. Müller¹,
¹Nuklearmedizinische Klinik, Düsseldorf, GERMANY, ²Röntgeninstitut, Mönchengladbach, GERMANY.

Aim: Application of dopamine (DA) transporter ligands such as methylphenidate (MP) leads to an inhibition of DA-reuptake, and thus to an increase of DA-concentrations in the synaptic cleft. This leads to a reduction of exogenous radioligand binding to the postsynaptic D2-receptor (D2R). In this study, the effect of various doses of MP on the binding of iodine-123-IBZM (IBZM) to the D2R in the rat striatum was assessed using small animal SPECT. **Materials & Methods:** D2R-binding was assessed in 53 rats in baseline (BAS, no treatment) and after pre-treatment with various doses of MP (gift of Medice Arzneimittel Pütter GmbH & Co.KG; 0.3mg/kg, n=14, 3mg/kg, n=11, 10mg/kg, n=11; 30mg/kg, n=11, 60mg/kg, n=6). IBZM (23 MBq) was injected into the tail vein 1h after pre-treatment with MP. Measurements were performed 45 min after radioligand administration with the TierSPECT. Striatal regions of interest (ROI) and cerebellar reference regions (REF) were defined with the MPI-Tool. For Baseline and MP-challenge, striatal equilibrium ratios ($V3''=V3''(ROI)/V3''(REF)-1$) were computed as estimation for the binding potential. Results: After MP, striatal $V3''$ was 1.61 ± 0.61 (MW±SD; 0.3mg/kg), 0.91 ± 0.44 (3mg/kg; mean±SD), 1.01 ± 0.44 (10mg/kg), 0.91 ± 0.34 (30mg/kg) and 1.02 ± 0.56 (60mg/kg). BAS values were 0.73 ± 0.48 , 1.32 ± 0.35 , 1.50 ± 0.27 , 1.82 ± 0.55 and 1.64 ± 0.44 , respectively. For the doses 3, 10, 30 and 60 mg/kg differences between BAS and MP were highly significant (paired t-test, two-tailed, $0.0001 < p < 0.005$). Comparison between BAS and 0.3mg/kg MP, however, yielded a p of 0.47. Thereby, in 6 of the 14 rats treated with 0.3 mg/kg MP $V3''$ was increased relative to BAS (MP: 2.08 ± 0.44 , BAS: 1.66 ± 0.21), whereas in 8 rats $V3''$ was decreased (MP: 1.25 ± 0.47 , BAS: 1.79 ± 0.62). Both differences were significant ($p=0.044$ $p=0.006$, respectively). Conclusion: Challenge with 3, 10, 30 and 60mg/kg MP reduced D2R-binding by 30, 33, 48 and 41%, respectively, whereas no significant reduction was evident after 0.3mg/kg. Interestingly, two subgroups could be distinguished, which displayed either a 26% increase or a 30% decrease of D2R-binding. The reduction of D2R-binding can be attributed to the increased availability of DA in the synaptic cleft induced by MP. The increase of D2R-binding, however, implies a different mechanism of action. Possibly, in a subgroup of animals the inhibition of the DA transporter and the increase of synaptic DA concentrations induce an enhanced activation of presynaptic D2-autoreceptors, which leads to a reduction of DA-release from synaptic terminals. Given the small numbers of rats in either subgroup, however, more investigations are needed to gain further insight into this matter.

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Morphine decreases 5-HT2A receptor binding measured with SPECT in the canine frontal cortex.

A. Adriaens¹, S. Vermeire¹, T. Waelbers¹, L. Duchateau¹, S. Sys¹, A. Dobbelaer¹, S. Van Dorpe¹, J. Eersels², B. De Spiegeleer³, K. Audenaert⁴, I. Polis¹, K. Peremans¹,
¹Faculty of Veterinary Medicine, UG, Merelbeke, BELGIUM, ²Nuclear Medicine and PET research, VU University Medical Centre, Amsterdam, NETHERLANDS, ³DruQuAR group, Faculty of Pharmaceutical Sciences, Ghent, BELGIUM, ⁴Faculty of Medicine, UG, Gent, BELGIUM.

The serotonergic and the opioid neurotransmitter systems play an important role in mood disorders and pain regulation. In this regard, interventions with both serotonergic as well as opioid agents have been suggested in depression and anxiety disorders. Electrophysiological and behavioral studies have previously demonstrated a physiological interaction between the serotonin-2A and μ -opioid receptors. Aim: to investigate the influence of a single injection of morphine on cerebral serotonin-2A receptor (5-HT2A) binding in dogs with ¹²³I-5I-R91150, a selective 5-HT2A receptor radioligand, and SPECT. Material and Methods: 5-HT2A binding was estimated with (M) and without (control) morphine pretreatment (0.5 mg kg⁻¹ intravenously (IV), 30 minutes prior radioligand injection) in eight 5-year-old female beagles. Scans were carried out with a triple head gamma camera (Triad, Trionix) 90 minutes after ¹²³I-5I-R91150 injection (15.07 ± 2.69 MBq kg⁻¹ IV). Dogs were premedicated with dexmedetomidine and anesthesia was induced with propofol and maintained with isoflurane in oxygen. Semiquantification, with the cerebellum (a region void of 5-HT2A receptors) as a reference region, was performed to calculate

the 5-HT2A receptor binding index (BI) in the frontal, parietal, temporal and occipital cortex and the subcortical region. Data were analyzed by mixed-model ANOVA. Significance was set at $p < 0.05$. Results: A significantly decreased 5-HT2A receptor BI was found after morphine administration in the right and left frontal cortices (resp. 1.41 ± 0.06 and 1.44 ± 0.08) compared to the blank scan (resp. 1.53 ± 0.10 and 1.55 ± 0.11) with $p = 0.012$ and 0.040 resp. No significant differences were noted for the other regions. Conclusion: morphine administration decreases frontocortical 5-HT2A receptor availability. This confirms an interaction between the serotonergic and the opioid neurotransmitter system. Whether the decreased radioligand binding is the consequence of decreased receptor density due to downregulation/internalization or the result of indirect actions, such as increased release of endogenous serotonin, remains to be elucidated. This study was supported by the Ghent University Special Research Fund (grant n°01J06109).

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Serotonin 2A receptor Imaging in Canine Behavioural Disorders: an Animal Model for Human Psychiatric Disorders

S. Vermeire¹, K. Audenaert², R. De Meester¹, E. Vandermeulen¹, T. Waelbers³, B. De Spiegeleer⁴, J. Eersels⁵, A. Dobbelaer¹, K. Peremans¹,
¹Dep. of Veterinary Medical Imaging and Small Animal Orthopaedics, Faculty of Veterinary Medicine, Ghent University, Merelbeke, BELGIUM, ²Dep. of Psychiatry and Medical Psychology, Faculty of Medical and Health Sciences, Ghent University, Ghent, BELGIUM, ³Dep. of Clinical Biology and Medicine of Small Animals, Faculty of Veterinary Medicine, Ghent University, Merelbeke, BELGIUM, ⁴Drug Quality and Registration group, Faculty of Pharmaceutical Sciences, Ghent University, Ghent, BELGIUM, ⁵Department of Nuclear Medicine & PET Research, VU University Medical Center, Amsterdam, NETHERLANDS.

Aim The serotonergic system is disturbed in different human behavioural and affective disorders, with especially the serotonin-2A (5-HT2A) receptor involved in impulsive aggressiveness and anxiety. The aim of the study was to evaluate the involvement of the brain 5-HT2A receptor in dogs with different behavioural disorders, as a model for human psychiatric diseases. **Materials & Methods** Three groups of drug naive dogs were studied: an impulsive aggressive group (n=22), an anxious group (n=22) and a reference group of normally behaving dogs (n=22). The 5-HT2A receptor was evaluated with Single Photon Emission Computed Tomography (SPECT) and the serotonin 2A receptor-selective radiopharmaceutical ¹²³I-R91150. Data were acquired with a triple head gamma camera (Triad, Trionix, USA) 90 minutes after ¹²³I-R91150 injection (8.26 ± 2.41 MBq kg⁻¹ IV) under general anaesthesia. A 5-HT2A receptor binding index (BI), proportional to the cortical receptor density, was calculated in 9 regions, with the cerebellum (a region void of 5-HT2A receptors) as a reference region. **Results** Significantly ($P < 0.0056$; Bonferroni corrected) different 5-HT2A receptor binding indices were found in the frontal, temporal and occipital cortical brain areas (bilateral) of the dogs behaving abnormally, with consistently increased BI in the impulsive aggressive group and decreased BI in the anxious group. **Conclusion** Our results provide evidence for a disturbed serotonergic balance in canine impulsive aggression and anxiety disorders, which is in line with the human psychiatric literature. Similar results between human and canine neuro-imaging in behavioural disorders strengthen the use of dogs as a model for human psychiatric diseases.

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Positron Emission Tomography Neuroimaging in Schizophrenia: Current and Future Avenues

N. S. Vyas, N. H. Patel, K. S. Nijran, B. K. Puri, A. Al-Nahhas; Imperial College Healthcare NHS Trust, London, UNITED KINGDOM.

Introduction: Positron emission tomography (PET) enables regional cerebral glucose metabolism and dopaminergic and serotonergic receptor function to be studied in schizophrenia. It has been used in drug development and in studying pharmacotherapeutic and repetitive transcranial magnetic stimulation treatments. PET offers a strategic imaging platform to provide a map of neural correlates associated with underlying cognitive deficits in schizophrenia. Individuals with schizophrenia show dopaminergic imbalances in the brain. PET offers a unique opportunity to study dopaminergic receptor functioning in relation to specific brain regions and their neurocognitive correlates in schizophrenia. **Method:** A synthetic approach was applied to conduct a literature review of the most recent PET studies investigating three dimensions: neurocognition, molecular genetics and imaging. **Results:** Evidence suggests significant differences in dopamine content in the prefrontal cortex, anterior cingulate gyrus and hippocampus between healthy controls and individuals with schizophrenia. Heightened density of D₂ receptors in the striatum and neural brain dysconnectivity are also observed. Cognitive impairments are a core feature of the disorder. Very few studies have investigated the relationship between D₁ dysfunction and working memory performance in medication-naïve patients with schizophrenia. Some studies report a decrease in prefrontal cortical D₁ receptor binding, while other studies show an increase in D₁ receptor binding. Some studies have also reported no differences between patients and healthy controls. A parsimonious explanation for these discrepancies may be the use of different PET radioligands, which show a differential response of dopamine depletion on internalisation and binding to the ligand. A paucity of PET studies have investigated the relationship between susceptibility genes (e.g. Catechol-O-methyltransferase, COMT; dopamine receptors 1-4, DRD) and cognitive functioning in schizophrenia. Some studies have used [¹¹C]NNC 112, showing heightened D₁R activation in the dorsolateral prefrontal cortex in schizophrenia and worse performance on working memory paradigms. Individuals with the at-risk variant (Val158 homozygosity) of the COMT Val¹⁵⁸Met polymorphism, showed greater cortisol [¹¹C] NNC 112 binding compared with other two genotypes (Met carriers). The [¹¹C] NNC 12 may be an important and reliable marker for low dopamine 'tone' as previously documented in schizophrenia. **Conclusions:** The use of PET neuroimaging in schizophrenia research, particularly in relation to neuropsychological changes, molecular genetic polymorphisms, and the development of novel pharmacotherapeutic agents, is likely to increase over the next five years. This will be aided by the continued development of new PET tracers. It is expected that this may help to identify genetic, biochemical, imaging and neurocognitive biomarkers for schizophrenia.

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The Development of [18F]-Flumazenil-PET for Localisation of the Epileptogenic Zone in Patients with Medically Refractory Focal Epilepsy

L. Vivash¹, M. Gregoire², S. Dedeurwaerdere¹, V. Boullieret¹, P. Roselt³, E. W. Lau³, R. E. Ware³, D. Binns³, A. Katsifis², R. J. Hicks³, D. E. Myers¹, T. J. O'Brien¹; ¹University of Melbourne, Melbourne, AUSTRALIA, ²ANSTO, Sydney, AUSTRALIA, ³Peter MacCallum Cancer Centre, Melbourne, AUSTRALIA.

Introduction: Studies of GABAA/central benzodiazepine receptor (GABAA/cBZR) distribution in the CNS using [11C]-flumazenil-PET (FMZ-PET) have enabled localisation of the epileptogenic zone (EZ) in patients with medically refractory epilepsy. [11C]-FMZ-PET images show a more restricted region of abnormality with increased sensitivity when compared with FDG-PET. However, use of [11C]-FMZ in routine clinical practice has been hindered by practical limitations of [11C]. The aim of the current study is to develop an [18F]-radiolabelled FMZ tracer with high specificity and improved imaging quality for EZ localisation in routine clinical practice. **Methods:** Preclinical studies: Presaturation, displacement and uptake PET scans were performed to define the kinetics of [18F]-FMZ binding in non-epileptic rats (n=8). Bmax (receptor density) and KD (binding affinity) were then quantified in the brains of epileptic (n=9; kainic acid-induced model of temporal lobe epilepsy) vs. non-epileptic control animals (n=10). Clinical study: 4 patient groups have been studied; healthy controls (n=20), patients with well-localised TLE from MRI scans (n=10), patients with lateralised TLE (n=7), and patients with other focal epilepsies (n=4). Each participant underwent a single 60 minute dynamic [18F]-FMZ-PET scan. Patients also underwent an FDG-PET scan. Blinded visual assessment of images to locate the EZ was performed. Parametric images of binding potential (BP) were generated. Data sets were processed using ROI analysis and SPM to assess differences in BP between patients and controls and localisation of the EZ in patients. **Results:** [18F]-FMZ was shown to be a suitable PET radiotracer for imaging GABAA/cBZR *in vivo*, with reversible and competitive binding and low non-specific binding. [18F]-FMZ-PET reliably detected decreased Bmax in the hippocampi of epileptic rats (left 16.3, right 15.9) compared with controls (left 20.9, right 19.8, p=0.022, p=0.049), with no change in KD (left 8.24 vs 8.46, p=0.82, right 7.43 vs 8.07 p=0.56). There were no changes in whole brain Bmax or KD. To date the visual assessment of the clinical data has shown [18F]-FMZ-PET to have high sensitivity (100%) and positive predictive value (100%) for the EZ in patients, with a more restricted localisation of the EZ compared to FDG-PET. Quantitative analysis is ongoing. **Conclusions:** The pre-clinical studies have demonstrated that [18F]-FMZ-PET is a reliable radiotracer for quantification of CNS GABAA/cBZR expression *in vivo*. Preliminary analysis in our current clinical study indicates that [18F]-FMZ-PET also has excellent imaging characteristics in humans, and shows promise as a new clinical tool for localising the EZ in TLE patients.

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A micro-PET study of effect of dextromethorphan against MDMA-induced serotonergic neurotoxicity in rat brain

K. Ma¹, W. Huang², M. Liao³, L. Shen³, C. Shiu²; ¹National Defense Medical Center, Taipei, TAIWAN, ²Tri-Service General Hospital, Taipei, TAIWAN, ³Institute of Nuclear Energy Research, Taoyuan, TAIWAN.

Aim: 3, 4-Methylenedioxymethamphetamine (MDMA) is an illicit drug that may induce neurotoxicity in brain serotonin system. The purpose of this study was to investigate the feasibility of N,N-dimethyl-2-(2-amino-4-[18F]-fluorophenylthio) benzylamine (4-[18F]-ADAM; a serotonin transporter imaging agent) in detecting the effect of dextromethorphan (DM) against MDMA-induced serotonergic degeneration in rat brain. **Methods:** Male Sprague-Dawley rats were co-treated DM (10 mg/kg, i.p.) with MDMA (5 mg/kg, s.c.) once a day for 6 successive days. Micropositron emission tomography (micro-PET) coupled with 4-[18F]-ADAM was performed on 6 and 30 days after the co-treatment. The specific uptake ratios (SURs) of 4-[18F]-ADAM were calculated by drawing the regions of interest (ROI) in various areas of rat brains in reference to the cerebellum (i.e., [ROI-cerebellum]/cerebellum). Immunohistochemistry was performed 7 days after the final micro-PET scan. **Results:** In MDMA-treated rats, the SURs of 4-[18F]-ADAM were obviously decreased in all brain regions. The SURs of 4-[18F]-ADAM in DM and MDMA co-treated rats was significantly higher than those of MDMA-treated rats in the midbrain (3.76±0.17 vs 2.51±0.40, p<0.01), thalamus (3.40±0.29 vs 2.02±0.31, p<0.01), hypothalamus (3.57±0.23 vs 2.41±0.43, p<0.01), hippocampus (2.59±0.25 vs 1.47±0.24, p<0.01), caudate putamen (3.24±0.19 vs 2.13±0.44, p<0.01) and frontal cortex (2.34±0.25 vs 1.28±0.27, p<0.01) one month after the treatment. The studies of serotonin transporter immunostaining were comparable to the PET imaging results in various brain regions. **Conclusions:** The results suggest that DM may provide neuroprotection against MDMA-induced loss of SERT and the 4-[18F]-ADAM and Micro-PET may be feasible to reflect such neuroprotection *in vivo*.

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Synthesis of tosylate and mesylate precursors for one-step radiosynthesis of [¹⁸F]FECNT

J. Pijarowska, A. Jaron, R. Mikolajczak; Institute of Atomic Energy Polatom, Otwock, POLAND.

Aim: Dopamine transporter (DAT) is critical to the regulation of dopamine neurotransmission and is decreased by Parkinson's disease. Several tropane analogues of cocaine have been developed and used in PET studies to evaluate the physiology and pharmacology of the dopamine transporter (DAT). However, low selectivity and unfavourable kinetics of most of the compounds limit their use in quantitative PET studies. The fluorine-18 labelled ligand 2-beta-carbomethoxy-3-beta-(4-chlorophenyl)-8-(2-fluoroethyl)-nortropone (FECNT) has promising properties and appears to be an excellent imaging PET agent. The development of automated [18F]FECNT synthesis system is a crucial because high amounts of radioactivity and availability of radiotracer for multiple PET study is necessary. We hypothesize that N-[18F] fluoroalkyl nortropone analogs could be synthesized at high yield by direct [18F] fluorination from appropriate precursors: N-tosylate and N-mesylate derivatives. A specific aims of this work were synthesis of non-radioactive FECNT as a standard and precursors for 18F labelling prepared in accordance with

requirements for Investigational Medicinal Product (IMP). **Methods:** The synthetic approach which we adopted based upon the published procedures with some modifications. The essential feature of this route was the reaction of Grignard reagent with the critical intermediate anhydroecgonine methyl ester, which was obtained from cocaine hydrochloride by hydrolysis in HCl and esterification with methanol. 3-β-substituted tropane derivative obtained in Grignard reaction was subjected to demethylation, as described. Non-radioactive FECNT was prepared by direct N-(2-fluoroethyl) alkylation of analytically pure 3-β-substituted nortropone precursor. The alkylating agent 2-fluoroethyl brosylate was prepared from 2-fluoroethanol and 4-bromobenzenesulfonyl chloride. The tosylate (TsOECNT) and mesylate (MsOECNT) precursors were synthesised from 3-β-substituted nortropone precursor in two steps by N-hydroxyethylation with 2-bromoethanol and subsequent tosylation of the obtained alcohol with appropriate anhydride. The crude products were purified by preparative HPLC. **Results:** In the present study we investigated and optimized synthetic route of non-radioactive FECNT, tosylate and mesylate analogs. Overall production yield were 74% for FECNT, 58% for TsOECNT and 81% for MsOECNT synthesis and a purity of these products were over 99% measured by the analytical HPLC(UV, 220 nm). The ¹H NMR and MS analysis confirmed a structure of these compounds. **Conclusions:** The synthesis method of tosylate and mesylate precursors were established and an automated radiosynthesis of [18F]FECNT will be evaluated. We expect that the new one-step method will provide a facile and reliable procedure for [18F]FECNT preparation in routine clinical applications. This study was funded in part by the EC - FP6-project DiMI, LSHB-CT-2005-512146

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Development of a PET Probe for Imaging of the Efflux Transport of Iodide from the Brain

T. Okamura, T. Kikuchi, M. Okada, K. Nagatsu, H. Wakizaka; National Institute of Radiological Sciences, Chiba, JAPAN.

Aim: There exist carrier-mediated systems for actively transporting iodide from the brain to the blood. The systems cause the low concentration of iodide in addition to the limited permeability of the blood-brain barrier (BBB). Methods for studying the *in vivo* efflux transport of iodide are expected to contribute to elucidating the physiological and biological implication of the transport systems. However, the currently available methods are limited to invasive evaluation by intracerebral injection of radioactive iodide. The purpose of this study is to develop a PET probe for the imaging of the efflux transport of iodide from the brain. **Materials and Methods:** The rationale for imaging the iodide efflux is as follows: a PET probe enters the brain, where it rapidly releases radioactive iodide. The kinetics of iodide can be evaluated after complete disappearance of the probe. In this study, 6-[¹²⁴I]iodo-9-pentylpurine ([¹²⁴I]1) was designed to penetrate the BBB and release ¹²⁴I⁻ by the reaction with glutathione. [¹²⁴I]1 was synthesized from the corresponding bromo derivative in a Br/¹²⁴I exchange reaction. Anesthetized mice were dynamically scanned for 30 min after intravenous injection of [¹²⁴I]1. ROI was placed on a PET image and transferred to all of the frames of images to generate time-activity curves. The kinetics of [¹²⁴I]1 was also evaluated in mice pretreated with perchlorate (3 mmol/kg), an inhibitor of iodide transport from the brain. **Results:** The radiochemical yield and purity were 45-60% and more than 93%, respectively. [¹²⁴I]1 showed high uptake in the brain of mice pretreated with perchlorate and control mice at 1 min after injection (4-5% injected dose/mL tissue). However, brain radioactivity in control mice was rapidly decreased from 1 min, while that in mice pretreated with perchlorate was slowly reduced. The efflux rate of ¹²⁴I⁻ in control mice was 5.4-fold higher than that in mice pretreated with perchlorate. The brain radioactivity after intravenous injection of Na¹²⁴I into mice was low during the period of 1 to 30 min, showing that the ¹²⁴I⁻ uptake from the blood to the brain would be negligible. **Conclusion:** These results suggest that [¹²⁴I]1 may be a promising PET probe for the imaging of the efflux transport of iodide from the brain.

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Development and pre-clinical evaluation of a novel class of ¹⁸F labelled PET ligands for evaluation of PBR/TSPO in the brain

V. Morisson-Iveson; GE Healthcare, Medical Diagnostics, Amersham, UNITED KINGDOM.

Introduction: The peripheral benzodiazepine receptor (PBR; otherwise known as TSPO (18kDa)) is a well-established target for imaging activated microglial cells and macrophages in inflammatory diseases such as MS, Alzheimer's disease and a wide range of both peripheral and brain diseases¹. Starting from a core tetracyclic indole pharmacophore², which displayed high affinity for the PBR, we have designed a series of molecules to assess the SAR around the pharmacophore and to determine the best site to introduce the radiolabel. **Methods:** Compounds have been assessed for PBR affinity in a radioligand binding assay and in a range of *in vitro* ADME assays. Following on from the *in vitro* assessments, promising compounds were radiolabelled and assessed *in vivo* for biodistribution and metabolism profiles. The compounds with the most appropriate profiles were assessed using autoradiography in the Facial Nerve Axotomy (FNA) model described by Banati *et al.*³ The corresponding data for the archetypal PBR ligand PK11195 was generated for comparison. **Results:** The olfactory bulb (OB) has high expression of PBR and is used to measure specific uptake, with the striatum used as a low expression area for comparative purposes. Key data obtained are summarised in the table below.

Compound (Ki)	Initial brain uptake (%ID/g)	OB @ 2 min (%ID/g)	OB @ 30 min (%ID/g)	2:30 Striatum ratio	OB : Striatum ratio (30 min)	Metabolism Profile - % Parent in brain at 60 min p.i.	FNA Model lesion : non lesion ratio (<i>in vitro</i>)
[¹¹ C]PK11195 (1.24nM)	0.28-0.48*	0.42	0.21	3.20	2.10	100	2.8**
[¹⁸ F]AH114011 (0.37nM)	0.32	0.39	0.31	1.73	2.07	96.0	2.3
[¹⁸ F]AH114629 (0.40nM)	0.42	0.51	0.28	4.75	3.50	97.6	NT

* Whole brain value not calculated ** [3H]PK11195 used for autoradiography studies **Conclusions:** Preclinical evaluation of the ¹⁸F labelled tetracyclic indole class of ligands for PBR

shows that this class of molecules represents a promising class of PET ligands that should be further evaluated. **Acknowledgement:** **References:** [1] Cagnin *et al.*, *Neurotherapeutics*, Vol. 4, No. 3, 443–452 (2007) [2] Okubo *et al.*, *Bioorg Med. Chem.* 12(2):423–438 (2004) [3] Banati *et al.*, *J. Neurocytol.* 26:77–82. (1997)

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Neurosciences: Clinical science

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Long Range Plasticity after Contralateral Cervical Nerve Transfer in Human Brain

C. Zuo, X. Hua, Y. Guan, W. Xu; Huashan Hospital of Fudan University, Shanghai, CHINA.

Aim. Peripheral nerve injury in a limb usually causes intra-hemispheric functional reorganization of the contralateral motor cortex. Recently, evidence is emerging for significant inter-hemispheric cortical plasticity in humans, mostly comes from studies of direct cortical damage. However, a long range inter-hemispheric plasticity was demonstrated in left BPAl (Brachial Plexus root Avulsion Injury) adults who had received a contralateral cervical nerve transfer in this study, much different to the BPAl induced intra-hemispheric cortical reorganization. **Methods.** Eight adult male patients with left BPAl were studied by using positron emission tomography (PET), while six healthy adult male subjects as control. All subjects performed the selective right shoulder adduction on the upper limb and PET scans were performed in rest and motor condition separately. **Results.** The results indicated that right shoulder adduction in the healthy side of the patients induced activation of the bilateral sensorimotor cortices (SMCs), with the left region being more significantly activated. However, the activation pattern of cortical structures in the BPAl patients was quite different: the bilateral SMCs were significantly activated, and the right supplementary motor area (SMA) was more activated. Corpus callosum was also found highly activated. **Conclusion.** It is concluded that BPAl-induced intra-cortical reorganization was reversed by a long range plasticity between two hemispheres following contralateral C7 nerve transfer, on mechanisms involving neural plasticity in the CNS. The activated corpus callosum suggests that it may be the essential bridge of long range plasticity between two hemispheres in the inter-hemispheric plasticity.

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Different Activated Cortical Areas in Tinnitus Patients under Auditory Blocking/Unblocking State

Z. Huang¹, C. Zuo¹, M. Li², Y. Guan¹; ¹Huashan Hospital of Fudan University, Shanghai, CHINA, ²Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, CHINA.

Aim. Whether strict auditory blocking is essential in tinnitus study has not been seriously discussed. The aim of the study is to show the different activated cortical areas in tinnitus patient with and without auditory blocking (AB) and to investigate the possible cause of tinnitus. **Methods.** 18F-FDG positron-emission-tomography (PET) scans of 3 chronic tinnitus patients (mainly in left side) were performed under AB and non-AB states. The image data of each patient was compared with data from 6 normal control subjects under AB state using Statistical Parametric Mapping (SPM). The acoustic stimulation was less than 10db under AB state and 30db under quiet non-AB environment. **Results.** Significant activation in the left primary auditory cortex (PAC) was found in the patients under non-AB state which was consistent with previous studies. However, under AB state, significant activation was found in part of the Wernicke's Area while decreased or no significant activation was found in the PAC. **Conclusion.** Our finding suggested that auditory blocking may always be performed in tinnitus study. Besides the PAC which was indicated in previous studies, the Wernicke's Area may played an important role in tinnitus in an unknown mechanism that related with the pathogenesis of tinnitus, further studies with larger collectives are needed to investigate this mechanism.

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Validation of the 'reversed Robin Hood syndrome' by acetazolamide-challenged HMPA-SPECT in patients with severe steno-occlusive disease of internal carotid or middle cerebral artery

A. K. Sinha, S. Lu, H. Teoh, G. Tsvigoulis, C. Ning, V. Chong, B. Ong, B. Chan, V. Sharma; NUHS, SINGAPORE, SINGAPORE.

Background: Intracranial stenosis is the commonest causes of stroke among Asian patients. An association exists between the degree of stenosis and recurrent stroke. In severe intracranial steno-occlusive disease, perfusion is maintained by the collateral pathways and cerebral autoregulation (CA). CA may be impaired due to inadequate cerebral vasodilatory reserve (CVR) & intracranial steal phenomenon, so-called the 'reversed-Robin Hood (RRH) syndrome'. Identification of patients with inadequate CVR may help in selecting high-risk patients who could benefit from various revascularization procedures. **Methods:** We prospectively included patients with symptomatic and severe intracranial steno-occlusive disease (of intracranial internal carotid artery and middle cerebral artery). Severe intracranial stenosis was defined according to validated transcranial Doppler (TCD) velocity criteria and blunted flow in distal segments. CVR was evaluated with TCD and a breath-holding index (BHI) <0.69 determined an inadequate reserve. RRH was detected as transient velocity reductions in affected artery at the time of velocity increase in the reference normal artery. Intracranial steal magnitude was calculated in these cases. Patients with RRH were further evaluated with acetazolamide-challenged HMPA-SPECT and net deficit in metabolic perfusion was calculated in all cases. **Results:** 74 patients (52 males, mean age 55yrs; range 23–78yrs) with severe intracranial stenosis fulfilled our TCD criteria of inadequate CVR on TCD. RRH phenomenon was observed in 31 (37%) patients with a median steal magnitude of 18% (inter-quartile range, IQR 10). Acetazolamide-challenged HMPA-SPECT

demonstrated significant metabolic perfusion deficit (median 8%; IQR 13%) in 30 out of these 31 cases (sensitivity 77%, specificity 97% with positive predictive value 97%). A strong relationship between RRH on TCD and acetazolamide-challenged HMPA-SPECT was noted on ROC curve analysis (area under curve 0.93; 95% confidence interval 0.88–0.98; p<0.00001). A linear relationship was noted between steal magnitude on TCD and acetazolamide-challenged HMPA-SPECT. Nine out of the 12 (75%) cases with RRH on best medical therapy developed subsequent cerebral ischemic events within 6 months. Surgical revascularization resulted in significant reduction in cerebral ischemic events, seen only in 3/18 cases (17%; p=0.001, absolute risk reduction 58%). **Conclusions:** Intracranial steal phenomenon in patients with severe intracranial stenosis is associated with very high risk of cerebral ischemic events. Acetazolamide-challenged HMPA-SPECT is reliable in the diagnosis of reversed Robin Hood syndrome in patients with severe steno-occlusive disease of intracranial internal carotid and middle cerebral artery ICA or MCA. Identification and quantification of intracranial steal magnitude helps in identifying a target group of patients for possible revascularization procedures.

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Subjective and Objective (SVM) analysis of Brain perfusion SPECT in migraine patients treated with acupuncture. Preliminary results of a pragmatic randomised controlled trial.

C. Ramos Font¹, J. Vas², A. C. Rebollo-Aguirre¹, M. Gómez-Río¹, D. Caballero¹, J. M. Górriz³, J. Ramírez⁴, J. M. Llamas-Elvira¹; ¹University Hospital Virgen de las Nieves, Granada, SPAIN, ²Pain Treatment Unit, Primary Care Center, Dos Hermanas, SPAIN, ³Dpt. Signal Theory and Communications (SIPBA Group). University of Granada, Granada, SPAIN, ⁴Dpt. Signal Theory and Communications (SIPBA Group). University of Granada., Granada, SPAIN.

Background: Migraine is a chronic neurologic disease that can severely affect the patient's quality of life. Acupuncture has emerged as an effective treatment for migrainic patients, but its use remains a controversial issue. Our aim was to determine whether acupuncture, applied under real conditions of clinical practice in the area of primary healthcare, was more effective than conventional treatment. **Methods/Design:** We designed a three-armed randomised pragmatic multi-centre controlled trial comparing the effectiveness of verum acupuncture with sham acupuncture, and with a control group receiving normal care only, all branches in blinded conditions. Inclusion criteria were patients presenting with migraine and for whom their General Practitioner (GP) considered referral for acupuncture. Consecutive selection and randomised allocation to the three branches of the study was centralised as followed: 1:1:1 distribution (verum acupuncture; sham acupuncture; conventional treatment). One patient in three was randomly selected from each acupuncture group for a regional brain perfusion SPECT study in a three head gammacamera ((Picker Prism 3000): 360° circular orbit; radius: 12.9cm; 3°/40 sec/step; 128x128 matrix; energy window: 140 ± 20 KeV. Base line scan was done with 260 MBq of 99mTc-ECD and another was done after first acupuncture session 925 MBq in the same day. Twelve weeks after treatment a third scan was acquired (925 MBq). Verum acupuncture consisted of 8 weekly sessions. Sham acupuncture group received 8 weekly sessions applied at non-acupuncture points. The control group was given conventional pharmacological treatment. Each patient filled a headache diary and several questionnaires to control migraine evolution. **Results:** Nowadays 15 patients have finished the protocol (86,7% female; 13,3% male); mean age 43,6 years old; 40% were settled in real acupuncture branch. Visual qualitative analysis of brain regional perfusion scan suggests inhomogeneous non specific ischemic pattern among basal studies, more significant when there is a concurrent migraine crisis. Significant changes occurred after verum in the acupuncture branch, not observed after sham acupuncture at the first post-acupuncture neither the final brain perfusion scan. Changes in visual analysis have been corroborated using an objective system of computer-aided-diagnosis (CAD) based on image parameter selection and support vector machine (SVM) classification. **Conclusion:** Preliminary results illustrate that basal brain perfusion scan resemble multi-infarct pattern in most of patients. Verum acupuncture induces modifications in global and regional brain perfusion in visual and SVM analysis. Clinical improvement analysis is still under blinded conditions.

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Reversible SPECT brain perfusion abnormalities (CBF) in Chronic Fatigue Syndrome (CFS): An evidence of systemic etiology

H. M. Abdel-Dayem¹, C. Love¹, S. Sadek¹, J. Yang¹, L. Rivera¹, N. Gandikota¹, S. Levine²; ¹SVCMC-NY, New York, NY, UNITED STATES, ²Susan Levine MD, New York, NY, UNITED STATES.

Introduction: CFS, aka Myalgic Encephalopathy, believed to be due to convergence of the following conditions: genetic factors, biochemical abnormalities, hyperactive immune system, viral or other infectious agents and psychiatric or emotional conditions. May be associated with elevated antibodies from: lyme disease, candida infection, herpes, HHV-6, HTCV, EBV, measles, coxackie B or cytomegalic. Up to 80% present flu like symptoms and non-specific complaints. Diagnostic criteria when symptoms persist > 6 mos most often used is described in 1994 "Fukuda" definition for CFS. SPECT CBF changes in CFS previously described focal hypoperfusion: frontal (63%), temporal (35%), parietal (53%), occipital lobe (38%) and basal ganglia (40%) (Ichise 1992). We previously reported diffuse supratentorial hypoperfusion (DSTH) and showed disassociation between Tc99m-HMPAO SPECT and F-18 FDG PET findings (1998). No long-term follow up (f/u) of SPECT CBF changes have been reported before. **Objectives:** Report initial Tc99m SPECT CBF changes in 6 CFS pts diagnosed according to CMS guidelines, f/u 12–14 yrs and correlate with clinical status. **Material and Methods:** 5 pts had Tc99m HMPAO SPECT CBF and one hypoperfusion of left frontoparietal region at initial diagnosis 1996–1998 and repeated: 1 pt (2000 and 2009), 5 pts (2009). Same acquisition, processing, display and interpretation. Images normalized to cerebellum. Grey matter activity < 70% or asymmetry > 10% considered abnormal. **Results:** All markedly improved to normal SPECT CBF in f/u studies in 2000 and 2009. Pts symptoms slightly improved yet did not parallel the marked improvement in CBF. **Conclusion:** Study is first report for long-term f/u in CBF changes in CFS and support that: 1.) The improvement of brain perfusion in this study favors the systemic etiology of CFS that improves with time. 2.) Clinical improvement of symptoms does not parallel improvement in CBF.

P296**Bain SPECT in evaluation of cerebral perfusion in metabolic syndrome patients: correlation with endothelial dysfunction and cognitive disorders**

N. Y. Efimova¹, V. I. Chernov¹, I. Y. Efimova¹, E. M. Idrisova², Y. B. Lishmanov¹; ¹Institute of Cardiology, Tomsk, RUSSIAN FEDERATION, ²Siberian Medical University, Tomsk, RUSSIAN FEDERATION.

Aim: to estimate role of endothelial dysfunction in development cerebral perfusion disturbance and cognitive disorders in patients with metabolic syndrome (MetS) **Material and methods:** The study involved 52 patients (8 males and 44 females, mean age 52±5) with MetS. Fifteen patients without angiographic signs of carotid atherosclerosis, ischemic disease and AH, neurological and psychiatric disorders were investigated as control group. All patients were investigated by perfusion brain SPECT with ^{99m}Tc-HMPAO and comprehensive neuropsychological testing. Endothelial function was assessed by flow-mediated dilation in brachial artery by vascular Doppler after pneumatic tourniquet stress at forearm according to D.Celermajer. Brain SPECT slices were divided into 14 symmetrical (right and left) regions of interest per patients: inferior and superior frontal lobes, temporal, anterior and posterior parietal, occipital lobes and cerebellar hemispheres. Regional cerebral blood flow (rCBF) (ml/100g/min) in these regions was calculated. **Results:** The results of Brain SPECT showed that cerebral perfusion was significantly decreased in regions of MetS patients in comparison with control group. The regional cerebral blood flow in patients with metabolic syndrome in decrease on 7.3% (p=0.003), 6% (p=0.028), 5.9% (p=0.024) was revealed in right and left anterior parietal cortex, in right posterior parietal region correspondingly, as well as with decrease on 8.3% (p=0.007), 6.6% (p=0.009) and 5% (p=0.041) in right superior frontal cortex, in right temporal and occipital regions, correspondingly, in comparison with control patients. Cognitive dysfunction was detected in 90% MetS patients. The flow-dependent vasodilatation in MetS patients was decrease on 41.3% in comparison with control group (p=0.021). In addition in 32 (61%) from 52 MetS patients was observed inadequate change of brachial artery diameter in reactive hyperemia peak, in 11 (22%) patients registered constricted response on reactive hyperemia and only in 9 (17%) patients detected normal response. Relationship between rCBF, cognitive function and indices of endothelial dysfunction was found. Significant correlation was shown between flow-dependent dilatation in MetS patients and rCBF in left superior frontal region (R²=0.126; p=0.023). The brachial artery diameter in phase of reactive hyperemia positive correlated with rCBF in left superior frontal cortex, temporal and right anterior parietal regions (R²=0.449; p=0.006, R²=0.320; p=0.277, R²=0.327; p=0.026, correspondingly), as well as with visualgnosis function (R²=0.415; p=0.009). **Conclusion** The brain SPECT is useful technique for evaluation the cerebral perfusion and understanding of cognitive disorders mechanisms in MetS patients. Deterioration of cognitive functions in MetS patients was associated with endothelial dysfunction and brain perfusion decreasing.

P297**An application of patlak plot method with TI-201 for identification of malignant lesions in brain., compared with benign lesions.**

M. Nakayama, A. Okizaki, M. Odashima, J. Sato, T. Aburano; Asahikawa medical college, Asahikawa, Hokkaido, JAPAN.

Aim: TI-201 imaging is useful for the diagnosis of brain tumor. Semiquantitative indexes, including tumor-to-nontumor activity ratio and retention index, have been used. We hypothesized that pharmacokinetics of TI-201 might indicate characteristics of brain disorders. The purpose of this study was to differentiate malignant lesions from benign ones with patlak plot method. **Materials & Methods:** A total of 22 lesions, in 20 patients with brain disorders, were studied. These lesions composed of 12 malignant and 10 benign lesions. After an injection of TI-201 (111MBq), dynamic SPECT was performed on a triple-headed digital gamma camera system for 15 minutes. ROIs were drawn manually over the abnormal uptakes of brain disorders. We analyzed TI-201 pharmacokinetics with patlak plot method, and estimated Ku as an index of influx rate constant and Vn as an index of distribution volume. These distributions were non-parametric. Therefore, Mann-Whitney's U test was performed to estimate whether there was a significant difference of Ku and Vn between the malignant and benign lesions. **Results:** The results were summarized in the table. The Ku in malignant lesions was statistically significantly lower than it in benign lesions. There was no significant difference of Vn. **Conclusions:** A statistically significant difference of Ku was seen between malignant and benign lesions (p < 0.05). Patlak plot method might be helpful to differentiate malignant lesions from benign ones in brain disorders.

Ku and Vn (average+/-SD)

Malignant lesions Benign lesions

Ku 0.0246+/-0.0151 0.0483+/-0.0321*

Vn 0.611+/-0.912 0.714+/-0.976

(*p < 0.05)

P298**¹⁸F-DG-PET/CT and MRI for evaluation of Primary CNS Lymphoma**

H. Munechika, T. Saginoya, Y. Miura, H. Shinjyo, K. Izaki, H. Goto, K. Watanabe; Southern Tohoku General Hospital, Koriyama, Fukushima, JAPAN.

Purpose: ¹⁸F-fluoro-deoxy-glucose positron emission tomography (PET/CT) has been reported to be useful for assessment of efficacy of therapy in patients with primary central nervous system lymphomas (PCNSL). However, it is necessary to verify that PET/CT is more useful than MRI in evaluation of PCNSL. This is a comparative study between PET/CT and MRI before and after treatment of PCNSL. **Materials and Methods:** PET/CT was compared with MRI in 31 lesions (16 pre-treatment and 15 post-treatment lesions) in 14 patients (male/female: 8/6, mean age: 65 year-old) with PCNSL. The histology included 13 cases of diffuse large B-cell lymphoma and one case of T-cell lymphoma. PET/CT or MRI was obtained within 7 days reciprocally. Gd-DTPA-

enhanced MRI was compared with PET/CT in axial images. **Results:** PET/CT was positive in 20 lesions and negative in 11 lesions. MRI was positive in 26 lesions and negative in 6 lesions. PET/CT and MRI were equivalent in 26 lesions (84%). MRI was positive and PET/CT was negative in 5 lesions (16%). There was no lesion of being negative in MRI but positive in PET/CT. **Conclusion:** Gd-DTPA-enhanced MRI and PET/CT were nearly equivalent in evaluation of PCNSL. However, Gd-DTPA-enhanced MRI was suited for evaluation of small lesions but non-specific. On the other hand, PET/CT was important to see residual lesion or response to treatment.

P299**Cognitive impairments in pediatric patients with Neurofibromatosis type 1 correlated with cerebral FDG PET - a retrospective series**

N. C. Nguyen¹, A. G. Abdelmalik¹, M. M. Osman¹, T. J. Geller²; ¹St. Louis University Hospital, Saint Louis, MO, UNITED STATES, ²Cardinal Glennon Children's Hospital, Saint Louis, MO, UNITED STATES.

Purpose: Cognitive impairments (CI) such as learning disabilities in patients with Neurofibromatosis type 1 (NF1) are associated with a dysregulation of Ras activity of the hippocampus. We examined a possible relation between CI and FDG hypometabolism of the hippocampus and other brain regions. **Methods:** Five NF1 pediatric patients underwent FDG PET/CT imaging including the brain, for evaluation of extracranial neoplasm. Cerebral PET images were evaluated by means of region-based Z-scores and asymmetry indices as well as voxel-based clusters. Two patients showed normal cognitive function and intelligence (group 1); the other 3 patients had CI, with either normal or low normal intelligence (group 2). **Results:** Thalamic and primary visual cortex hypometabolism was noticed in group 1 and 2 subjects (mean Z-score -1.3 and -3.4 and -2.4 vs. -2.5). The Z-scores of the hippocampus and parahippocampal region were normal in group 1 and decreased in group 2. The FDG metabolism of the frontal-temporal-parietal (FTP) lobes and cingulate gyrus-precuneus-retrosplenial area (CPR) region was normal in both groups. The results of cluster-based analysis appeared to correlate well with those of region-based analysis, in that abnormal clusters were mostly present in those regions with decreased FDG uptake (negative Z-scores). **Conclusions:** FDG hypometabolism of the thalamus and primary visual cortex is a consistent pattern in NF1 patients, which may be independent of cognitive impairments. A relation between FDG hypometabolism of the hippocampus and parahippocampal region, and CI in NF1 pediatric patients may exist and should be further investigated.

P300**Timing of a static ¹¹C-methionine brain PET imaging**

Z. Hascsi¹, B. Szucs¹, L. Balkay², I. Garai¹; ¹PET-CT Medical Diagnostic Ltd., Debrecen, HUNGARY, ²Institute of Nuclear Medicine, University of Debrecen, Debrecen, HUNGARY.

According to EANM Procedure Guidelines for Brain Tumour Imaging using Labelled Amino Acid Analogues (2006) for brain tumor ¹¹C-methionine (MET) PET investigation image from 20 to 40 min post injection is proposed for the clinical reading. **Aim:** The aim of this study was to optimize the timing of a short static imaging in brain tumor evaluation, as an early start is preferred using a short lived radionuclide for imaging. **Methods:** Forty six consecutive patients with known or suspected brain lesions were investigated. Dynamic study was performed 10-15 min post injection (0.15mCi/kg) for 20 min, consisting of equal 1 minute frames. The time course of the mean activity in normal brain tissue and tracer accumulating abnormalities was determined. ROI was placed on a representative transversal brain slice (at level of the thalamus) and applied for each 1 min dynamic frame. For lower contrast intracranial tracer accumulations free hand ROI's were drawn around regions of the tumors demonstrating the greatest activity. Threshold-based VOI's were defined for highly methionine-avid tumors. **Results:** In all cases the brain time-activity curve appeared constant during the 20 min acquisition. Visualized lesions either showed decreased MET concentration or no apparent change. More than 10% tracer washout could be demonstrated in 11 of 34 suspected tumors. Eight of them were histologically confirmed (three oligodendroglioma grade II, one astrocytoma grade II, three meningioma, one craniopharyngeoma). However, none of the MET uptake curves showed remarkable rise. **Conclusion:** Our results indicate, that the tumor to background ratio depends only on the tracer kinetics of the neoplasm, since normal brain MET concentration is stable for at least 20 min, 10-15 min after the administration. Our observation of steady or slow washout of MET within tumor tissue would support earlier image acquisition (i.e. 10 min p.i.) for static MET PET investigation.

P301**Evaluation of Cortical Metabolic Reactivation of Suppressed Brain Tissues Adjacent to Epileptic Focus after Amygdalohippocampectomy with FDG PET**

N. A. Selcuk¹, T. Toklu¹, U. Ture², C. A. Bingol³; ¹Yeditepe University Hospital, Dept. of Nuclear Medicine, ISTANBUL, TURKEY, ²Yeditepe University Hospital, Dept. of Neurosurgery, ISTANBUL, TURKEY, ³Yeditepe University Hospital, Dept. of Neurology, ISTANBUL, TURKEY.

Aim: The aim of this study was to evaluate post operative changes in the cerebral glucose metabolism of patients with mesial temporal lobe epilepsy (MTLE), using statistical parametric mapping (SPM) analysis on pre- and post-operative ¹⁸F-fluorodeoxyglucose PET (FDG-PET) images. **Materials and Methods:** Six patients who underwent amygdalohippocampectomy for medically refractory mesial temporal lobe epilepsy (5 had left MTLE and 1 had right MTLE) were included in this study. All patients showed hippocampal sclerosis by brain MRI. Pre-operative FDG-PET scans were performed one to five months before surgery, while post-operative FDG-PET scans were performed at least 12 months after surgery. All patients underwent 20-minute PET/CT scan after injection 314±48 MBq ¹⁸F-FDG and 45-minute uptake time. To determine the operation site each patient underwent MRI after the operation. Volumes of interests (VOIs) drawn on MR images were used as mask when registering images to the template image supplied by SPM. To take into account activity and uptake time differences, all the images were normalized to mean global cerebral glucose metabolism. FDG images of the patient with right MTLE were flipped horizontally so that the epileptogenic zone was lateralized to the left side in all patients. A paired

t-test was used for the voxel-wise group comparison of the FDG-PET images before and after surgery. **Results:** All patients had hypometabolism in the temporal cortex ipsilateral to the epileptogenic region and adjacent area on FDG PET scans. After operation, reduced metabolic activity was observed in operation site due to resection of the brain tissue. On the other hand, cortical metabolic reactivation was determined in neighboring cortical area ($p < 0.01$). All patients achieved a good post-operative seizure outcome. **Conclusion:** Restricted temporal lobe epilepsy surgery can preserve healthy cortical structures to improve patients' life standard. In addition to this, cortical metabolic reactivation of patients operated with such a surgical process can be successfully evaluated using FDG PET.

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Functional vs. structural neuroimaging in whiplash syndrome

R. Nieto-Serrano, M. Carrero-Lérida, M. Bermúdez-Morales, C. Dávila Arias, M. Mariscal-Cerrato, A. López-Ruiz, M. Arenas-Aguaza, D. Becerra-García, J. Martínez-Sampere; H.U. San Cecilio, Granada, SPAIN.

BACKGROUND AND OBJECTIVES: Whiplash Syndrome (WS) is due to neck hyperextension after road traffic accident with no associated head injury. Derived neurological symptoms are due to indirect axonal injury. This study sets out to describe and study the correlation between SPECT functional neuroimaging (FN) findings and CT/MR structural neuroimaging (SN) findings after WS has occurred. **METHODS:** 69 WS patients (43 female and 26 male) with a mean age of 39 years were included. They all had both SN and FN (Brain perfusion SPECT using ^{99m}Tc -ECD on a double-headed Fan-Beam gamma-camera) scans. **RESULTS:** Out of 69 patients, 8 showed an abnormal SN scan (2 female and 6 male). Both females had a normal FN scan (i.e., 43 year old woman with calcified spots at the base nuclei and a 64 year old woman showing an intraparenchymal hemorrhage at right semi-oval centre). On the contrary, all 6 men subjects had an abnormal FN scan (1 had left frontal-parietal alteration, 2 showed global spread alterations, 2 had a left frontal-temporal alteration and 1 had both right parietal and left temporal abnormalities). Out of those 61 patients with normal SN scans (41 female and 20 male, mean age 43), 30 also had a normal FN scan (20 female, 10 male) and 31 had an abnormal FN scan (17 female, 14 male). Among the latter, the most prevalent (65%) abnormality was on left hemispheric and, particularly, it affected more frequently (55%) the left frontal-temporal area. Also among these 31 patients, 9 had a mixed right-left alteration whilst the right cortex was altered in two other patients. **CONCLUSIONS:** Brain perfusion SPECT is of extraordinary value in assessing organic impairment after WS, exhibiting a superiority when compared to SN tests. Thus, whilst SPECT showed brain abnormalities in 54% of WS patients, SN just detect such abnormalities in 11% of WS patients.

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Brain single photon emission computed tomography (SPECT) with ^{99m}Tc -MIBI or ^{99m}Tc -ECD in comparison to MRI in Multiple Sclerosis

M. Assadi¹, H. Salimpour², M. Seyedabadi¹, H. Javadi³, I. Nabipour¹, R. Nemati¹, J. Saberifrad¹; ¹Bushehr Research Center for Nuclear Medicine, The Persian Gulf Biomedical Sciences Institute, Bushehr University of Medical Sciences, Bushehr, IRAN, ISLAMIC REPUBLIC OF, ²Department of Neurology, Faculty of Medicine, Bushehr University of Medical Sciences, Bushehr, IRAN, ISLAMIC REPUBLIC OF, ³Department of Nuclear Medicine, 5th Azar Hospital, Golestan University of Medical Science, Gorgan, IRAN, ISLAMIC REPUBLIC OF.

Aim: To evaluate whether or not brain single photon emission computed tomography (SPECT) with ^{99m}Tc -MIBI or ^{99m}Tc -ECD (ethyl cysteinate dimer) can detect any abnormality in patients with definite MS. We then compared these values with the results of T1, T2 and FLAIR in magnetic resonance imaging (MRI). **Materials & Methods:** Sixteen patients with proved MS were enrolled in the study and the MRI with and without gadolinium contrast and also brain SPECT with ^{99m}Tc -MIBI (8 cases) or ^{99m}Tc -ECD (8 other cases) were performed. **Results:** MRI studies was performed in 16 patients (13 women and 3 men, aged 16–38 years) and an average of 10.47, 3.7, 5.3, 1.7, and 0.9 lesions was found in respect in periventricular WM, juxtacortical WM, corpus callosum, cerebellar peduncles and brainstem, whereas brain SPECT with neither ^{99m}Tc -MIBI nor ^{99m}Tc -ECD detected no abnormality. In addition, six cases had some degree of contrast enhancement. **Conclusion:** It seems that brain SPECT with ^{99m}Tc -MIBI or ^{99m}Tc -ECD would not improve this insufficiency. The small sizes of some plaques, particularly in chronic atrophic form of lesions, and the possibility of deeper anatomical positions of plaques can to some extent explain why the MS lesions were impossible to delineate on brain scan. However, positron emission tomography (PET) can be complementary to other diagnostic techniques in the evaluation of MS, although additional studies are needed.

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Evaluation of regional brain perfusion in patient with pseudoexfoliation syndrome

E. Kaya¹, F. Öztürk²; ¹Acibadem Hospital, Kayseri, TURKEY, ²Uluçanlar Eye Education and Research Hospital, Ankara, TURKEY.

Pseudoexfoliation syndrome (PXS) is characterised by the accumulation of abnormal extracellular fibrillar material in ocular tissue by aging which can lead to some ocular complications like glaucoma, cataract, zonular damage, keratopathy. It was shown that extraocular accumulation of pseudoexfoliation matter can occur in other tissues like heart, lung, liver, kidney, cerebral meninx, aorta and adventitia layer of cerebral arteries. Acute vascular complications were seen commonly by the involvement of systemic vasculature. It was reported that PXS has been found in dementia and stroke patients. We aimed to study regional brain perfusion of PXS patients in this study. **Material and Methods** Twenty four patients who has pseudoexfoliation (14 female, 10 male) and 19 healthy volunteer (10 female, 9 male) were included to the study. There was no any cerebrovascular or psychiatric complaint in neither patient nor control group and all of them were right handed. Brain perfusion SPECT images were taken by low energy general purpose collimator of single headed gamma camera after IV injection of 25 mCi technetium-99m-hexamethylpropylene amine oxime (Tc-99m-HMPAO). To get the cortico-cerebellar ratio by semiquantitative analysis 3x3 pixel region of interests were

drawn on transaxial sections and the counts of frontal, temporal, parietal and occipital regions were divided to the counts of cerebellar region bilaterally. **Results** We showed the mean value and comparison of clinic and cortico-cerebellar ratio of patient and control group in Table 1. **Conclusion** We found that there was decrease in frontal, temporal, parietal and occipital cortex perfusion of PXS patients bilaterally. **Keywords** Pseudoexfoliation syndrome, regional brain perfusion. **Table 1:** The mean value and comparison of clinic and cortico-cerebellar ratio of patient and control group.

	Patient (n=24)	Control (n=19)	p*		
Age	67.83±9.03	64.52±6.88	0.181		
Gender (F/M)	14/10	10/9	0.708		
Blood Pressure					
Systolic	120.0±9.2	122.9±9.2	0.291		
Diastolic	80.5±2.3	80.7±4.6	0.089		
Heart Rate	63.9±9.5	65.7±5.6	0.124		
Glaucoma					
Right eye	10	-	-		
Left eye	8	-	-		
Right and Left eye	6	-	-		
Cortical Region	Cortex/Cerebellum OD±SH	Cortex/cerebellum OD±SH	Decrease (%)	p**	
Frontal	Left	0.54±0.13	0.60±0.06	10.0	0.049
	Right	0.55±0.11	0.62±0.08	11.2	0.012
Temporal	Left	0.53±0.11	0.63±0.05	15.8	0.003
	Right	0.54±0.14	0.61±0.05	11.4	0.030
Parietal	Left	0.53±0.09	0.61±0.07	13.1	0.001
	Right	0.53±0.13	0.62±0.06	14.5	0.005
Occipital	Left	0.53±0.08	0.61±0.04	13.1	0.001
	Right	0.53±0.06	0.62±0.05	14.5	0.001

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^{99m}Tc HMPAO brain SPECT in children with phace syndrome treated with propranolol

M. D. Marin¹, D. Garcia², A. C. Hernandez¹, J. Coia¹, M. Coronado¹, S. Rodado¹, C. Escabias¹, I. Santos¹, J. C. Lopez¹, D. Mendez¹, L. M. Martin¹; ¹La Paz Hospital, Madrid, SPAIN, ²Hospital Universitario de Salamanca, Salamanca, SPAIN.

We evaluated three brain perfusion SPECT (BPS) of children with PHACE syndrome (PS) in order to detect perfusion abnormalities that may be caused by propranolol therapy. **INTRODUCTION** PHACE syndrome is an uncommon congenital neuro-cutaneous syndrome defined by segmental facial hemangioma associated with structural anomalies of the brain, cerebral vasculature, eye, aorta and chest wall. The most frequently extracranial manifestations has been reported on central nervous system (45%), and cerebro-vascular anomalies (35%). Propranolol has proven to be effective in hemangioma treatment despite lack of information about its effects on the cerebral vascularization. **MATERIAL AND METHOD** We have evaluated three patients with mayor criteria of PS, who underwent: magnetic resonance angiography (MRA); ophthalmology, neurology and cardiology evaluation and brain perfusion SPECT (BPS); all of them received propranolol at 2-3 mg/kg/day in order to treat stridor or avoid ophthalmologic impairment. Informed consent was first obtained from the parents. SPECT imaging was performed one hour after intravenous administration of 13 MBq/kg (0.35 mCi/kg) Tc-99m HMPAO. Reconstruction was performed in transaxial, sagittal, and coronal positions by filtered back-projection using a Butterworth Filter (cut-off frequency 0.34 Nyquist, power factor 5). Brain SPECT was analyzed by two observers, evaluating the level of uptake decrease as mild, moderate, severe or absence. **RESULTS** Patient 1: A 15 years old girl with a large left facial hemangioma extended to fronto-nasal, temporal and maxillar regions (S4,S1,S2 segments). She presented seizures and was under antiepileptic therapy. MRI showed left temporal lobe hypotrophy and BPS revealed no uptake on left temporal lobe. Patient 2: A 3 years old boy with a large right facial hemangioma (S4, S2, S1 segments). He did not had neurological symptoms. MRA did not demonstrate pathological significant findings. BPS showed mild decrease uptake on right temporal lobe. Patient 3: A 9 year old boy with a right side facial hemangioma (S4,S1). Recently he presented migraine symptoms. MRA did not demonstrate pathological significant findings. BPS showed mild decrease uptake on right temporal lobe. **CONCLUSION** Alterations in brain perfusion ipsilateral to the hemangioma seem to be associated to PS. The present data suggest that Tc-99m HMPAO brain SPECT is a sensitive imaging modality that provides information about cerebral perfusion follow-up of patients with PS considered at risk of neurovascular impairment.

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Thalamic glucose uptake and functional improvement of the patients with severe brain injury in the chronic stage - Evaluation of the improvement using newly designed score and FDG-PET-

Y. Uchino, M. Odaki, S. Onodera, H. Endou, T. Uchida, N. Oka; Chiba Ryougo Center, Chiba, JAPAN.

[Objective] It is generally believed that the patients with severe traumatic brain injury do not improve in the chronic stage. However, improvement was observed in some patients even in several years after the injury. We focused on the thalamic glucose metabolism of the patients with severe brain injury in the chronic stage, and discussed the usefulness of the newly designed scoring system (CHIBA score, <http://chiba-ryougo.jp/>). [Methods] Twenty five patients (20 males,

5 females) were involved in this study, ranging from 21 to 66 years old (40±14, mean±SD). Duration from the accident to the first PET scan was 3.9±2.2 yrs. The second scan was scheduled 22 months after the first PET scan. Cases with thalamic damage on the CT/MR images in the acute stage and diabetic cases were excluded. The cases were divided into two groups, those were 20 cases with improved score less than 5 pts (A group), and 5 cases with improved score 5 pts or more (B group). Volumes of interests (VOIs) were drawn automatically on bilateral thalamus, and each average standardized uptake values (SUVs) was measured. [Results] In the A group, the SUVs of thalamus were not changed between two scans (right 4.2±1.0 to 4.3±1.1, left 4.3±1.3 to 4.3±1.1, respectively), while in the B group, SUVs were improved in bilaterally (right 4.2±1.7 to 5.5±2.3, left 5.7±1.1 to 7.1±1.3, respectively). [Conclusion] Even in the chronic stage of traumatic brain injury, some patients have potential to improve. From this study, the patients can be evaluated by the scoring system, since increased thalamic FDG accumulation of the dominant side reflected the functional improvement.

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Serum calcitonin gene related peptide (CGRP) levels correlate with mini mental state examination (MMSE) in patients with cognitive diseases.

V. Papantoniou¹, A. Tsaroucha¹, A. Fothiadaki¹, T. Karianos¹, A. Archontaki¹, P. Valsamaki², G. Gerostergios³, A. Rizoulis⁴, N. Kanellou⁴, T. Liotsou¹, S. Tsiouris⁵, N. Sifakis¹, A. Stipsanelli¹, A. Papadimitriou¹, ¹Alexandra University Hospital, Athens, GREECE, ²Pammakaristos Hospital, Athens, GREECE, ³Hospital of Tripoli, Tripoli, GREECE, ⁴University of Thessaly, Larisa, GREECE, ⁵Ioannina University Hospital, Ioannina, GREECE.

Aim: To assess the variation of CGRP neuropeptide expression between patients with different status of cognitive impairment and in healthy normal individuals in relation to age. **Materials and Methods:** 11 patients (mean age ± sd :79.5±19, 2) were submitted to mini mental state examination(MMSE). Serum CGRP levels were measured with RIA method and compared (t-test) with normal controls (group c₁, n=5) matched for age (mean ± sd :72±15) and younger normal volunteers (group c₂, n=5) (mean ± sd :31,8±12) in order to evaluate change in CGRP expression with ageing. CGRP expression was correlated (linear regression analysis) with MMSE. **Results:** MMSE evaluation for patients with cognitive dysfunction was (mean ± sd :14±7.2 (range 12-24). CGRP in patients, group c₁ and group c₂ was (mean ± sd) 190±46.76, 128.8±24 and 89.7±33 respectively. CGRP levels in patients with dementia were significantly higher as compared to group c₁ and c₂ (p=0.009 and p=0.0008 respectively). Linear regression analysis revealed a significant coefficient of correlation between CGRP serum value and MMSE score in patients group (r=0.854, p<0.0001). **Conclusion:** Serum CGRP is over expressed in patients with cognitive diseases. Its correlation with MMSE shows a decrease of CGRP along with the severity of the disease. CGRP seems to increase with age in the normal healthy population.

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Brain perfusion gammagraphy performed with a portable gammacamera (Sentinella®) as a support tool for brain death diagnosis.

C. Calvo, P. De la Riva, T. Cambil, M. Molina, A. Bonilla, A. Fernández, J. Castro; Hospital Virgen Macarena, Sevilla, SPAIN.

AIM: Check the use of a portable gammacamera on patients to confirm the diagnosis of clinical brain death (b.d.). **MATERIAL AND METHOD:** We have performed an evaluation of the brain perfusion in 13 patients (10 male and 3 female) that presented clinical criteria of brain death and in some of them discordance or impossibility of performing some of the instrumental tests (Transcranial Doppler and EEG). A brain perfusion gammagraphy was performed in all of them immediately in dynamic phase and later in static phase, 20 minutes after an i.v. injection of 1111 MBq of 99m Tc -HMPAO, acquiring images with a pinhole collimator in anterior projection and both lateral, using a portable gammacamera (Sentinella®) at the bed side of the patient at the ICU. **RESULTS:**

	Patient	HMPAO	DOPPLER	EEG
	1	+	+	+
	2	-	+	+
Hemorrhagic stroke	3	-	+	+
	4	+	*	+
	5	-	+	-
	6	+	+	*
CET ¹	7	+	*	+
	8	+	+	+
	9	+	+	+
	10	-	+	-
Ischemic stroke	11	+	+	+
	12	+	+	+
Sepsis	13	+	+	+

¹ CTE: craniocencephalic trauma(+) compatible with b.d. (-) not compatible with b.d. (*) Test not performed in the patients where no brain perfusion was observed, b.d. diagnosis was confirmed. In patients 2 and 5 a conserved perfusion was observed in the whole brain parenchyma, except in the area corresponding to the hematoma. In patient 3 the perfusion was normal and in patient 10 the perfusion was localized only in the posterior fossa. **CONCLUSION:** The brain blood flow perfusion is recommended in Spain, through the "Real Decreto 2070/1999", to shorten the observation period, in those circumstances where the clinical diagnosis may be difficult or complicated or in the case of judicial patients. The brain perfusion gammagraphy performed with portable gammacamera is valid to detect both the absence of brain perfusion, and conserved

perfusion, identifying hematoma areas and correctly evaluating the posterior fossa. The presence of portable gammacameras allows intensive care specialists access to a useful tool such as the perfusion brain gammagraphy, with highly proven clinical value, but underused. In our case, it also eliminates the important obstacle of transporting the patient from the ICU to the Nuclear Medicine department, this being the main advantage of this new diagnostic tool.

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^{99m}Tc-HMPAO SPECT in estimate of cerebral perfusion in patients with cardiovascular diseases: correlation with cognitive function

I. Y. Efimova, N. Y. Efimova, Y. B. Lishmanov; Institute of Cardiology, Tomsk, RUSSIAN FEDERATION.

Aim: to estimate brain perfusion (BP) and cognitive function (CF) in patients with cardiovascular diseases. **Material and methods:** Seventeen pts with chronic atrial fibrillation (CAF), 70 pts with coronary artery disease (CAD) and 42 pts with essential arterial hypertension (AH) were involved in the study. Fifteen patients of similar age without angiographic signs of carotid atherosclerosis, cardiac arrhythmia, CAD and AH, neurological and psychiatric disorders were investigated as control group. All pts underwent brain SPECT with ^{99m}Tc-HMPAO, standard neurologist examination and comprehensive neuropsychological testing. **Results:** All patients had no focal neurological symptoms. BP was decreased in pts with CAF as compared with control group. The most significant BP decrease was revealed in the inferior frontal and posterior parietal brain lobes (on 14-21%). In lesser degree (on 7-12%) hypoperfusion was marked in the anterior parietal, superior frontal, temporal and occipital regions. The CF disturbance was marked in 94 % CAF pts. Worsening of immediate verbal memory was correlated with BP decrease in the superior frontal cortex (R²=0,25; p=0,04) and deterioration of attention was correlated with BP decrease in the inferior frontal cortex (R²=0,26; p=0,03). There was negative correlation between psychomotor speed and BP in the inferior frontal cortex (R²=0,47; p=0,003). The BP was decreased in pts with CAD on 12-15% as compared with control group. Direct correlation between psychomotor speed and BP in the superior frontal lobe was revealed (R²=0,121;p=0,046). Deterioration of immediate verbal memory and attention correlated with decrease BP in the anterior parietal cortex (R²=0,120; p=0,041 and R²=0,134; p=0,031, correspondingly). The greatest BP decrease (on 15-20%) in AH pts was marked in the frontal, posterior parietal and temporal regions. Hypoperfused was present to a lesser degree (on 8-13%) in the anterior parietal and occipital brain lobes. There was positive correlation between mentation and BP in the frontal lobe (R²=0,214; p=0,008). Deteriorations of attention and psychomotor speed were connected with BP impairment in the frontal (R²=0,436; p=0,003), parietal (R²=0,346; p=0,003) and temporal (R²=0,194; p=0,012) lobes. **Conclusion:** Our results suggest that perfusion brain SPECT permit to detect of the signs of brain hypoperfusion in patients with cardiovascular disease it even if they have no focal neurological symptoms and hemodynamic significant lesion of carotid arteries. BP disorders serve as pathogenetic part of neurocognitive dysfunction development in these patients.

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Acetazolamide Challenged HMPAO SPECT Plays Important Role in Decision Making for Superficial Temporal Artery-Middle Cerebral Artery (STA-MCA) Bypass in Patients With Severe Steno-occlusive Disease Of Intracranial Internal Carotid And Middle Cerebral Artery

A. K. Sinha, S. Lu, V. Sharma, V. Chong, B. Ong, C. Ning, T. Hock L, B. Chan; NUHS, SINGAPORE, SINGAPORE.

Background- The International Cooperative Study of Extracranial / Intracranial arterial anastomosis (EC/IC Bypass) study in patients with symptomatic carotid artery disease failed to demonstrate a reduction in the risk of subsequent ischemic stroke. Subsequent reports found that superficial temporal artery-middle cerebral artery (STA-MCA) bypass surgery improved the cerebral oxygen extraction fraction and possibly useful in patients with impaired cerebral hemodynamic and vasodilatory reserve (VR). We evaluated cerebral hemodynamics and VR in patients with symptomatic distal internal carotid (ICA) or middle cerebral artery (MCA) severe steno-occlusive disease to select patients who could benefit from STA-MCA bypass surgery. **Methods-** Diagnostic transcranial Doppler (TCD) and vasomotor reactivity (VMR) testing with voluntary breath-holding, according to a standard scanning protocol, were performed in patients with severe ICA or MCA steno-occlusive disease. We defined severe stenosis according to previously published criteria, blunted flow in the distal arterial segments and breath-holding index (BHI) <0.69. Artery-to-artery embolization was excluded by extended TCD monitoring for spontaneous emboli. Patients with inadequate BHI were further evaluated with acetazolamide-challenged HMPAO-SPECT. Patients with significantly impaired metabolic perfusion and VR on SPECT imaging were offered STA-MCA bypass surgery. Cerebral hemodynamics and VR were re-evaluated in all patients at 6 months and they were followed up for cerebral ischemic events. **Results-** 72 patients (51males, mean age 55yrs; range 23-78yrs) fulfilled our TCD criteria of inadequate CVR. Acetazolamide-challenged HMPAO-SPECT demonstrated impaired CVR in 35 patients and 22 of them underwent STA-MCA bypass surgery. There were no perioperative complications and during subsequent follow up (mean 10months; range 3 to 28months). Early morning headache and lethargy noted in 16 patients resolved completely. 3(14%) in the surgery group developed new cerebral ischemic event during follow up. Acetazolamide-challenged HMPAO-SPECT repeated at 5±2months after STA-MCA bypass surgery revealed significant improvement in CVR in all cases. In comparison, 9 out of the 13 (69%) patients with inadequate CVR and on best medical therapy developed new cerebral ischemic events during follow up. **Conclusion-** Patients with symptomatic severe intracranial steno-occlusive disease and impaired vasodilatory reserve carry a high risk of cerebral ischemic events. Assessment of cerebral vasodilatory reserve and quantification of metabolic hypoperfusion by acetazolamide-challenged HMPAO-SPECT may be used to select patients who would benefit from STA-MCA bypass surgery

P26 — Monday, October 11, 2010, 16:00 — 16:30, Hall Z

Neurosciences: Dementia and psychiatric disorders**P312****Semi-Quantitatively Measured Cerebral Blood Flow in Patients with Mild Cognitive Impairment - Relation to Progression at Follow-Up**

J. Freden Lindqvist¹, Å. Edman², M. Nilsson¹, A. Wallin², L. Edenbrandt¹;
¹Dept of Nuclear Medicine, Sahlgrenska University Hospital, Göteborg, SWEDEN, ²Inst of Neuroscience and Physiology, Sahlgrenska Academy, Mölndal, SWEDEN.

Aim Mild cognitive impairment (MCI) is a heterogeneous condition between normal cognition and dementia, that might progress to dementia. Markers for progressive MCI will be essential for future treatment selection. Cerebral blood flow (CBF) single photon emission tomography (SPECT) has been used in several studies, usually with either Alzheimer Dementia (AD) or subcortical vascular dementia (VD) as endpoint, although a combination is probably often present. The aim of this study was to explore patterns of CBF reduction at baseline in patients with progressing MCI (PMCI) to early dementia, compared to those with stable MCI (SMCI). **Materials and Methods** From a longitudinal MCI-study, the nineteen first patients diagnosed with MCI (score 3 on the Global Deterioration Scale), who at follow-up 1-3 years later had clinically converted to dementia were included. Eighteen matched patients who were stable at follow-up were included as controls. There were no statistical differences in age (PMCI 66.9 ± 6.7 years, range 51-78; SMCI 66.5 ± 7.4 years, range 54-77) or gender (PMCI 11 women, SMCI 7 women). The PMCI group converted to AD (n=7), VD (n=3), and mixed (n=7). The CBF-SPECT investigation was performed on a 3-headed Picker Irix gamma-camera (Philips Medical Systems) 45 minutes after injection of 1000 MBq ^{99m}Tc-hexamethyl propylene amine oxime (HMPAO). In a semi-quantitative analysis (Exini brain™, Exini Diagnostics, Sweden), the relative CBF values in the four lobes (ten brain regions; frontal dx/sin/med, temporal dx/sin, medial temporal dx/sin, parietal dx/sin, occipital) were compared in relation to three different reference regions (total cortex, total cortical cerebellum, maximum cerebellum intensity) to the corresponding values of a normal database, and z-values were calculated. **Results** At baseline 12 of 19 PMCI patients had an abnormal finding in at least one of the four lobes, as compared to 5 of 18 SMCI patients. With cerebellar maximum as reference, 8 of 19 PMCI patients had abnormal CBF in the left medial temporal lobe, as compared to 1 of 18 SMCI patients (p=0.019). There were no other statistically significant differences between the patient groups in other lobes. Lower CBF on the left side in at least one of the four lobes was found in 7 PMCI patients and in 4 SMCI patients. **Conclusion** Semi-quantitative CBF reduction in the left medial temporal region might be a marker in predicting deterioration into overt dementia in MCI patients, potentially guiding patient selection for future preventive treatment. Further studies are needed for confirmation.

P313**Different Hypoperfusion Patterns in SPECT/CT in Suspected Early Dementia may Predict Conversion to Clinical Dementia**

S. Pukkila¹, M. Hakulinen¹, A. Sutela², K. Timonen¹, M. Hallikainen³, R. Vanninen⁴, P. Hartikainen⁵, E. Vanninen⁶;
¹Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, FINLAND, ²Department of Radiology, Kuopio University Hospital, Kuopio, FINLAND, ³Department of Neurology, University of Eastern Finland, Kuopio, FINLAND, ⁴Department of Radiology, Kuopio University Hospital and University of Eastern Finland, Kuopio, FINLAND, ⁵Department of Neurology, Kuopio University Hospital and University of Eastern Finland, Kuopio, FINLAND, ⁶Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital and University of Eastern Finland, Kuopio, FINLAND.

Early diagnosis of dementia is important but challenging. The established SPECT-criteria for Alzheimer's disease (AD) are based on cases already fulfilling clinical diagnostic criteria. The frontal or anterior temporal hypoperfusion in SPECT is included in clinical diagnostic criteria of frontotemporal dementia (FTD). **AIM.** To evaluate early cerebral hypoperfusion patterns in patients presenting with different symptoms indicative of possible neurodegenerative dementia. **PATIENTS AND METHODS.** We studied 63 patients with suspected dementia and 18 matched control subjects (9 men/9 women, mean age±SD 74±7 years) with ^{99m}Tc-ECD-SPECT/CT and SPM5 software (uncorrected p<0.001, extension threshold 125 voxels). An experienced neuroradiologist rated CT-images according to cortical atrophy pattern and severity. Thirty-two patients originally presented with mild cognitive impairment (MCI) and 31 with symptoms or findings of possible FTD. During the 4-year follow-up, 15 patients showed stable MCI (9/6, 72±6 years) and 13 MCI-patients converted to AD (MCI-AD, 7/6, 73±6 years). Of the patients with suspected FTD, 12 were later clinically confirmed to have FTD (5/7, 64±7 years) and 5 were diagnosed to have AD (FTD-AD, 1/4, 62±5 years). For further analyses the MCI-AD- and FTD-AD-groups were combined as converted Alzheimer's cases (AD). **RESULTS.** In CT, 4 controls and 19 patients showed moderate to severe cortical atrophy, mainly in fronto-temporal areas. FTD-group tended to show more frontal lobe atrophy than AD-group (p = 0.078/0.098, right/left). When compared to controls, stable MCI-group showed hypoperfusion in right temporal neocortex and right frontal lobe, while in AD-group the hypoperfused areas were more widespread and included also left frontobasal and right hippocampal areas. When compared to stable MCI-group AD-group had significantly reduced perfusion in right posterior cingulum, bilateral striatum and right frontal operculum. FTD-group also showed extensive hypoperfusion in right fronto-temporal cortical areas combined with small hypoperfusion areas in left frontal lobe and thalami when compared to controls. FTD-group showed more severe hypoperfusion in right perisylvian area and left superior parietal gyrus when compared to stable MCI-group. Compared to FTD-group AD-group had more severe right posterior hippocampal hypoperfusion. Interestingly, there were no more severe hypoperfusion in FTD-group when compared to AD-group. **CONCLUSIONS.** All patient groups with variable clinical presentation indicative of dementia demonstrated hypoperfusion in right frontal and temporal lobes and cortical atrophy in CT when compared to controls. However, more detailed hypoperfusion patterns were different

between the stable and clinically progressing patient groups. ^{99m}Tc-ECD-SPECT/CT and voxel-based quantification may provide a surrogate marker for early diagnosis of dementia.

P314**Perfusion in posterior cingulate correlates with verbal learning independently of temporal atrophy in MCI patients: an MRI and perfusion SPECT study**

C. A. Sánchez Catasús¹, J. Samper², P. Valdés- Sosa³, M. Pagani⁴, L. Galán³, A. Aguila¹, Y. Ginarte⁵, R. Rodríguez-Rojas¹, E. Barroso⁶, L. Alvarez-González¹, J. Llibre-Rodríguez², Y. Fernández³;
¹CIREN, Havana, CUBA, ²University Hospital "Carlos J. Finlay", Havana, CUBA, ³Cuban Neuroscience Center, Havana, CUBA, ⁴Institute of Cognitive Sciences and Technologies – CNR, Rome, ITALY, ⁵Iberoamerican Center for the Third Age, Havana, CUBA, ⁶Institute of Neurology and Neurosurgery, Havana, CUBA.

Aim: to our knowledge, there are no studies analyzing functional, structural and cognitive data in the same group of MCI patients in a single correlative analysis. Our aim was to explore the interconnections between hypoperfusion, atrophy and cognitive dysfunction in MCI patients, in order to analyze the cognitive dysfunction in the context of the functional/structural association reported by other authors. We also performed the same analysis in control subjects. **Material and Methods:** 29 MCI patients, characterized by memory and learning deficits, and 29 age, gender and education matched-controls underwent resting-state ^{99m}Tc-ECD- SPECT (double-head), high-resolution T1-MRI and cognitive function assessment. For group comparison, voxel-based morphometry (VBM) and voxel-based analysis (VBA) on SPECT data were carried out. Marsbar toolbox was used to create volumes of interest (VOI) using the statistical maps obtained for each image modality. For each subject, normalized regional perfusion was extracted from SPECT images and grey-matter volume from MRI images within the VOIs representative of hypoperfusion and atrophy, respectively (significant clusters). The correlations between perfusion VOIs (pVOIs), grey-matter volume VOIs (gVOIs) and neuropsychological variables (significantly different between groups) were separately tested for each group, controlling for age, gender and education. **Results:** VBM showed two clusters representing atrophy in MCI patients in both temporal lobes, comprising the hippocampus, parahippocampal, temporal inferior and fusiform gyri. VBA showed two clusters representing hypoperfusion: one comprising the angular and supramarginal gyri and the inferior parietal region on the right hemisphere; the other comprising the bilateral posterior cingulate cortex and the adjacent right precuneus. The pVOI in the bilateral posterior cingulate region and the hard-word pairs learning score (HWPLS) from the Wechsler memory scale showed the strongest partial correlation (r=0.65, p < 0.0005) in the MCI group. This VOI also correlated with the pVOI in the right parietal region (r=0.55, p < 0.005) and with the gVOI in the right temporal lobe (r=0.39, p < 0.05). Exploring further the result, we found that the significant correlation observed between the pVOI in the posterior cingulate and the HWPLS survived after controlling for nuisance variables (r=0.62, p < 0.01). We didn't find any significant partial correlation in the control group. **Conclusion:** perfusion in the posterior cingulate correlated with verbal learning independently of grey matter atrophy in MCI patients at risk for Alzheimer's disease (AD), probably due to other hypoperfusion-inducing factors, in agreement with recent studies suggesting an interaction between vascular, cholinergic and "amyloid β" hypotheses of AD.

P315**Frontotemporal Dementia and Alzheimer's Disease: Evaluation of Brain Perfusion in Specific Brodmann Areas Using Automated 3-D Voxel Based Analysis.**

V. Valotassiou¹, J. Papatrifiatyllou², N. Sifakis³, I. Tsougou¹, C. Tzavara¹, A. Fothiadaki³, K. Makrypoulas³, C. Zerva³, P. Georgoulas¹;
¹University Hospital of Larissa, Larissa, GREECE, ²G. Gennimatas Hospital, Athens, GREECE, ³Alexandra University Hospital, Athens, GREECE.

Aim: Brain perfusion studies with single-photon emission computed tomography (SPECT) have been applied in demented patients to provide better discrimination between frontotemporal dementia (FTD) and Alzheimer's disease (AD). The aim of our study was to assess the perfusion of specific Brodmann (Br) areas of the brain cortex in FTD and AD patients, using NeuroGam processing program to provide 3D voxel by-voxel cerebral SPECT analysis. **Materials-methods:** We studied 51 consecutive patients from an outpatient Memory Clinic. We used the established DSM-IV criteria for the diagnosis of dementia and the specific established criteria for the diagnosis of FTD and AD. All the patients had a neuropsychological evaluation with a battery of tests including the mini mental state examination (MMSE). All the patients underwent a CT and/or MRI of the brain in order to exclude the presence of vascular or structural brain lesions. Thirty nine patients received the clinical diagnosis of FTD (24 males, 15 females, age 68.76±6.51 years, MMSE 16.69±9.89, education 11.81±4.25 years) and 12 patients (all females, age 71.25±10.48 years, MMSE 12.5±3.89, education 10±4.6 years) the clinical diagnosis of AD. All the patients underwent a brain SPECT scan 20 min after the intravenous administration of 740MBq of ^{99m}Tc-HMPAO. We applied the NeuroGam™ software on the reconstructed data, for the evaluation of brain perfusion in specific Br areas in the left and right hemispheres. Count normalization was performed using cerebellum (least affected area in degenerative dementias) as the reference area. **Results:** Continuous data are expressed as mean±standard deviation. The normality assumption of continuous variables was evaluated using Kolmogorov-Smirnov criterion. In order to test differences of the rCBF in Br areas between the AD and FTD groups, the unpaired Student t-tests were used. All p values reported are two-tailed. Statistical significance was set at 0.05. Analyses were conducted using the STATA statistical software. Perfusion was significantly lower in AD compared to FTD patients in the following Br areas: 7R and 39R (p<0.05). Significant hypoperfusion was found in FTD patients compared to AD patients, in the following Br areas: 11L (p<0.0001), 11R, 20L, 20R, 32L, 38L, 38R, 44L (p<0.001), 32R, 36L, 36R, 45L, 45R, 47R (p<0.01), 9L, 21L, 44R, 46R, 47L (p<0.05). **Conclusion:** The application of NeuroGam processing protocol offers a more detailed and objective evaluation of rCBF and may contribute to a better discrimination between FTD and AD patients.

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Brain perfusion scan (SPECT) in primary progressive aphasia

S. Rodríguez Martínez de Llano¹, R. Piñeiro Bolaño², I. Candal Casado¹, P. Pais Silva¹, ¹Centro Oncológico de Galicia. Nuclear Medicine., La Coruña, Galicia, SPAIN, ²Hospital Xeral-Calde. Neurology, Lugo, Galicia, SPAIN.

Introduction Primary progressive aphasia (PPA) is a clinical syndrome characterized by a progressive deterioration of language with relative preservation of other cognitive functions, which underlie different clinical-pathological entities (Alzheimer's disease, frontotemporal dementia, cortico-basal degeneration). **Aim** To evaluate the usefulness of SPECT perfusion scan in the PPA as well as the pursuit of a characteristic pattern of hypoperfusion that allow to identify different underlying entities and guide treatment. **Materials and methods** We performed a retrospective study in the last year (2008-2009), selecting patients referred to our department with clinical suspicion of APP. We contacted the referring physicians for confirmation of clinical diagnosis. All patients underwent cerebral perfusion SPECT with 99mTc-ECD (NEUROLITE), the injected dose was 740MBq. The results were assessed qualitatively by two experienced nuclear physicians and semiquantitatively, extracting the average percentage from each defined region and calculating R / L (Right / Left) ratios, using the cerebellum as a reference. **Results** A total of 6 patients were included in the study (5W/1M), all submitted from the Neurology department with clinical suspicion of progressive non-fluent aphasia, with a mean age of 70.3 years and an average of 2 year symptom duration. All cases showed left temporal atrophy (MRI), with the ipsilateral frontal region affected in two cases. The qualitative analysis of cerebral perfusion studies showed perfusion defects in the left temporal region of 83.33% as well as in the contralateral temporal, parietal region was affected in two cases, one case was normal and no case had occipital involvement. The semiquantitative analysis showed a R / L ratio of 0.98 (± sd 0.07) in the temporal region, 1 (± sd 0.01) occipital, 1.04 (± sd 0.07) parietal and 1.01 (± sd 0.07) in frontal. **Conclusions** A temporal perfusion defect supports the clinical picture of primary progressive aphasia. Our sample showed a lower R / L ratio in the temporal region. **Results** suggest two patterns, one bilateral and another unilateral. **Studies** with more patients are needed to establish a formal method of analysis.

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Differential diagnosis for Dementia with Lewy Bodies(DLB),Parkinson disease with dementia (PDD) and Alzheimer Disease(AD) using cortico-subcortical index in SPECT study

B. M. Brockhuis¹, P. Lass², D. Wiczorek³, E. Sitek⁴, M. Derejko⁵, J. Teodorczyk¹, W. Cytawa¹, G. Romanowicz¹, J. Slawek⁶, ¹Medical University in Gdansk, Nuclear Medicine Department, Gdansk, POLAND, ²Medical University in Gdansk, Nuclear Medicine Department, Gdansk, POLAND, ³Medical University in Gdansk, Department of Rehabilitation, Gdansk, POLAND, ⁴Medical University in Gdansk, Department of Neurological and Psychiatric Nursing, Gdansk, POLAND, ⁵Neurophysiology Department, Institute of Psychiatry and Neurology, Warsaw, POLAND, ⁶Department of Neurology, St Adelbert Hospital, Gdansk, POLAND.

Introduction: In some cases distinction between patients with DLB and those with AD or PDD may be difficult because of overlapping clinical features. Clinical criteria do not allow to make an early and specific diagnosis in many patients. Early diagnosis in DLB seems to be important to avoid the disease progression after treatment with classical neuroleptics (what increases the mortality rate and the risk of nursing-home placement). **Aim:** The purpose of this study was to perform rCBF study in patients with DLB, PDD and AD to find a parameter which can help to distinguish patients with dominated cortical pathology like AD versus patients with subcortical pathology typical for PDD or DLB. We calculated cortico-subcortical index in order to distinguish DLB versus AD and PDD versus AD. **Method:** We studied 50 subjects: DLB (N=13), PDD (N=18), AD (N=19), age 54-88 and controls (N=14). All patients we recruited according to established clinical diagnostic criteria. In all patients magnetic resonance imaging (MRI) or computed tomography study (CT) was done. SPECT study was performed after intravenous injection of 20 mCi (740 MBq) ^{99m}Tc-ECD (FAM, Lodz, Poland) with three head gammakamera Multispect (Siemens, Erlangen, Germany) using low-energy, high resolution parallel-hole collimator. Cortico/subcortical index, which is mean value of cortical perfusion to mean value of subcortical structures was calculated. **Results:** Analysis of three groups of patients and controls showed significant statistical differences between controls and DLB group (decreased value of cortico/subcortical index). There has been also a marginally significant trend for PDD group and controls (p=0.054). **Conclusion:** Cortico-subcortical index may help to differentiate DLB patients (with dominated subcortical pathology) and AD patients (with dominated cortical pathology).

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Preliminary evaluation of the usefulness of originally established normal database of Brain perfusion SPECT for the statistical analysis using 3D-SSP software.

A. Taniguchi¹, H. Otake², T. Higuchi³, Y. Takahashi¹, H. Shimada², Y. Arisaka⁴, G. Miyashita⁵, N. Oriuchi⁴, K. Endo⁴, ¹Department of Nuclear Medicine Technology, Gunma Prefectural College of Health Sciences, Maebashi, JAPAN, ²Department of Radiological Technology, Gunma University Hospital, Maebashi, JAPAN, ³Diagnostic Radiology and Nuclear Medicine, Gunma University Graduate School of Medicine, Maebashi, JAPAN, ⁴Department of Diagnostic Radiology and Nuclear Medicine, Gunma University Graduate School of Medicine, Maebashi, JAPAN, ⁵Department of Stomatology and Oral Surgery, Gunma University Graduate School of Medicine, Maebashi, JAPAN.

Aim: Statistical software, 3D-SSP and SPM are widely used to detect decreased perfusion are in brain perfusion SPECT. However, variable result form different database remained and induces variety of artifacts and different severity of fdcreased perfusion. To solve these problem, we

developed our original database and it was compared with those developed in other institution. **Materials and methods:** Original I-123 IMP brain perfusion normal database obtained from 24 volunteers (12 male and 12 female) with the mean age of 65.2±8.5 (51 to 76) confirmed as normal neuropsychological test and MRI were established. Age distribution are as below. 50-59; 7 (3male, 4 female), 60-69; 9 (4 male, 5 female), 70-79; 8(5 male and 3 female). NDB from other institution are compared with our own NDB in normal volunteer and mild cognitive disorder (MCI) by the case by case analysis using SEE methods in aspect of artifact, extent and severity score in posterior cingulate gyrus. **Results:** Artifact in normal volunteer was reduced in our own NDB. Furthermore, extent and severity score in posterior cingulate gyrus showed different pattern between two NDB base analysis. **Discussion:** The results of 3D-SSP were affected by used NDB. Standard deviation (SD) and variable coefficient might affect the results. It is important to understand the characteristics of each NDB and enough consideration of characteristics should be paid during image analysis.

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Qualitative (QL) and 3D Quantitative (QN) analysis of 123I-iodoflupane SPECT in possible Alzheimer's Disease (AD), Lewy Body Dementia (LBD) and Vascular Dementia (VD) differential diagnosis

S. Nuvoli¹, A. Nieddu², A. Rotondo², R. Salvo², F. Chessa¹, A. Spanu¹, G. Madeddu¹, ¹Nuclear Medicine DPT, University of Sassari, Sassari, ITALY, ²Geriatrics DPT, Policlinico Sassarese, Sassari, ITALY.

Aim: We evaluated the usefulness of QL and QN analysis of 123I-iodoflupane SPECT in Dementias differential diagnosis. **Material and Methods:** We enrolled 96 consecutive patients (54F; 42M), aged 52-84 yrs, positive for DSM-IV criteria. According to International Consensus Criteria, 61 cases were classified as possible AD (NINCDS-ADR-DA) 16 as possible LBD (LBD Consortium International Workshop) and 19 as possible VD (NINDS-AIREN); Parkinson's disease was clinically excluded; CT/MR were normal or not specific (atrophy, leukoariosis and gliosis) in all cases. All patients underwent Brain SPECT, 3-4 hrs after 148 MBq 123I-iodoflupane (DaTSCAN[®], GE Healthcare Medical Diagnostic) i.v. injection. SPECT were evaluated by both QL and QN, the latter by a 3D dedicated software (NEUROTRANS 3D; Segami Corp.) which defines striatal dopaminergic activity as Binding Potentials (BP) applying attenuation/partial volume effect corrections (Talairach atlas). Caudate and putamen BP normal values (cut off: 3.3) were previously calculated in 20 sex-age matched normal subjects. **Results:** QL was pathological in 21/96 (21.9%) cases, 16 LBD, 4 AD and one VD with reduced tracer uptake in 13/42 (30.9%) caudate and 31/42 (73.8%) putamen. QL was normal in the remaining 75/96 (78.1%) patients, 57 AD and 18 VD. In QL pathological cases, QN showed BP values 3.3 in the remaining 12/42 caudate (28.6%). In QL normal cases, QN showed BP>3.3 in 71/96 (73.9%), 53AD and 18 VD and BP<3.3 in the remaining 4/96 cases (4.2%) who had been clinically classified as AD. The 25 patients with QN <3.3 had mean caudate and putamen BP values (1.94±0.78, and 1.31±0.71, respectively) significantly (p<0.000001) lower than our controls (4.9±0.71 and 4.6±0.67, respectively), while in the remaining 71 patients with QN>3.3 BP values were not statistically different. Globally, QL better discriminated LBD from non LBD (AD/VD) dementias than Consensus Criteria alone: its use allowed to confirm clinical diagnosis in 93.5% AD, 100% LBD and 94.4% VD, while suggesting further investigation, in 6.5% AD and 5.6% VD with reduced uptake. Comparing QL and QN results there was QL/QN concordance in 92/96 (95.8%) cases while in 4/96 (4.2%) only QN correctly classified LBD. **Conclusions:** 123I-iodoflupane SPECT QL and QN analyses represent valuable tools in supporting Dementia diagnosis since, in our cases, they better discriminated LBD from non LBD (AD/DV) in respect of Consensus Criteria. Moreover, QN with BP calculation, especially in the initial phase of the disease, seems to improve QL performance.

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Does Periventricular White Matter Hyperintensities as Seen on MRI Images Effect Cerebral Glucose Metabolism? A Retrospective Study

A. G. Abdelmalek¹, H. R. Farghaly¹, A. S. Nassif¹, A. S. Nelson², M. M. Osman¹, N. C. Nguyen¹, ¹St. Louis University Hospital, Saint Louis, MO, UNITED STATES, ²MIMVista Corp., Cleveland, OH, UNITED STATES.

PURPOSE Periventricular white matter hyperintensities (PWH) are commonly seen on brain MRI of elderly individuals. In this retrospective study, we seek to determine whether PWH effects cortical metabolism using F-18 FDG PET. **METHOD AND MATERIALS** We included 20 cancer patients (pts) that did not undergo recent chemotherapy (>10 months) and had no brain metastasis at MRI. MRI demonstrated PWH in 8/20 (40%) pts - 5 female, 3 male (group P). PWH were absent in the remaining 12/20 (60%) pts - 1 female, 11 male (group N). Time interval between their MRI and PET scans was < 1 month. PET images of the brain were extracted from the true-whole body PET scans performed for oncological staging/restaging, and compared with a normal database (MIMneuro 4.1, MIMVista Corp.) that contained 43 normal controls and provided Z-score evaluation based on single brain or probabilistic mapping. The Z-scores of 47 brain regions were compared between the two groups using independent t-test. Patients' age, gender and cerebrovascular risk factors were also compared. **RESULTS** PWH ranged from 0.5-1.6 cm and were unilateral in 5/8 pts and bilateral in 3/8 pts. Pts in group P were statistically older than those in group N (mean age 67 vs. 47, p = 0.007). PWH were more frequent in females than males (p = 0.05). Hypertension was present in 2 pts in each group which was not statistically significant. The Z-scores in all 47 regions were not statistically significant between the two groups (p > 0.05). **CONCLUSION** The presence of PWH is highly associated with older age. PWH, as seen at brain MRI, may not affect cortical FDG metabolism despite the age difference found in pts with PWH and those without PWH.

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Cerebral Glucose Metabolic Rate (CMR_{glu}) changes before and after ventricular shunt placement in patients with normal pressure hydrocephalus (NPH)

M. L. Calcagni¹, M. Lavalle¹, A. Mangiola², L. Leccisotti¹, L. Indovina³, L. Rigante², C. Anile², A. Giordano¹, ¹Institute of Nuclear Medicine, Catholic

University of Sacred Heart, Rome, ITALY, ²Neurosurgery Unit, Catholic University of Sacred Heart, Rome, ITALY, ³Medical Physics Unit, Catholic University of Sacred Heart, Rome, ITALY.

Aim: to evaluate regional Cerebral Glucose Metabolic Rate (CMR_{glu}) values before and after ventricular shunt placement in patients with normal pressure hydrocephalus (NPH). **Materials & methods:** ten patients (mean age of 69±18 years) with NPH syndrome (gait disturbance, urinary incontinence, and cognitive dysfunction), and radiological signs of NPH underwent to dynamic Cerebro Spinal Fluid (CSF) study and dynamic 3D ¹⁸F-FDG PET-CT (185MBq) before (3 days) and after (7 days) ventricular shunt placement. CMR_{glu} was calculated drawing regions of interest (ROIs) over both grey matter (superior, middle, and inferior frontal regions, temporal and parietal regions, caudate, putamen and thalamus), and white matter (frontal, parietal and periventricular area). CMR_{glu} was measured in each ROI using a 2-compartmental model. CMR_{glu} values before and after shunt placement were compared using a paired T test. **Results:** after shunting, 7/10 patients (70%) showed an improvement of all three symptoms and a significant increased of CMR_{glu} of all bilateral cortical and subcortical cerebral regions: superior, middle, and inferior frontal region (p=10⁻³), temporal (p=10⁻³) and parietal (p=10⁻³) region, caudate (p=10⁻⁴), putamen (p=10⁻⁴) and thalamus (p=10⁻⁴). Only 2/10 patients (20%) showed a clinical improvement of one out of three typical NPH symptoms: urinary incontinence (1 patient), and gait disturbance (1 patient). In these patients, CMR_{glu} did not show a significant improvement in any cortical regions, while only bilateral subcortical regions showed a significant CMR_{glu} improvement: caudate (p=0.01), putamen (p=0.02), and thalamus (p=0.007). Finally, only 1 patient did not show any significant clinical and CMR_{glu} improvement in all cortical and subcortical regions. In all patients, CMR_{glu} values of white matter did not show any significant difference before and after shunting. **Conclusions:** dynamic ¹⁸F-FDG PET-CT procedure allows to get easily the CMR_{glu} values. Our preliminary data, obtained in a small but highly selected sample of NPH patients, demonstrate that CMR_{glu} values increases in all cerebral regions after shunt placement only in patients with complete clinical response. This finding suggests that ventricular drainage has an effect also on cerebral glucose metabolism, as well as on cerebral blood flow, as already reported. The exclusive improvement of CMR_{glu} in the bilateral subcortical regions of patients with partial clinical response allows to hypothesize the earlier involvement of basal ganglia in NPH patients. Consequently, in order to verify if metabolic changes precede clinical response, our next step is to repeat both clinical evaluation and ¹⁸F-FDG PET-CT scan after six-months follow-up.

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Value of 18FDG-PET in the differential diagnosis of spongiform encephalopathies in patients with dementia.

I. Dominguez-Prado, J. Arbizu, E. Prieto, S. Ortega, M. Gonzalez-Forero, M. Carmona, C. Vigil, C. Caicedo, M. Riverol, J. A. Richter; Clinica Universidad de Navarra, Pamplona, SPAIN.

Objectives: Clinical diagnosis of the different human forms of spongiform encephalopathies (HSE) may be difficult since dementia is the main symptom. For this reason many other neurodegenerative disorders should be included in the differential diagnosis. However, a well defined ¹⁸F-FDG metabolism pattern has not been described in the short bibliography published up to date. The aim of this study is to describe the ¹⁸F-FDG brain distribution pattern in the different forms of HSE, and to consider its usefulness as a diagnostic tool. **Patients and methods:** Nine patients with a final diagnosis of HSE were included (median age of 51 years; range: 39-71 years). All of them had developed rapidly progressive dementia with or without parkinsonism symptoms. A ¹⁸F-FDG-PET was performed in order to carry out a differential diagnosis among neurodegenerative disorders. Additional brain imaging techniques (MRI), electroencephalography, laboratory examinations of cerebrospinal fluid (CSF) for proteins such as 14.3.3 and genetic analysis (PRNP gene) were achieved. A voxel-based statistical analysis (SPM) of the FDG-PET studies was performed individually and per groups. A healthy population (n=18, median age: 67, range: 64-71), was included as a control group. Age was considered as a covariable in the analysis, and a p-value of 0.001 was defined as threshold for statistical significance. **Results:** The diagnosis of definitive sCJD was confirmed in 6 patients and FFI in 3 patients. The PET findings are shown in the table.

Patient	Diagnosis	Hypometabolism			
		Cortex	Thalamus	Basal ganglia	Cerebellum
1	sCJD	+	+	-	-
2	sCJD	+	+	+	+
3	sCJD	+	+	+	-
4	sCJD	+	+	-	-
5	sCJD	+	-	+	-
6	sCJD	+	+	+	-
7	FFI	+	-	-	-
8	FFI	-	+	-	-
9	FFI	+	+	+	-

MRI findings were compatible with HSE in 5/8 patients. PRNP gene mutation was studied in 4/9 patients (mutated in 2 FFI, 1 sCJD and non-mutated in 1 sCJD). The analysis of the 14.3.3 protein in CSF was performed in 6/9 patients (positive in 2 sCJD and in 1 FFI). **Conclusions:** The hypometabolism in thalamus and basal ganglia was present in all HSE. The cortex involvement is more extensive and frequent in sCJD than in FFI cases. This pattern adds a valuable information in the differential diagnosis of neurodegenerative diseases.

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Differential Diagnosis of Mild Cognitive Impairment from Early-stage of Alzheimer's Dementia Using F-18 FDG Brain PET

H. Song¹, B. Kim², A. Chong¹, T. Kim³, S. Choi², M. Kim², K. Cho², G. Jeong³; ¹The Department of Nuclear Medicine of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF, ²The Department of

Neurology of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF, ³The Department of Radiology of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF.

Purpose: The purpose of this study is to evaluate the characteristic, hypometabolic areas to discriminate mild cognitive impairment (MCI) from early stage of Alzheimer's disease (ESAD) using F-18 FDG brain PET and statistical parametric mapping (SPM). **Materials and Methods:** Sixteen healthy controls (59.6 ± 6.7 yrs), 7 patients with MCI (71.6 ± 7.5 yrs) and 6 patients with ESAD (73.0 ± 8.8 yrs) underwent F-18 FDG brain PET under the same scanning conditions and Seoul neuropsychological screening battery. Severity of dementia was rated with global deterioration scale. We selected age- and sex-matched normal control without cognitive impairment. Voxel-based morphometric analysis was performed using SPM software (version 2). F-18 FDG PET images were compared each patient's subgroups with healthy controls using SPM. **Results:** MMSE scores were 30 in all healthy control, 25.7 ± 2.2 in patients with MCI, and 23 ± 4.2 in patients with ESAD. MMSE scores of MCI and ESAD were significantly lower than those of healthy control (p < 0.001). However, there was no statistically significant difference between MMSE scores of MCI and ESAD (p = 0.1635). Compared with healthy control group, MCI group showed reduced glucose metabolism in the frontal, superior and inferior temporal lobes, parietal lobe excluding superior parietal area, anterior and median cingulate gyri, whereas glucose metabolism of both the frontal, temporal, parietal, cingulate gyrus, basal ganglia and limbic lobes were reduced in ESAD group. A significant difference in F-18 FDG uptakes between MCI and ESAD groups was the spared glucose metabolism in the left inferior temporal, fusiform gyrus, left superior parietal lobe, posterior cingulate gyrus, limbic lobe and basal ganglia in MCI group. **Conclusion:** This preliminary data suggests that F-18 FDG brain PET is a useful imaging modality to diagnose MCI which will later convert to ESAD.

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Computer-assisted system for diagnosis of Alzheimer's disease using database-independent estimation using FDG PET and 3D-SSP

K. Ishii¹, T. Uemura², N. Miyamoto², T. Yoshikawa²; ¹Kinki University School of Medicine, Osakasayama, JAPAN, ²Hyogo Brain and Heart Center, Himeji, JAPAN.

Purpose: To produce and evaluate an automatic diagnosis system using database-independent estimation system for the diagnosis of mild Alzheimer's disease (AD). **Methods:** We retrospectively selected 66 subjects, including 33 patients with AD (mean age ± SD, 71.2 ± 2.5), and 33 age-matched healthy volunteers (NC) (mean age ± SD, 70.6 ± 4.2). The mean mini-mental state examination (MMSE) scores of the AD and NC groups were 22.8 ± 1.7 and 29.9 ± 0.4, respectively. Individual brain metabolic images were obtained using fluorodeoxyglucose and positron emission tomography (FDG-PET). These were transformed using three-dimensional stereotactic surface projections (3D-SSP). We then produced a computer-assisted diagnosis with a database-independent system (CADDIES), which compares the parietal and sensorimotor metabolic counts using t-tests. If parietal metabolism was significantly lower than the sensorimotor metabolism, the subject was automatically diagnosed as AD. The FDG-PET images were also analyzed using a previous automatic diagnosis system (CAAD) that is dependent on the construction of a 'normal database' of healthy brain images. **Diagnostic performance** was compared between the two methods. **Results:** The CADDIES method exhibited similar diagnostic accuracy to the CAAD method. The mean area under the ROC curve of CADDIES was 0.940. The mean areas under ROC curves of the CAAD method in the parietal and posterior cingulate gyri were 0.843 and 0.939, respectively. **Conclusion:** The CADDIES method demonstrated a similar diagnostic accuracy to the CAAD system. Our results indicate that this method can be applied to the detection of early AD patients in routine clinical examinations, with the benefit of not requiring the generation of a normal database.

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An attempt to improve the diagnostic performance of structural MRI for the detection of Alzheimer's disease: comparison with FDG PET

W. P. Chen¹, I. Matsunari¹, K. Shima², M. Samuraki², Y. Miyazaki¹, M. Yoshita², K. Ono², T. Tamaki³, W. P. Chen³, S. Nishimura¹, M. Yamada²; ¹The Medical and Pharmacological Research Center Foundation, Hakui, JAPAN, ²Department of Neurology and Neurobiology of Aging, Kanazawa University Graduate School of Medical Science, Kanazawa, JAPAN, ³Nagoya Radiological Diagnosis Foundation, East Nagoya Imaging Diagnosis Center, Nagoya, JAPAN.

[Aim] Prior structural MRI studies have demonstrated that Alzheimer's disease (AD) associated brain atrophy may involve not only the hippocampal area (Hipp) but also the posterior cingulate gyri (PCG). Our aim was to test the hypothesis that the diagnostic performance of structural MRI and voxel-based morphometry (VBM) could be improved by taking PCG atrophy as an additional marker of AD to the conventional Hipp atrophy in comparison with FDG PET. **[Materials & Methods]** 97 AD patients and 105 healthy subjects underwent both 3D-T1 MRI and FDG PET on a single day. Normal databases for both MRI and PET were generated using additional age-matched 56 healthy subjects. For VBM z-score maps, regions of interest (ROI) were placed on Hipp and PCG. For PET, ROI was placed on PCG. **[Results]** The diagnostic performance of VBM and FDG PET was tested to discriminate 97 AD patients from the 105 normal subjects using those ROIs. A receiver-operating characteristic (ROC) analysis was performed to determine the optimal threshold for each ROI. **[Conclusions]** As summarized in Table, the use of PCG ROI in addition to Hipp significantly improved the sensitivity of VBM, resulting in overall accuracy comparable to that of PET. **[Conclusion]** Our data indicate that the diagnostic performance of VBM for the detection of AD can approach to that of FDG PET by ROI optimization.

	PET	VBM	
Regions of Interest	PCG	Hipp	Hipp+PCG
Sensitivity	84.4%	77.1%	85.6%
Accuracy	88.3%	83.4%	87.6%

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Effect of cognitive stimulation on brain glucose metabolism in patients with senile dementia of Alzheimer's type: SPM5 quantification in FDG-PET studies.

L. Ruffini¹, C. Ghetti², C. Cidda¹, M. Scarlattei¹, O. Ortenzia², G. Serreli², L. Concarini³, S. Gardini³, S. Copelli⁴, F. Dieci⁴, F. Ferrari Pellegrini⁴, P. Caffarra²; ¹Nuclear Medicine Department, AOU di PARMA, Parma, ITALY, ²Medical Physic Department, AOU di PARMA, Parma, ITALY, ³Department of Neuroscience, AOU di PARMA, Parma, ITALY, ⁴Outpatient Clinic for the Diagnosis and Therapy of Cognitive Disorders, Parma, ITALY.

Aim of the study was to quantify the differences of cerebral metabolic rates for glucose (CMRglc) in patients with senile dementia of Alzheimer's type (SDAT) before and after cognitive stimulation therapy (CST). **Materials and methods:** CST is a group treatment for patients with mild-to moderate dementia, based on the idea of really orientation and memory improvement, increased autonomy and a better quality of life. It involves sessions of themed activities which typically run twice a week over a 3 months period. We have enrolled 10 SDAT patients; they were asked to perform cognitive tests (Mini Mental State Examination, Clinical Dementia Rating, Instrumental Activities of Daily Living Scale and Base Activity of Daily Life) and a FDG-PET scan before and after the CST. All brain PET scans were acquired under standard resting conditions using a GE Advantage DST scanner in 3D mode. The PET/CT camera has an axial field of view of 15.4 cm in 47 planes with a plane spacing of 3.27 mm; the axial resolution is 4.8 mm FWHM. Thirty minutes after injection of about 200 MBq 18F-FDG the images were acquired and reconstructed using the CT scan for attenuation correction. PET images were analyzed using SPM5 (<http://www.fil.ion.ucl.ac.uk/spm>) implemented on Matlab 7.01, the image set was spatially normalized using the SPM5 PET template and smoothed with a Gaussian filter of 8 mm FWHM. Differences in CMRglc (before vs. after and after vs. before CST) were assessed on a voxel-by-voxel basis using a paired t-test. Finally, with SPM5 tools it was possible to identify, in a stereotaxic coordinate system, the clusters in which the CST determined CMRglc variations statistically significant. **Results and Conclusions:** Cognitive tests have highlighted an improvement in patients performance and quality of life after CST; SPM5 analysis has shown an increase of CMRglc in limbic lobe, and in particular in right cingulate gyrus (Brodmann Area 23) and in left thalamus. Even if these results can be considered preliminary, the voxel-by-voxel analysis method applied to brain PET is able to detect and quantify small variation of CMRglc probably related to stimulation: cingulate gyrus, which is particularly affected during the preclinical phase of dementia, seemed to have an increased metabolism.

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Quantification of PET Amyloid and Tau Ligand [F-18]FDNP in early Alzheimer disease

C. Tauber¹, J. Vercoillie¹, V. Kepe², E. Beauvils³, Y. Venel³, J. Baulieu³, D. Gendre⁴, J. Barrio², J. Cottier³, K. Mondon³, C. Hommet⁵, V. Camus³, D. Guilloteau⁵; ¹UMRS INSERM U930 - CNRS ERL3106 - Université de Tours, Tours, FRANCE, ²Department of Molecular and Medical Pharmacology, D. Geffen School of Medicine, UCLA, Los Angeles, CA, UNITED STATES, ³CHRU de Tours, Hôpital Bretonneau, Tours, FRANCE, ⁴Centre d'Investigation Clinique CIC U202, Tours, FRANCE, ⁵CHRU de Tours, INSERM U930, CIC IT 806, Tours, FRANCE.

Aim: We evaluated the feasibility of a non-invasive quantification of [F-18]FDNP to detect amyloid-beta plaques and tau neurofibrillary tangles in early Alzheimer disease (AD). Our aim was to discriminate early AD patients from healthy controls (HC). This abstract presents the preliminary results on a cohort of 4 AD and 2 controls. **Methods:** Patients and cognitively normal controls underwent PET imaging with [F-18]FDNP, and MRI. All subjects underwent neuropsychological assessment evaluating global efficiency (MMSE), episodic memory (free and cued recall test), language (French naming test of 80 pictures), executive functions (semantic fluency task, Trail Making Test). [F-18]FDNP distribution volume ratios (DVR) parametric images were generated using Logan graphical analysis with the cerebellum grey matter as a reference region (PMOD 3.1). Regions of interest (ROIs) were defined in the posterior cingulate, parietal, frontal and temporal regions. The DVR scores were measured as the mean DVR values of each of these regions. A global score was calculated as the mean DVR scores of all these regions. **Results:** [F-18]FDNP scans were positive for all the AD patients by visual inspection, while all the HC had negative scans. Global values of [F-18]FDNP-PET binding were significantly higher ($p=0.045$) in the AD group (1.18 ± 0.06) than in the control group (1.06 ± 0.03). Similar results were obtained in several individual ROIs, namely the frontal and medial temporal regions.

	AD	HC	
MMSE	20±2.97	27.5±0.71	
Frontal	1.21±0.07	1.06±0.01	$p=0.077$
Med. temp.	1.17±0.03	1.08±0.02	$p=0.044$
Lat. temp.	1.16±0.05	1.06±0.03	$p=0.087$
Post. cing.	1.17±0.07	1.06±0.05	$p=0.34$
Parietal	1.11±0.06	0.99±0.03	$p=0.11$

A cross analysis with the results of the neuropsychological tests clearly indicates some correlations. The patient with the lowest MMSE score (15) has the highest global DVR score (1.27) among the group, and inversely the AD patient with the highest MMSE score (23) has the

lowest global DVR score (1.12) among the AD group. Similar correlations were obtained for language and executive functions and the DVR found in the associated cerebral areas. **Conclusions:** The global fixation of the tracer is significantly higher for the AD than for the HC. These data suggest that the [F-18]FDNP can be used to discriminate non-invasively AD subjects from HC. Moreover, the specificity of the fixation seems to be correlated with the evolution of the pathology and the results of the neuropsychological tests. **Acknowledgements:** FP6-project DiMI, LSHB-CT-2005-512146, PHRC IR 2007 STAFF, Planiol Fondation 2006.

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Florbetapir F 18 PET brain amyloid deposition and MRI Pattern of Atrophy: relation between SUVr and SPARE-AD index

G. Romanowicz¹, C. Davatzikos², J. Doshi², C. M. Clark³, K. Saha³, D. M. Skovronsky³; ¹Medical University of Gdansk, Gdańsk, POLAND, ²University of Pennsylvania, Philadelphia, PA, UNITED STATES, ³Avid Radiopharmaceuticals Inc., Philadelphia, PA, UNITED STATES.

Objective: Clinical diagnosis of Alzheimer Disease (AD) may be incorrect thus reliable biomarkers are investigated. We compared amyloid PET brain images quantified by SUV normalized to cerebellum (SUVr) with MRI atrophy pattern quantified by SPARE-AD index (which takes positive values in the presence of patterns of atrophy characteristic of AD). **Method:** MRI and florbetapir F18 PET images of 19 subjects (clinically diagnosed 7 AD and 12 HC) were analyzed. PET images were acquired for 10 minutes, 50 minutes post IV injection of 370MBq florbetapir F18. For the amyloid deposition quantification, PET images were spatially normalized to MNI space and counts extracted from VOIs (frontal, temporal, precuneus, parietal, anterior and posterior cingulate and cerebellum) to calculate average SUVr values. The SPARE-AD score was developed using pattern classification and machine learning methods, using a group of cognitive normal individuals and a group for AD patients. The spatial pattern of brain atrophy that best separated these two groups in a highly multi-variate nonlinear way was determined from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. When applied to new scans, including the ones herein, it produces the SPARE-AD score. Positive SPARE-AD implies the presence of AD-like spatial pattern of atrophy and vice-versa. SUVr and SPARE-AD values were compared. **Results:** There is good correlation ($r=0.68$) between both indices. In all HC SUVr values are below 1.1 (0.92-1.06) and SPARE-AD values are negative (-1.15 to -0.12) with one exception where index was 0.34 and SUVr 0.97, indicating the presence of AD-pattern atrophy but no significant amyloid plaque deposition. In AD group there was one patient with low both SPARE-AD and SUVr values (-0.97 and 0.96 respectively), suggesting that neither AD-pattern atrophy nor amyloid deposition contributed to the cognitive impairment in this subject. All other AD subjects had SUVr values ranging from 1.51 to 1.62. SPARE-AD indexes for those patients were positive (0.51-1.1) with exception of one subject having borderline SPARE-AD of -0.12 but SUVr of 1.54 (highly indicating low AD-pattern atrophy in spite of considerable amyloid presence). **Conclusions:** We found significant correlation between both imaging biomarkers however in two cases the biomarker indexes were discrepant. Given small number of studied cases it is unclear whether it is result of method limitations or represents true difference between the occurrence of amyloid deposition and the development of an atrophy pattern. More studies are required to establish clinical role of different modalities in subsequent stages of AD.

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Clinical Manifestations and I-123 ADAM Uptake in Different Brain Areas in Patients with Major Depressive Disorder

W. Huang¹, S. Huang¹, T. Chung¹, P. Huang¹, L. Shen², K. Ma³; ¹Tri-Service General Hospital, Taipei, TAIWAN, ²Institute of Nuclear Energy Research, Taoyuan, TAIWAN, ³National Defense Medical Center, Taipei, TAIWAN.

Objective: Serotonergic dysregulation is an important factor in developing major depressive disorder (MDD) while serotonin transporter (SERT) is a main target in evaluating pathophysiology of MDD. We used I-123 ADAM brain SPECT to observe SERT uptake in different brain areas, clinical manifestations and therapeutic response in MDD patients. **Methods:** 36 MDD (M/F=16/20; mean age: 33.4 y [SD, ± 12.4 y]; age of onset: 28.6 y [SD, ± 9.7 y]) based on DSM-IV criteria and 10 age-matched controls (M/F=7/3; mean age: 31.6 y [SD, ± 10.8 y]) were enrolled. Merikangas et al., 1998 K.R. Merikangas, D.E. Stevens, B. Fenton, M. Stolar, S. O'Malley, S.W. Woods and N. Risch, Co-morbidity and familial aggregation of alcoholism and anxiety disorders, *Psychol. Med.* 28 (1998), pp. 773-788. **Full Text** via CrossRef | View Record in Scopus | Cited by in Scopus (147) Severity of MDD was measured by 21-item Hamilton Depression rating Scale (HDRS). All patients were drug-naïve or drug-free 6 weeks before SPECT and re-imaged 2 months after SSRI treatment. The SPECT was performed as described (Huang et al. 2004). The specific uptake ratios (SUR) of I-123 ADAM in different brain areas [i.e. midbrain (MB), striatum (ST), thalamus (TH) and pons (PO)] were measured using the cerebellum as a reference. The post therapeutic SUR and HDRS were observed in 28 MDD patients. **Results:** There was significant decrease of SUR after SSRI compared to that of pre-treatment (0.67±0.25 vs. 1.20±0.40; $p<0.001$). The HDRS is also significantly decreased after therapy (30.36±4.59 vs. 10.64±7.04; $p<0.001$). The midbrain SUR appeared to be positively correlated with post-therapeutic HDRS in the MDD group. However, no significant difference in mean SUR values were found in any brain region between drug-free MDD patients (ST=1.12±0.41; TH=1.21±0.51; MB=1.94±0.56; PO=1.37±0.38) and healthy controls (ST=0.96±0.10; TH=1.13±0.30; MB=1.78±0.45; PO=1.35±0.36). The SERT availability was also not influenced by age, gender, and severity of MD. **Conclusion:** The significant decrease of midbrain I-123 ADAM uptake and HDRS after SSRI at a trend of positive relationship between SUR and post-therapeutic HDRS indicated the potential role of I-123 ADAM SPECT in SERT availability and SSRI occupancy.

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FDG PET/CT in patients with treatment resistant depression.

G. Capriotti, S. Rigucci, F. Cicone, P. Pizzichini, V. Lanni, A. Festa, M. Sasanelli, M. Martini, F. Trapasso, D. Prosperi, R. Tatarelli, G. Nicolò, S. Ferracuti, F. Scopinaro; II Faculty of Medicine, Rome, ITALY.

Purpose: Depression is a widely diffused syndrome, usually treated with anti-depressant treatments. Depression is usually considered resistant ("treatment resistant depression", TRD) or

refractory when at least 2 appropriate trials of antidepressants from different pharmacologic classes fail to produce significant improvements. There are no definitive, consensual, standardized operational criteria to treat TRD. To our knowledge, there are no PET studies identifying the resting metabolic abnormalities associated with TRD. The aim of this study was to evaluate whether ^{18}F FDG PET-TC brain scans show specific abnormalities pattern in depressed resistant outpatients. **Material and Methods.** Eight outpatients with TRD were recruited, 2 male, and 6 female. Mean age was 44 (range 32–55). All patients were right-handed. To exclude diagnoses other than TRD, prior to FDG PET/CT scan all patients underwent physical examination, electroencephalography, laboratory tests, and Magnetic Resonance (MRI). All patients were assessed through neuropsychological tests and psychopathological evaluation. Ten healthy volunteers, 8 female and 2 male with a mean age of 52 were enrolled as controls. Nine out of ten controls were right-handed. To minimise visual and auditory stimuli, patients were positioned in a comfortable, silent and dark room. A fasting state >4 hours was mandatory, blood glucose were <160 mg/dl in all cases. Images were acquired on a scanner 20 to 30 minutes after the intravenous injection of 185MBq ^{18}F FDG. Region of Interests (ROIs) were drawn over three transaxial slices encompassing the following cortical regions: frontal, temporal, occipital, and parietal, bilaterally. Mean SUVs obtained within ROIs in each region were averaged and compared to those obtained in the contralateral hemisphere as well as to those obtained in controls. All images were also qualitatively analysed. **Results.** Neuropsychological battery: most of our patients did not achieve a fulfilling cognitive performance, especially on frontal functions domains. Working memory, planning, abstraction, categorization and mental shift abilities were significantly impaired. PET scans were normal and symmetric in all volunteers and in 2 patients with TRD. Six out of 8 patients showed 30–40% and 40–50% lower averaged SUV in left fronto-temporal region compared to the contralateral and to that of normal subjects. **Conclusion.** Our data suggest that left fronto-temporal hypo-metabolism might be related to poor response to antidepressant treatment and to cognitive impairment.

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Increased Striatal Dopamine Transporter Density in First-Episode Drug-naïve Patients with Schizophrenia

F. Sedaghat, S. Spyridi, I. Nimatoudis, A. Papazisi, M. Arnaoutoglou, A. S. Dimitriadis, S. J. Baloyannis, G. Kaprinis; Aristotle University, Thessaloniki, GREECE.

Successful treatment with dopamine antagonists suggests a crucial role of the neurotransmitter dopamine in the pathophysiology of schizophrenia. Little is known, however, about the dopaminergic function in schizophrenia and there is a controversy among different studies. We evaluated the pre-synaptic dopamine transporter density with SPECT using 123I-PP-CIT (DaT Scan), in 13 patients (8 F, 5 M) (26±3 years old) with first-episode drug-naïve schizophrenia and 20 (12 F, 8 M) (30±8 years old) controls. All the patients underwent MRI, perfusion SPECT using HMPAO and DaT Scan. A significant increase of striatal radiotracer uptake in DaT scan was shown in our patients with schizophrenia compared to normal group ($p=0.000$), while rCBF in these regions didn't show any significant difference. Also significant negative correlations between 123I-PP-CIT binding ratios in right and left striatum with positive symptoms of patients were found. Elevated density of presynaptic dopamine transporters, may be part of the neuronal abnormality associated with dopaminergic activity in schizophrenia.

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Voxel-based and VOI-based analysis of ^{99m}Tc -ECD perfusion SPECT at rest and activation by Wisconsin Card Sorting Test in patients with schizophrenia

A. Nocuń, J. Pawęzka, B. Chrapko, K. Szymona, A. Smoleń, H. Karakula; Medical University of Lublin, Lublin, POLAND.

The aim of our study was to assess patterns of brain activation by Wisconsin Card Sorting Test (WCST) and to examine the relations between regional cerebral blood flow (rCBF) and psychotic symptoms in schizophrenia. **Materials & methods:** We examined 12 men with schizophrenia (mean age 29±1.2 years). Patients were evaluated for negative symptoms using the Scale for the Assessment of Negative Symptoms and for positive symptoms using the Scale for the Assessment of Positive Symptoms. Brain perfusion SPECT was performed with ^{99m}Tc ethyl cysteinate dimmer (ECD), injected at rest and during WCST. SPECT was carried out with double-head gamma camera (Varicam). Semiquantitative assessment was performed with Brain SPECT Quantification software (Compant, Poland). Images were automatically matched with the anatomically standardized, stereotactic template. Count normalization was to the whole brain. For comparison of rest and activation SPECT with voxel-based approach, the relative difference was computed $\{(A-R)/[(A+R)/2]\} \times 100$, where A and R represent counts at activation and rest. The cut-off value of the relative difference was 10% in a cluster volume of 10 ml. Volume of interest (VOI)-based analysis of relative rCBF was performed in 20 VOIs (left and right: prefrontal, frontal, parietal, temporal, occipital, cerebellum, thalamus, basal ganglia, anterior and posterior cingulate). Comparison between rest and activation rCBF was performed by the Wilcoxon test (paired variables). The Spearman test was applied to study correlations between rCBF and scores of positive or negative symptoms. $P \leq 0.05$ was considered statistically significant. **Results:** In voxel-based analysis, the patterns of rCBF decrease and increase varied between patients, with combinations of different brain regions involved. In VOI-based analysis the only statistically significant difference between rest and activation was rCBF decrease in the left basal ganglia ($p=0.028$). The score of positive symptoms (2–31; mean 16.5±9.7) correlated with rCBF in the right frontal at rest ($r=-0.8$; $p=0.005$) and activation ($r=-0.6$; $p=0.02$). The score of negative symptoms (16–69, mean 39.3±16.9) showed correlation with rCBF in the right occipital lobe at rest ($r=0.6$; $p=0.04$) and activation ($r=0.7$, $p=0.01$), in the right prefrontal only after activation ($r=-0.6$; $p=0.04$), in the left anterior cingulate only after activation ($r=-0.6$, $p=0.03$). **Conclusions:** Patterns of WCST activation and deactivation differ between patients. Our results suggest the relations between the positive symptoms and the right frontal region, negative symptoms and right occipital, right prefrontal and left anterior cingulate. WCST allows for augmentation of rCBF pattern and detection of more correlations than the resting stage.

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Inter-observer agreement in 360° versus 180° rotation DaTSCAN SPECT

E. Moralidis, G. Gerasimou, I. Hilidis, T. Aggelopoulou, E. Papanastasiou, A. Gotzamani-Psarrakou; AHEPA Hospital, Thessaloniki, GREECE.

Aim. An 180° rotation has been proposed instead of the routine 360° SPECT in DaTSCAN studies, but observers' agreement has not drawn particular attention. This study aimed to evaluate the clinical performance of the 180° DaTSCAN SPECT in terms of inter-observer agreement, using the 360° SPECT acquisition as the reference standard. **Method.** One-hundred and twelve consecutive patients (52 male) with movement disorders were recruited. Patients were submitted to routine 360° SPECT imaging 3–4 hrs after intravenous injection of 5mCi ^{123}I -ioflupane. Frames corresponding to an 180° rotation over the anterior parts of the brain (from the left to the right lateral projection) were separated. Acquired data of both datasets were reconstructed in a standard manner, the two most central slices of the striatum in the transverse plane were summed up and in this composite image predefined ROIs were placed to encompass the caudate and putamen nuclei of the left and right side and also the inferior part of the occipital cortex (non-specific activity). The caudate/occipital count density in both the left and right side (LC and RC, respectively) and also the putamen/occipital count density of both sides (LP and RP) were calculated. ROIs were drawn by two observers independently and in separate sessions for each dataset. In addition, the 180° and 360° SPECT images were interpreted visually by two experienced, independent observers in different sessions, using a 3-point scale (normal, equivocal, abnormal) separately for the left and right side. **Results.** In visual analysis inter-observer agreement for the 360° rotation was moderate for both the left ($\kappa=0.558$, $p<0.001$, identical readings in 75% of cases) and the right side ($\kappa=0.583$, $p<0.001$, identical readings in 77% of cases). In the 180° SPECT inter-observer agreement was fair for the left ($\kappa=0.346$, $p<0.001$, identical readings in 64% of cases) and moderate for the right side ($\kappa=0.419$, $p<0.001$, identical readings in 70% of cases). In quantification the following results were provided for the 360° rotation (Pearson's coefficient of correlation (r), 95% limits of agreement according to the Bland-Altman statistic): LC $r=0.939$ ($p<0.001$), -0.02 ± 0.48 ; RC 0.935 ($p<0.001$), -0.03 ± 0.51 ; LP $r=0.861$ ($p<0.001$), 0.02 ± 0.57 ; RP $r=0.874$ ($p<0.001$), -0.03 ± 0.56 . For the 180° SPECT the results were: LC $r=0.923$ ($p<0.001$), 0.05 ± 0.61 ; RC 0.905 ($p<0.001$), 0.06 ± 0.69 ; LP $r=0.799$ ($p<0.001$), 0.02 ± 0.71 ; RP $r=0.831$ ($p<0.001$), 0.01 ± 0.67 . **Conclusion.** The use of an 180° rotation in DaTSCAN deteriorates inter-observer agreement in both the visual and quantitative analysis of images, in comparison to the standard 360° SPECT acquisition.

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Creation of a customized Normal Database for 123I-PP-CIT SPECT studies in a major Nuclear Medicine department in Northern Greece

K. Badiavas¹, I. Iakovou², E. Molyvda³, M. Tsolaki⁴, K. Psarrakos³, N. Karatzas², ¹Medical Physics Dept, General Hospital "G. Papageorgiou", Thessaloniki, GREECE, ²3rd Nuclear Medicine Dept, Aristotle University, General Hospital "G. Papageorgiou", Thessaloniki, GREECE, ³Medical Physics Dept, Aristotle University, Thessaloniki, GREECE, ⁴Neurology Dept, Aristotle Univ., General Hospital "N. Papanikolaou", Thessaloniki, GREECE.

Aim. Following the European recommendations and trend, we set up a database of normal values for the 123I-PP-CIT SPECT studies performed in our department during the previous 4 years in order to use them as reference in future studies. Materials and methods. For a number of years we used multiple semi-quantification methods for every exam and ended up in a preferred set that best fit the clinical background of our patients. For the database construction we chose to use physiological and technically correct exams from 47 patients aged 66.0±14.0 years, diagnosed with essential or pharmacological tremor and no sign of neural degeneration nor vascular parkinsonism. We used individualized manual ROI creation, referred to as method 1, and two semi-automated methods - the so called "crescent" and "two box" methods - available in the QuantiSPECT software package, referred to as method 2 and method 3 respectively. Results. For the manual method, where no attenuation correction has been applied, we found the normal uptake values for the striatum, caudate nucleus, putamen, percent difference of the unilateral putamen, putamen to caudate and percent difference of the unilateral putamen to caudate to be 2.62±0.45, 3.32±0.57, 1.95±0.46, 0.09±0.07, 0.58±0.09 and 0.11±0.10 respectively. The QuantiSPECT "crescent" method, after Chang attenuation correction, gave 1.68±0.44, 0.80±0.10, 0.09±0.06, 1.37±0.41 and 0.13±0.14 for the striatum, putamen to caudate, percent % difference of the unilateral putamen to caudate, putamen and percent difference of the unilateral putamen respectively. Finally, the specific binding index values, derived from the QuantiSPECT "two box" method after Chang attenuation correction, were 5.77±0.97 for the striatum and 0.06±0.05 for the percent difference of the unilateral striata. All values presented, if not otherwise stated, are the average values of left and right structures. Conclusion. As is common for every department performing 123I-PP-CIT SPECT studies we constructed a normal database from non-Parkinson patients showing no sign of neurodegenerative disease with the specific radiopharmaceutical. We consider crucial, adding to qualitative assessment, the absolute values given by the semi-quantification methods, as well as, the percent difference of the unilateral structures, especially those concerning the putamen. In the future, we plan to apply more strict criteria in order to lower the standard deviation of our measurements and expand the normal database using different age groups to cover the age dependency of the normal values.

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Aging Effects on Striatal F-18 FP-CIT Binding in Normals and Hemiparkinsonian Patients

S. Baek¹, J. Kim¹, S. Oh¹, D. Moon¹, J. Lee²; ¹Department of Nuclear Medicine, Asan Medical Center, University of Ulsan College of Medicine,

Seoul, KOREA, REPUBLIC OF, ²Department of Neurology, Asan Medical Center, Univ. of Ulsan College of Medicine, Seoul, KOREA, REPUBLIC OF.

Purpose: Dopamine transporter (DAT) imaging studies have consistently shown significant aging effects in the striatum of normal subjects. It is not known whether similar aging effects appear in the striatum of Parkinson's disease (PD) patients. We evaluated aging effect on F-18 FP-CIT binding of the striatum in the normal and hemiparkinsonian patients, and estimated the symptomatic threshold of striatal FP-CIT binding in Parkinson's disease. **Methods:** We prospectively performed F-18 FP-CIT PET/CT in 32 healthy normal volunteers and 21 drug naive hemiparkinsonian (H&Y stage I PD) patients. All patients were assessed for the severity of parkinsonism with UPDRS-III before PET imaging. PET/CT images were acquired 3 hours after intravenous injection of F-18 FP-CIT (185MBq). Specific to non-specific binding ratios (SNBRs) of FP-CIT were obtained in bilateral caudate and putamen using occipital cortex as a reference region. **Results:** Age was 50.0±17.2 yrs (mean±SD, range 24–82 yrs) in normal and 52.8±13.9 (range 31–78 yrs) in PD group. UPDRS-III scores of PD group were 12.1±6.2. Caudate and putamen SNBRs of normal group decreased linearly with aging ($y = -0.059 \cdot \text{age} + 10.897$ and $-0.052 \cdot \text{age} + 11.225$, respectively). Ipsi- and contra-lateral putamen SNBRs in PD group also decreased linearly with aging ($y = -0.054 \cdot \text{age} + 7.479$ and $y = -0.056 \cdot \text{age} + 6.781$, respectively). Our data showed significant aging effects on FP-CIT binding of the normal striatum, which were similar in the caudate and putamen, amounting to 4.6 to 5.4% of the value at birth per decade. Assuming that striatal FP-CIT binding of the newly diagnosed early PD patients was close to the symptomatic threshold, motor sign of PD group started when the loss of FP-CIT binding in the putamen was 44–53% of the age matched normal. **Conclusion:** There were significant aging effects on striatal F-18 FP-CIT binding in normal and also PD patients. The symptomatic threshold in the putamen FP-CIT binding of PD was 44–53% of the age matched normal.

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Semi-Quantification of DAT SPECT Images - Survey of Normal Reference Limits Used at Different Hospitals

K. Riklund¹, S. Jakobson Mo¹, A. Larsson², F. Jonasson Collett³, L. Edenbrandt⁴, E. Broedsgaard⁵, M. Nowak Lonsdale⁵, L. Friberg⁵; ¹Dept. of Radiation Sciences, Diagnostic Radiology, Umeå University, Umeå, SWEDEN, ²Dept. of Radiation Sciences, Radiation Physics, Umeå University, Umeå, SWEDEN, ³Dept. of Molecular and Clinical Medicine, Sahlgrenska University Hospital, Gothenburg, SWEDEN, ⁴Dept. of Clinical Medicine, Skåne University Hospital, Malmö, SWEDEN, ⁵Dept. of Clinical Physiology & Nuc. Med., Bispebjerg Univ. Hosp., Copenhagen, DENMARK.

Background: Interpretation of dopamine transporter (DAT) SPECT examinations comprise a visual inspection as well as a semiquantitative evaluation of the regional striatal up-take ratios of ¹²³I-labelled tracers correlated to a reference (background) region. Specific DAT binding traditionally is calculated from ROIs placed on transaxial slices as count rates (CR) in striatum and striatal subregions (caudate nucleus, putamen) divided by CR obtained from ROIs defining occipital cortex, cerebellum or the entire brain. Establishing normal values and significant thresholds are important to assist the interpretation. The aim of this survey was to compare different reference limits from four different hospitals where data was analysed using an automated, 3-D algorithm in defining the striatal ROIs and the reference region (whole brain). **Methods:** Normal values (mean, SD) and reference limits (mean-2 SD) for specific DAT uptake were collected from four different hospitals, using four different SPECT systems. Information about population, imaging parameters and calculated uptake-values are given in the table below. The EXINI DAT software was used for automated quantification at all hospitals. In two hospitals, groups of 'true' healthy volunteers were examined, whereas in the two other hospitals patients that retrospectively were found to have a normal DAT scan and no clinical signs of striatal affection. **Results:** The results are presented in the table below. Threshold values for putamen/caudate ratios were almost similar at all hospitals, but the values for specific uptake varied among hospitals. The reference limits for the three hospitals using OSEM, scatter- and attenuation correction (CT or line source) were roughly found within the same range, whereas the hospital using filtered backprojection and uniform attenuation correction (Chang) presented much lower values. Among the three hospitals using OSEM and non-uniform attenuation correction algorithms, the highest specific uptake values were found in the group of normals with the lowest mean age (60 years vs 66/67 years). **Conclusions:** Calculation of specific uptake ratios for DAT brain SPECT studies are dependent on the type of camera, collimator, acquisition, and reconstruction parameters and, hence, are not easily transferred among hospitals. However, calculation of the internal ratio between radioactivity in putamen and the caudate nucleus seems to be a fairly robust parameter comparable among data obtained with different SPECT systems.

Specific Uptake	Bispebjerg	Umeå	Malmö	Gothenburg
Mean (SD)				
Caudatus	7.5 (1.3)	6.1 (0.7)	5.6 (0.6)	5.1 (1.1)
Putamen	5.8 (1.1)	4.5 (0.7)	4.1 (0.5)	3.9 (0.8)
Striatum	6.6 (1.1)	5.2 (0.7)	4.8 (0.4)	4.4 (1.0)
Putamen/Caudatus	0.83 (0.05)	0.82 (0.04)	0.81 (0.05)	0.85 (0.05)
Lower Limits				
Caudatus	4.9	4.6	4.5	2.8
Putamen	3.6	3.1	3.2	2.3
Striatum	4.3	3.9	3.9	2.5
Putamen/Caudatus	0.73	0.73	0.71	0.76
Material				
Subjects	Normal volunteers	Normal volunteers	Patients	Patients
Number (Female/Male)	30 (17/13)	25 (11/14)	7 (4/3)	22 (15/7)
Age; mean (range)	60 (42/73)	67 (48-78)	66 (52-80)	60 (21-86)
Methods				
Camera	Prism 3000	Infinita GE	Siemens Symbia TG	GE Millennium
Collimator	LEUHR Fan beam	LEGP	LEHR	LEHR
Reconstruction	OSEM	OSEM	OSEM	FBP
Attenuation corr	Gd-153 line source	Low dose CT	Low dose CT	Chang
Scatter corr	Yes	TEW	DEW	No

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¹²³I-ioflupane (DaTSCAN™) dopaminergic brain SPECT: establishing semiquantitation reference values in a normal Greek population

S. Tsiouris, A. Papadopoulos, D. Dristiliaris, J. Al-Boucharali, T. Exarchopoulos, X. Xourgia, A. Georgiou, E. Koletsi, M. Tsironi, C. Bougias, E. Gkika, A. Fotopoulos; Univ. General Hosp. of Ioannina, GREECE.

Aim: ¹²³I-ioflupane (DaTSCAN™) brain SPECT is an established imaging modality to diagnose neurodegenerative parkinsonism (Parkinson disease and Parkinson-plus syndromes) and differentiate them from non-degenerative movement disorders like essential or drug-induced tremor. Although qualitative visual image reading yields high diagnostic accuracy, tracer uptake semiquantitation offers a non-subjective adjunct to visual interpretation, particularly useful in assessing images with subtle neuron deficits and quantifying tracer uptake decline between exams. We aimed to establish normal (reference) values of image semiquantitation in a Greek population. **Methods:** We retrospectively evaluated 77 individuals (35 males, 42 females) with normal visual brain SPECT interpretation that were studied in our department between 2004 and 2009. All ¹²³I-ioflupane scans were performed on the same gamma-camera (dual-head General Electric Millennium VG™), following a standardized data acquisition and reconstruction protocol: imaging 3.5–4.0 hours post-injection of 148–185 MBq tracer activity; LEHR collimation; matrix 128x128 pixels; 360° circular orbit in 120 frames (3°-angular step-and-shoot); frame time 40 sec; zoom factor 1.5; slice thickness 2.95 mm; Butterworth-filtered backprojection reconstruction algorithm (cut-off frequency 0.5 cycles/cm, filter order 7); Chang attenuation correction algorithm (linear attenuation coefficient 0.11/cm). We performed semiautomatic semiquantitative tracer uptake analysis on the 3 consecutive reconstructed transversal SPECT slices with maximal striatal tracer uptake, by manually defining ROIs over the left (L) and right (R) caudate nucleus (CAUD) and the putamen (PUT) and over the occipital cortex serving as background (BKG). From the mean counts within each ROI we calculated the following ratios: STR(L+R)/BKG (STR: total striatal activity = CAUD+PUT activity); CAUD(L+R)/BKG; PUT(L+R)/BKG; and PUT(L+R)/CAUD(L+R). We compared our results against a German normal database (Competence Web Parkinson: University Hospitals of Berlin, Essen, Kiel, Marburg, Munich) that came preinstalled in our imaging hardware. **Results:** Our results are summarized in the table:

Tracer uptake ratio	German reference database	Studied non-degenerative Greek population (77)	Males (35)	Females (42)
Mean ± SD				
STR/BKG	3.23±0.50	3.65±0.55	3.62±0.59	3.67±0.52
CAUD/BKG	3.64±0.53	3.80±0.59	3.74±0.62	3.84±0.56
PUT/BKG	3.02±0.56	3.50±0.53	3.50±0.57	3.49±0.49
PUT/CAUD	0.83±0.07	0.92±0.05	0.94±0.05	0.91±0.05

Compared to the reference database, all ratios in our population tended to be relatively higher, yet with comparable standard deviations denoting similar levels of results' uncertainty. **Conclusion:** Semiquantitative analysis is a useful adjunct to visual image reading. Since marked differences in ¹²³I-ioflupane uptake ratios have been described between different SPECT systems, each department should build its own reference database of normalcy. This will probably differ from the reference values coming preinstalled-in-hardware or in the literature, since they directly reflect and depend on the specific data acquisition and image processing parameters used within each individual imaging chain. Furthermore, these normal values could be influenced by racial or other factors related to each studied population.

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Could FP-CIT SPECT Detects Bilateral Impairment of Nigrostriatal Pathway in Parkinson Disease Hoehn & Yahr 1 Stage?

C. Lorenzo-Bosquet¹, J. Hernández-Vara², G. Cuberas-Borrós¹, J. Álvarez-Sabín², J. Castell-Conesa¹; ¹Nuclear Medicine Service, Hospital Universitari Vall d'Hebron, Barcelona, Catalonia, SPAIN, ²Neurology Service, Hospital Universitari Vall d'Hebron, Barcelona, Catalonia, SPAIN.

Aim: To evaluate nigrostriatal impairment in "de novo" Parkinson's disease (PD) patients with unilateral disease using ¹²³I-FP-CIT SPECT. **Material and methods:** 46 patients were included (28 women), mean age 61.72±10.42 with diagnosis of PD according to established clinical criteria, stage Hoehn-Yahr I. A complete neurological evaluation (including UPDRS motor subscale) and a ¹²³I-FP-CIT SPECT was performed to all of them. SPECT images were qualitatively and quantitatively analysed using volumes of interest (VOIs). SPECT quantitative values were compared to a reference group (20 patients with essential tremor (ET), 3-years follow-up, mean age 61.5 ± 16.4). **Results:** 35 patients showed bilateral decreased uptake in FP-CIT. PD patients showed lower FP-CIT uptake in the putamen contralateral to the affected side. Quantitative uptake values are summarized in the following table:

	Maximum (ipsilateral)	Minimum (contralateral)
ET putamen	2.73 ± 0.32 (2.35 - 3.65)	2.57 ± 0.30 (2.14 - 3.23)
PD putamen	2.33 ± 0.29 (1.56 - 2.83)	2.11 ± 0.33 (1.42 - 2.74)
ET caudate	2.35 ± 0.33 (1.76 - 3.34)	2.24 ± 0.31 (1.70 - 2.99)
PD caudate	2.29 ± 0.23 (1.80 - 2.74)	2.09 ± 0.29 (1.45 - 2.73)
	<i>mean ± SD (min-max)</i>	

Quantitative analysis in PD patients compared to the reference group, showed significant ($p < 0.0001$) reduction in both ipsilateral and contralateral putamen uptakes, being more evident in the putamen contralateral to the affected side. No significant differences between groups in caudate uptake were observed. **Conclusion:** FP-CIT SPECT is able to detect bilateral nigrostriatal dysfunction in patients with one-side symptoms and might be a useful tool to identify neuronal loss in presymptomatic or premotor phases of the disease.

P339**Usefulness, Etiology and Diagnostic relevance of a normal presynaptic dopamine transporter 123I-FPCIT SPECT Scan (DaTSCAN)**

J. Pou, A. M. Alvarez, A. Serena, F. Loira, S. Valle, J. Barandela, J. M. Nogueiras, L. Campos; Hospital Do Meixoeiro (CHUVI), VIGO, SPAIN.

Aim: A normal DaTSCAN rule out a degenerative disorder of the nigrostriatal pathway. The aim of the study was to access the meaning, diagnostic relevance and security of these normal findings in our hospital complex. **METHODS:** Review of normal DaTSCAN records evaluated by visual assessment from 2005-2009. A clinical form was completed by experienced neurologist pointing out the main (MainDx) and possible alternative diagnosis (AltDx) in three times: (A) PRE-DaTSCAN, (B) POST-DaTSCAN and (C) FOLLOW-UP. Every patient was classified according to the security level of the diagnosis from 1 (low) to 5 (very probable), the therapeutic modifications in the follow up and the usefulness of the test. **RESULTS:** 94 Normal scans from 370 studies. 55/94 (59%) responses. 55 patients reviewed. (A) **PRE-DaTSCAN:** Mean age: 66.9 years-old; Average follow-up: 53.4 months; Predominant symptoms: 54.5% Tremor; 22%-rigid-akinetic; 20%-equivalent; 3.6% other. Dopaminergic therapy: 42.9% (response: 21.4%-poor, 16.1%-regular). MainDx pre-scan: Essential Tremor (ET) 21.4%, 17.9% Pharmacological Pk; Early PD 19.6%; 10.7% Atypical/incomplete PD; 14.3% other degenerative Pk; 14.3% others. Diagnostic Security PRE: 37.4% Probable, 3.6% Very Probable; Mean security level: 3.33. (B) **POST-DaTSCAN:** Normal scan results modified the MainDx in 42.9% (28.6 to AltDx, 14.3% to a new diagnosis). MainDx post: 48.2% ET; 17.9% drug Pk, 5.4% vascular Pk, 14.3% PD or other degenerative diseases. 46.3% evidenced of therapeutic modifications (53% without changing Dx), antiparkinsonian medication withdrawal in 13. Diagnostic security POST was increased in 64.3%: 33.9% Probable; 44.6% Very Probable; Mean level: 4.24. (C) **Follow-up:** 100% maintains MainDx, except those who were lost in the follow up. Mean security level: 4.52. Average follow-up: 66 months (mean 14 months after scan). **Usefulness:** 76.8% considered DaTSCAN as a very or fairly useful test; 7.6% false negative or a confusion factor (2 EPI/SWEDD 1 LBD, all of them pending evolution). **CONCLUSIONS:** 1) In our hospital complex, ET has been the most frequent cause of a normal DaTSCAN (48%), almost half of them previously considered a Degenerative Parkinsonism; 18% of normal DaTSCAN had a pharmacological cause, 90% previously suspected. 2) A normal DaTSCAN finding often modifies the diagnosis and/or therapeutic attitude, 3) The assured diagnosis by the normal scan remains in follow-up, 4) More than 75% of clinicians consider the test useful 5) However, in 14% the normal DAT is not concordant with clinical suspicion, most cases expecting a longer follow-up.

P340**123I-ioflupane FP-CIT (DaTSCAN) in differential diagnosis of Parkinson's disease**

L. Brajkovic¹, M. Svetel², V. Kostic², E. Stefanova², I. Petrovic², T. Stojkovic², S. Pavlovic¹, D. Sobic-Saranovic¹, V. Artiko¹, V. Obradovic¹; ¹Center of nuclear medicine, Belgrade, SERBIA, ²Institute of Neurology, Belgrade, SERBIA.

Brain SPECT with DaTSCAN is objective neuroimaging method for assessment of nigrostriatal dopaminergic system integrity and degeneration. Pathological degenerative nigral cell loss leads to decreased concentration in presynaptic dopamine transporters (DAT) and decreased uptake of 123I-FP-CIT (DaTSCAN) in striatum in Parkinson's disease (PD). Objective: To evaluate usefulness of brain SPECT with 123I-ioflupane FP-CIT in differential diagnosis of PD. Materials and methods: We performed brain SPECT-DaTSCAN in 75 patients (41 males, 34 females) age 21-80 with clinically unclear parkinsonism. Study was performed 3-5 hours after intravenous injection 145-185MBq 123I-ioflupane-FP-CIT (DaTSCAN, Amersham, GE Healthcare) Image acquisition was carried out with a Mediso Nuclear Spirit, double-headed gamma camera equipped with low-energy, parallel-hole, high-resolution collimators. Images were acquired using a full 360 rotation in step and shoot mode (128 projections, matrix 128x128, pixel size 3, 84mm, 40 seconds per projection). Image reconstruction was performed using Filtered back projection method, with Butterworth filter (cut off 0.5 order 7) and attenuation correction (Chang method, factor 0.12) The images were evaluated by visual and semiquantitative analyses. For the analyses of striate binding, the ratio of specific- striate to non specific-occipital binding was calculated. Regions of interest (ROI) were positioned on the referents transverse slice (representing the most intense striatal uptake) on both striatal (caudate n, putamen) and occipital regions, and calculated ratio. Results: In 38 patients brain-SPECT have shown decreased uptake of DaTSCAN in striatum, bilaterally, symmetrically or asymmetrically, especially in putamen, and confirmed Parkinson's disease diagnosis (10 patients with young onset Parkinson's disease, 9 patients in early stage of disease). 18 patients with Parkinsonian syndromes (PS) (7 with autonomic dysfunction and suspected multiple system atrophy (MSA), 5 patients with suspected progressive supranuclear palsy (PSP), 4 patients with Dementia Lewy body (DLB) and 2 patients with suspected corticobasal degeneration (CBD) have reduction of accumulation 123I-ioflupane in striatum. Five patients with suspected Dystonia and 9 patients with atypical statoposturokinetic tremor and uncertain diagnosis-Parkinsonian syndrome or Essential tremor (ET) have normal DaTSCAN, and confirmed diagnosis Dystonia (D) and ET. Five patients with suspected drug induced parkinsonism (DIP) have normal DaTSCAN. Conclusion: Our results indicate that DaTSCAN is a useful diagnostic procedure for detecting nigrostriatal degeneration and differentiating neurodegenerative disease (PD, MSA, PSP, DLB, CBD) from other conditions such as ET, DIP, and D. DaTSCAN especially useful in young patients with atypical clinical signs and early stage of PD.

P341**Statistical parametric mapping of FP-CIT SPECT reveals regional differences in striatal dopamine transporter density between tremor-dominant and akinetic-rigid subtypes of early Parkinson's disease**

A. Maschur, J. Spiegel, A. Grgic, A. P. Hellwig, G. Farmakis, U. Dillmann, K. Fassbender, C. M. Kirsch, D. Hellwig; Saarland University Medical Center, Homburg, GERMANY.

Aim: Recently we demonstrated that striatal dopamine transporter (DAT) density as determined by region-of-interest (ROI) analysis of FP-CIT SPECT differs between tremor-dominant (TD) and akinetic-rigid (AR) subtypes of early Parkinson's disease (PD). These results were both confirmed and denied by other researchers. Automated voxel-based statistical methods, such as statistical parametric mapping (SPM) has been shown to be more sensitive and operator independent compared to ROI analysis. Thus, we performed an SPM analysis to further characterize the regional differences in striatal DAT density between TD and AR subtypes of early PD. Patients and methods: This retrospective study included a total of 48 patients (58±10 years) with early PD with symptoms duration 2 years follow-up. Subscores of the Unified PD Rating Scale (UPDRS) were used to define a TD subtype (n=19), an AR subtype (n=14), and a mixed subtype. All patients underwent SPECT imaging 4 h after injection of 185 MBq I-123-FP-CIT. SPECT images were iteratively reconstructed. A FP-CIT normal template for SPM was generated after supervised coregistration (MultiModalityTool, HERMES Medical Solutions, Sweden) of SPECT images from normal controls with the T1 weighted normal MRI template from SPM99. For SPM analysis all SPECT images were normalized to uptake in their posterior cortex (self made MATLAB program), mirrored for patients with left sided symptoms and coregistered with our new FP-CIT template which was transferred into SPM99. Voxelwise independent t-tests of FP-CIT SPECT images between TD and AR were performed with SPM99. Specific binding ratios (SBRs) were measured by ROIs in putamen and caudate nucleus contralateral to the clinically affected side. Results: SBRs in clinically contralateral putamen and caudate nucleus were higher in patients with TD subtype than in AR subtype (putamen: 1.32±0.44 versus 0.78±0.28; caudate nucleus: 1.45±0.37 versus 0.99±0.33; p<0.02). Conclusions: The loss of DAT density in AR subtype in comparison to the TD subtype is located in the lateral parts of the clinically affected contralateral putamen and caudate nucleus and might be used to further characterize the subtypes of early PD.

P342**A study about the integrity of the striatal dopamine transporters in early-onset Parkinson's disease in a Spanish family using 123I-ioflupane**

J. Herrera-Henríquez¹, M. Isla-Gallego¹, F. Armas-Serrano¹, M. Santana-Borbones¹, M. Ochoa-Figueroa¹, J. Miranda-Ramos¹, O. Lorenzo-Betancor², M. Hernández-Briz¹, P. Pastor²; ¹Hospital Universitario Insular de Gran Canaria, Las Palmas, SPAIN, ²Clínica Univ. de Navarra, Pamplona, SPAIN.

A study about the integrity of the striatal dopamine transporters in early-onset Parkinson's disease in a Spanish family using ¹²³I-ioflupane. Introduction: The Early-Onset Parkinson's Disease (EOPD) is an autosomal recessive syndrome whose phenotype is characterized by an early onset, before 50 years, and an adequate levodopa responsive parkinsonism. The syndrome has been associated to three mutated genes: *PARKIN*, *PTEN-induced putative kinase 1 (PINK1)* y *DJ-1*, with variable results according to several studies. On the other hand, ¹²³I-ioflupane is useful in the assessment of patients with Parkinsonism. Objective: To analyze visually and quantitatively the striatal dopamine transporters binding ¹²³I-ioflupane in a Spanish family with several members with Parkinsonism who were carriers *PINK1* mutated gen. Materials and methods: We studied 31 members of an early-onset Parkinson's disease Spanish family with 6 affected individuals. All family members underwent a neurological examination and genetic analysis, and in eight individuals ¹²³I-ioflupane Brain SPECT examination was also performed. Tracer specific ¹²³I-ioflupane uptake binding ratio (¹²³IUBR), right/left asymmetry ratio for different ROI (Asym) and putamen-caudate uptake ratio (PC) were calculated. SPECT acquisition was analyzed visually. Results: Two segregating pathogenic *PINK1* mutations were found: an exon 7 deletion (g.16089_16383del293;c.1252_1488del) and a splicing mutation in exon 7 (g.16383A>G;c.1488+1G>A).

Results in 123I-ioflupane Brain SPECT examination.

Patien	Sex/ Age	Symptoms/Desea se duration	Genotype	Visual analysis	¹²³ IUBR R/L	Asym P/C/Whole striatum	PC R/L
1	F/63	Asymptomatic	Exon 7 deletion carrier	Normal	3.13/3.0 2	1.04/1.06/1.0 3	0.92/0.9 4
2	M/36	Asymptomatic	Homozygous (splicing mutation)	Bilateral putamen hypointens y	3.01/3.1 9	1.03/0.98/1.0 1	0.64/0.6 0
3	M/38	PD/<1	Heterozygou s, double mutations	Bilateral putamen hypointens y	3.23/2.9 3	1.18/1/1.10	0.70/0.6 0
4	M/17	Minor Parkinson's disease signs/3	Heterozygou s, double mutations	Absence of signal in right putamen, left putamen hypointens y	1.12/1.4 6	0.75/0.88/0.7 7	0.51/0.5 9
5	M/40 , Exitu s	PD/6	Heterozygou s, double mutations	Absence of signal in putamen, left caudate hypointens y	0.96/0.8 8	1.04/1.08/1.0 9	0.35/0.3 6
6	F/40	PD/9	Homozygous (splicing mutation)	Bilateral putamen hypointens y	1.93/1.8 8	1.11/1.05/1.0 3	0.37/0.3 8

7	M/36 PD/9	Heterozygous, double mutations	Absence of signal in putamen, caudate	1.82/1.7	0.92/1.03/1.0	0.43/0.4
			hypointensity	7	3	9
8	F/67 PD/22	Heterozygous, double mutations	Absence of signal in putamen, caudate	1.80/2.1	1.03/0.80/0.8	0.58/0.4
			hypointensity	0	6	5

Conclusions: ^{123}I -Ioflupane Brain SPECT revealed a posterior-anterior gradient similar to idiopathic Parkinson's disease. We found no correlation between nigrostriatal denervation and disease duration and no difference in patterns of dopaminergic activity between homozygous and heterozygous carriers, suggesting a similar biological effect of both mutations.

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Clinical diagnostic value of dopamin transporter imaging with ^{123}I -ioflupane (DaTSCAN) - two years of experience

R. Petrovic¹, T. Samardzic¹, S. Telarovic², N. Klepac², L. Unusic², M. Relja²; ¹Clinical Department of Nuclear Medicine and Radiation Protection, Clinical Hospital Centre Zagreb, Zagreb, CROATIA, ²Neurology Clinic, Clinical Hospital Centre Zagreb, Zagreb, CROATIA.

Aim: to evaluate clinical effectiveness of ^{123}I -ioflupane brain SPECT as useful diagnostic tool in detection of nigrostriatal neuronal integrity in patients with clinical diagnosis of Parkinson's disease (PD) and essential tremor (ET). **Materials and methods:** In group of 93 patients, 49 males and 44 females with clinical diagnosis of PD (43) and ET (50) a dose of 185 MBq of ^{123}I -ioflupane was administered and SPECT conducted 4 hours after radiotracer injection. Images were analyzed qualitatively (visually classifying SPECT images as: 0-normal or positive for PS as: 1-mild, 2-moderate, 3-severe) and semiquantitatively using ROI based method calculating specific (caudate, putamen and striatum) versus nonspecific uptake (occipital). **Results:** In a group of 50 patients (54% of all patients) clinically suspected to have ET the ^{123}I -ioflupane brain SPECT was normal in 17 (34%) patients while 33 (66%) others showed mild to severe pathologic reduction in striatal uptake. This findings resulted in immediate therapy change for those 66% of patients. In group of 43 patients with clinical suspicion of PD, pathologic reductions in striatal ^{123}I -ioflupane uptake were found in 35 (81%) patients, while 8 (19%) patients have normal scans. Clinical disease severity of those patients with pathological scans was assessed using the Hoehn and Yahr (H&Y) rating scale. Striatum, caudate and putamen uptake ratios were significantly reduced, even in early stage of disease and S/NS ratios highly correlated with the disease stages and severity assessed by H&Y rating scale, and also with the duration of disease. Looking at whole group of all 93 patients there was confirmation of clinical PD diagnosis in 35 (38%) patients (thus increasing clinical confidence), non-PD confirmation in 17 (9%) patients (decreasing clinical confidence), diagnose is changed to PD in 33 (35%) patients and changed to non-PD in 8 (18 %) patients. All patients benefited from ^{123}I -ioflupane SPECT, mostly the group of 35% patients whose diagnose switched from suspected ET to PD (new therapy was initiated). Specific therapy was withdrawn in 18% of patients while 38% patients confirmed as PD gained mostly from avoidance of other preplanned tests and fewer follow-ups. **Conclusion:** ^{123}I -ioflupane brain SPECT has an important (sometimes even crucial) role in detecting and monitoring nigrostriatal dopaminergic degeneration and should be routinely used in clinical practice to support the diagnosis of PD and differentiate between other conditions. Moreover, ^{123}I -ioflupane brain SPECT can be used as important contribution to the early diagnosis of PD.

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Investigating Diagnostic Possibilities of SPECT Imaging in Early Parkinson's Disease

P. Tomše¹, B. Starovasnik¹, I. Slodnjak¹, J. Fettich¹, M. Grmek¹, Z. Pirtošek², M. Trošt²; ¹University Medical Centre, Nuclear Medicine Department, Ljubljana, SLOVENIA, ²University Medical Centre, Neurology Department, Ljubljana, SLOVENIA.

Parkinson's disease (PD) manifests with many motor and non-motor signs and symptoms. It is assumed that these abnormalities are related to altered activity of specific brain regions. The aim of our study was to investigate brain perfusion changes of PD patients with perfusion Single Photon Emission Computed Tomography (SPECT) images and to relate them with results of the neuropsychological testing. Twelve patients with early "de novo", stage of PD (mean age: 55 ± 9 yrs; male/female: 8/4; education level: 12 ± 2 yrs) and 13 healthy volunteer controls (mean age: 54 ± 8 yrs; male/female: 8/5; education level: 13 ± 2 yrs) were included in the study. $^{99\text{m}}\text{Tc}$ -ECD brain perfusion images of controls (CTR) and patients prior to (PD1) and following the 3-month treatment with dopamine agonist pramipexole (PD2) were acquired. Regional cerebral perfusion of the three groups was compared using voxel by voxel image analysis with statistical parametric mapping (SPM8; Institute of Neurology, London, UK). Additionally, we assessed the effect of pramipexole therapy on motor and executive functions, using Unified Parkinson's Disease Rating Scale motor subscale (UPDRS-II) and the Tower of London Test (TLT) test in both groups across two sessions. SPECT image comparison CTR:PD1 revealed PD1 having relative hypoperfusion in parietal cortex (BA 7, 19, 40), in primary visual cortex in occipital lobe (BA 17) and in frontal cortex in supplementary motor area (BA 6) ($p < 0.005$). PD2:PD1 comparison showed hypoperfusion of PD1 in the areas involved in dopaminergic cortico-striato-thalamo-cortical loops [1,2,3]: BA 9, 17, 18, 24, 40, 46, and again in BA 6 ($p < 0.005$). In neuropsychological TLT significant differences were found between CTR:PD1 ($p < 0.014$), but not anymore between CTR:PD2 ($p < 0.42$). UPDRS-II motor subscale score was significantly different for PD1:PD2 ($p < 0.001$). PD patients' hypoperfusion in BA 7, 19 and 40 relative to controls is in agreement with previous findings [2,3] whereas observed hypoperfusion in BA 6 can be associated to inhibition of movements planning and is supported with results in CTR:PD1 and CTR:PD2 neuropsychological TLT. PD2:PD1 SPECT image comparison confirms increased perfusion after dopaminergic therapy and is supported by UPDRS-II scores. Results of SPM analysis of SPECT images are thus well

supported by clinical and neuropsychological observations and our study illustrates that despite of limiting resolution of SPECT imaging modality voxel-based analysis of $^{99\text{m}}\text{Tc}$ -ECD SPECT images holds considerable potential for assessing brain activity abnormalities in early PD patients, as well as the effect of dopamine agonist therapy.

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$^{99\text{m}}\text{Tc}$ -HMPAO and ^{123}I -FP-CIT SPECT Imaging in Patients with Essential Tremor

P. Tamayo, C. Montes, J. Cacho, E. Martin, R. Ruano, D. Garcia, F. Gomez-Camirero, A. Rosero, J. R. Garcia-Talavera; University Hospital of Salamanca, SALAMANCA, SPAIN.

INTRODUCTION. Essential tremor (ET) is one of the most prevalent neurological disorders but the exact pathophysiology is still unknown. It has been hypothesized that ET could be a neurodegenerative disease with cerebellar involvement. However, there are some controversial data on the literature about the role that cerebellum plays in ET. **The aim** of this study was to assess the presence of regional cerebral blood flow (rCBF) abnormalities in the cerebellum in nondemented patients with ET. **MATERIAL AND METHODS.** We have assessed 23 patients (ten males; mean age 75 years) without dementia who met published diagnostic criteria for ET with $^{99\text{m}}\text{Tc}$ -HMPAO and ^{123}I -FP-CIT SPECT techniques and 22 neurological normal subjects (8 males; mean age 70 years) as controls with $^{99\text{m}}\text{Tc}$ -HMPAO brain SPECT imaging. All subjects remained at rest conditions 10 minutes before and 10 minutes after a bolus intravenous injection of 740 MBq of $^{99\text{m}}\text{Tc}$ -HMPAO SPECT images were analysed with the SPM5 software package using a two-sample t-test was used to investigate differences of rCBF between patients and controls. The significance threshold was set at $p < 0.001$ uncorrected for multiple comparisons and $k > 50$ voxels for cluster extent. **RESULTS.** All patients showed normal striatal ^{123}I -FP-CIT uptake, revealing integrity of the presynaptic nigrostriatal dopaminergic system. However, our results did not show statistical differences in rCBF in the cerebellum between patients and controls. **CONCLUSIONS.** Our results showed that SPECT with FP-CIT, a dopamine transporter ligand, is a reliable means to identify patients with ET. In addition, our study could not find rCBF abnormalities in the cerebellum of patients with ET, which raises doubt about the role that cerebellum plays in ET.

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The contribution of I-123 ioflupane SPECT in diagnosis of patients with parkinsonian syndromes

E. Zaromitidou¹, M. T. Siabanopoulou², C. Bairaktaris³, S. El-Mantani Oroulidis²; ¹Nuclear Medicine Dept. Kavala General Hospital, Kavala, GREECE, ²Nuclear Medicine Dept., Biomed Diagnostics, Thessaloniki, GREECE, ³Department of Neurology, 401 Army Hospital, Athens, GREECE.

Background: Parkinsonism is diagnosed when a patient presents two out of the following three symptoms: resting tremor, rigidity and bradykinesia. There is an overdiagnosis of Parkinson's disease in about 25% of patients. Dopamine transporter imaging (DAT) is a sensitive method to detect presynaptic dopamine neuronal dysfunction, which defines neurodegenerative parkinsonism. DATscan can therefore assist the differentiation between conditions with and without presynaptic dopaminergic deficit. Diagnosis of Parkinson disease or tremor disorders can be achieved with high degrees of accuracy in cases with full expression of classical clinical features. **Objective:** This study investigates the correlation between striatal dopamine transporter (DAT) binding, measured with ^{123}I -FP-CIT SPECT, and motor handicap in a group of 35 patients diagnosed with Parkinson's disease. Patients were examined using the motor subscale of the Unified Parkinson's Disease Rating Scale (UPDRS) and the modified Hoehn and Yahr (H&Y) scale. **Methods:** Over a year 35 patients with the diagnosis of Parkinsonism or uncertain tremor disorder were screened and enrolled in our study. Patients were examined by neurologists and were classified as neurodegenerative or non- neurodegenerative disorders. Each patient was subjected to SPECT imaging using I-123 ioflupane. Patients ratio of caudate nucleus-occipital/occipital (CN/O) lobe and putamen-occipital/occipital (P/O) lobe was estimated and compared with a control group. **Results:** Our results demonstrated a statistically significant negative correlation between H&Y and UPDRS motor score (i.e. with disease stage and motor handicap) and the binding ratio for the right and left caudate and putamen regions. Thus, the loss of DAT binding correlates with disease severity and motor handicap in patients with Parkinson's disease. **Conclusions:** DATscan, in conjunction with the clinical data, is considered as of significant clinical importance, not only for the objective confirmation of presynaptic nigrostriatal degeneration, but also and in particular for the early differential diagnosis from nondegenerative movement disorders. SPECT with I-123 ioflupane may prove a cost effective method aiding the neurologist in the evaluation and therapeutic intervention of patients presenting with clinically uncertain parkinsonian syndromes or patients with emerging diagnostic doubt.

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Brain SPECT with ^{123}I ioflupane (FP-CIT)-DATSCAN in differential diagnosis of Dopa-Responsive Dystonia and Young-Onset Parkinson's disease

L. Brajkovic¹, M. Svetel², V. Kostic², E. Stefanova², I. Petrovic², T. Stojkovic², S. Pavlovic¹, D. Sobic-Saranovic¹, V. Artiko¹, V. Obradovic¹; ¹Center of Nuclear Medicine, Belgrade, SERBIA, ²Institute of Neurology, Belgrade, SERBIA.

Dopa-responsive dystonia (DRD) is genetic disorder characterized by childhood onset dystonia, dominant inheritance, diurnal symptoms fluctuation and positive levodopa response. Adult-onset disease is frequently combined with Parkinsonism and can be mistaken with young onset Parkinson's disease (YOPD). Both conditions are caused by dopamine deficiency, due to nigral cell loss in YOPD, and enzymatic defects in dopamine synthesis in dopaminergic neurons in DRD. DaTSCAN is sensitive neuroimaging method for assessment of nigrostriatal dopaminergic system integrity and degeneration. The loss of neurons leads to decreased concentration in presynaptic dopamine transporters (DAT) and decreased uptake of ^{123}I -FP-CIT in striatum in YOPD. **Purpose:** To evaluate usefulness of SPECT-DATSCAN in differential diagnosis of DRD and YOPD. **Method:** We performed brain SPECT with ^{123}I -FP-CIT in 13 patients (11 patients with YOPD and two with genetically proved DRD). Study was performed 3-5 hours after intravenous injection 145-185MBq

123I ioflupane-FP-CIT (DaTSCAN, Amersham, GE Healthcare) Image acquisition was carried out with Mediso Nuclear Spirit, double-headed gamma camera (128 projections, matrix 128x128, pixel size 3, 84mm, 40 seconds per projection). Images were reconstructed using Filtered back projection method, with Butterworth filter (cut off 0, 5, order 7) and attenuation correction (Chang method, factor 0, 12). The images were evaluated by visual and semiquantitative analyses (ROI). The ratio of specific- striatal to non specific-occipital binding was calculated. Results: Thirteen patients (7males, 6 females), age 20-58 years, with mean age of onset 31years, with early onset parkinsonian symptoms (11) and DRD (2) were analysed. Ten out of 11 patients with YOPD had decreased accumulation of DaTSCAN in striatum, especially in putamen, what are typical findings for Parkinson's disease. In three patients DaTSCAN was normal-symmetric tracer uptake in both striata (caudate n, putamen) and the diagnosis of DRD was hypothesized. Two patients with initial dystonic symptoms, with genetically proved DRD have normal DaTSCAN. In one patient initial diagnosis YOPD after normal DaTSCAN finding was changed to diagnosis DRD. ROI analyses have shown significantly lower [123I]-FP-CIT binding ratios in YOPD than those in DRD in all regions of interest: striatum(1,95±0,32) : (2,76±0,10) p<0,001, putamen (1,76±0,25) : (2,84±0,14) p<0,0001, caudatus (2,37±0,51) : (3,27±0,14) p<0,01. Conclusion: Our preliminary results indicate that DaTSCAN is an objective neuroimaging method competent to distinguish YOPD from DRD and clarify clinical dilemma. Clarification of the diagnosis is important for the treatment, prognosis and genetic counselling of patients and families.

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Preliminary evaluation of nigrostriatal dopaminergic pathway with I123-iodoflupano SPECT in patients with Machado-Joseph disease

A. C. Hernandez Martinez, M. D. Marin, J. Coia, D. Mendez, S. Rodado, C. Escabias, I. Santos, R. Cazorla, J. Arpa, L. M. Martin; Hospital La Paz, Madrid, SPAIN.

AIM: Spinocerebellar ataxia type 3 (SCA 3) or Machado Joseph disease (MJD) is an unusual neurodegenerative hereditary disease characterized by cerebellar ataxia and occasionally Parkinsonian symptoms. The aim of our study is to evaluate the nigrostriatal dopaminergic pathway (NDP) in symptomatic patients with I123-iodoflupano brain SPECT. **MATERIAL AND METHODS:** From March 2009 to February 2010 we performed eleven I123-iodoflupano brain SPECT in patients with symptomatic MJD (mean age 55.2, age range 27-72). All patients were genetically confirmed (expansion of the CAG trinucleotide repeats). We assessed age at disease onset, disease duration, abnormal CAG repeat length, family history MJD, and clinical involvement using SARA score (values between 0-40, meaning 0 score asymptomatic and 40 score severe symptoms). To evaluate brain SPECT we performed visual analysis of the imaging and we divided it in 3 groups according to the level of the NDP damage: mild (unilateral), moderate (bilateral, both putamenes), severe (bilateral, both putamenes and uni/bilateral caudates). **RESULTS:**

Patient	Age (years)	Age at disease onset (years)	Disease duration (years)	Family history (yes/no)	SARA score	Expanded CAG repeats	Level damage (brain SPECT)
1	72	45	7	Yes	12,65	65	Mild
2	65	56	9	Yes	10	61	Mild
3	60	55	5	Yes	8,25	63	Mild
4	60	31	29	Yes	26,75	70	Moderate
5	54	42	12	No	15	72	Moderate
6	73	62	11	Yes	15	65	Moderate
7	45	43	2	Yes	8,25	68	Moderate
8	48	42	6	Yes	2	72	Moderate
9	60	55	5	Yes	8	65	Severe
10	43	21	22	Yes	8	72	Severe
11	27	25	2	Yes	6	75	Severe

Pathological findings were found in all patients. We did not find statistically significant differences between level of NDP damage and the other evaluated parameters (p>0.05). **CONCLUSIONS:** I123-iodoflupano brain SPECT was able to evaluate nigrostriatal dopaminergic pathway damage in all symptomatic Machado Joseph disease patients and might be helpful for understanding the disease and the management of affected patients. There was no correlation between the level of nigrostriatal dopaminergic pathway damage in brain SPECT and age at disease onset, disease duration, SARA score and expanded CAG repeats, however it would be necessary a larger sample of patients to establish definitive conclusions.

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Significance of dopamine transporter imaging (I-123 ioflupane SPECT) in patients with Wilson disease

T. Samardzic, R. Petrović, M. Relja; University Hospital Zagreb, Zagreb, CROATIA.

AIM: Wilson's disease, known as progressive hepatolenticular degeneration is an autosomal recessive disorder of impaired copper metabolism, characterized by hepatic and neurological symptoms. Except liver symptoms, the most common neurological manifestations are parkinsonism and dystonia due to striatal damage. The aim of our ongoing study is to evaluate the effectiveness of brain SPECT with I123-iodoflupane as a useful and effective diagnostic tool in detection of presynaptic nigrostriatal dopaminergic deficit in Wilson's disease. **Materials and methods:** In carefully selected group of 12 patients, 9 men and 3 women, mean age of 40,7 years (range from 28 to 61), identified by strict predefined criteria from experienced neurologist, with clinical diagnosis of hepatolenticular degeneration a dose of 185 MBq of I123-iodoflupane was administered and SPECT imaging performed 3-6 hours after radiotracer injection. Images were reconstructed and reoriented on Odyssey FX820 workstation and analyzed visually and semiquantitatively using region-of-interest based method. The ratio of the mean specific-to-nonspecific striatal binding for the entire striatum (S/NS) was calculated in all patients and compared with those from literature. **Results:** In a group of twelve patients diagnosed as

hepatolenticular degeneration the I123-iodoflupane brain SPECT was normal only in 3 patients while 5 patients showed mild pathologic reduction of striatal uptake. Mild to moderate reduction in striatal uptake was found in one patient while other 3 patients had moderate pathologic reduction of striatal uptake. So, in 9/12 patients (75%) the I123-iodoflupane scans were pathological, and in the other 3 patients findings were normal (25%). In majority of examined patients with hepatolenticular degeneration apparent loss of the I123-iodoflupane uptake in the striatum suggested significant damage in presynaptic nigrostriatal dopaminergic nerve terminals. **Conclusion:** Our experiences shows that a great number of our patients with Wilson's disease have pathological striatal uptake. Because of those findings, we think that I123-iodoflupane brain SPECT have an important role in detecting and monitoring nigrostriatal dopaminergic degeneration and could be routinely used in clinical practice to support the diagnosis and follow-up of patients with hepatolenticular degeneration.

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Contribution of FP-CIT-I-123 in the differential diagnosis between Parkinson's disease and multiple system atrophy subtype P. Evaluation of quantitative parameters.

E. Ramos-Moreno, M. Martinez del Valle-Torres, S. Ortega-Lozano, T. Amrani, S. Sanz-Viedma, J. Jimenez-Hoyuela; University Hospital "Virgen de la Victoria", Malaga, SPAIN.

Aim: To assess the individual contribution of several parameters extracted from the quantitative evaluation of tomographic scan with FP-CIT in the differential diagnosis between Parkinson's Disease (PD) and multiple system atrophy subtype P (MSA-P). **Material and Methods:** The study include 23 patients with probable clinical diagnosis of MSA(mean age: 67.3 ± 11.2) and 25 PD (63.16 ± 10.60), according the established criteria for each entity. Using ROIs, we calculate the ratio between specific and nonspecific activity (S/O = average counts in striatum / average counts in occipital), asymmetry index (AI = average counts in striatum with more activity / striatum with less activity) and index of regional involvement (C/ P = average counts in caudate / average counts in putamen). For each index is calculated the area under the curve and another parameters by ROC curve analysis. **Results:** The average value of analyzed indexes showed: **S/O:** PD: 1.29 ± 0.15, MSA: 1.13 ± 0.16 (p = 0.001); **AI:** PD: 7.44 ± 2.02, MSA: 3.39 ± 2.04 (p = 0.00); **C/P:** PD: 1.26 ± 0.14, MSA: 1.15 ± 0.12 (p = 0.01). ROC curve analysis: **S/O Index:** Az: 0.810 (95% CI: 0.671-0.909). Optimal cutoff: 1.24, sensitivity (S): 91.3%, specificity (Sp): 72.0%, LR +: 2.48. **AI Index:** Az: 0.890 (95% CI: 0.767-0.962). Optimal cutoff: 3 (S: 73.9%, E: 100%, LR +: 9.24. **C/P Index:** Az: 0.702 (95% CI: 0.552-0.825). Optimal cutoff: 1.2 (S: 69.6 % E: 72%, LR +: 2.48. **Conclusions:** The asymmetry index (AI) extracted from quantitative analysis of FP-CIT study, is the parameter which provides better predictive power for the differential diagnosis between PD and MSA-P.

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I123-FP-CIT striatal uptake and I123-MIBG heart scintigraphy in CADASIL patient affected by parkinsonism

A. Berbellini, G. Cacchiò, E. Di Luzio, F. Di Marzio, L. Pianese, F. Ottalevi, M. Scarella, M. Ragno; Ospedale Mazzoni, Ascoli Piceno, ITALY.

Aim: to describe I123- FP-CIT SPECT data in 4 patients affected by CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarct and Leukoencephalopathy) and parkinsonism. Background: Parkinsonian features are not part of the CADASIL phenotype and, so far, only two patients presenting with parkinsonism have been reported. Both patients showed no response to levodopa treatment and imaging showed functional integrity of the nigro-striatal dopaminergic system in one of them. Our report shows clinical features and imaging data in 4 patients affected by CADASIL and parkinsonism (C+P+). **Material and methods:**I123- FP-CIT SPECT was performed in 4 CADASIL patients with parkinsonism (3 males, age: 50-74 years) and in 3 patient an hearth I123-MIBG scan was performed to exclude Parkinson disease (PD). Only in one patient the I123-FP-CIT study was performed twice (the second 13 months after). We also included for comparison 2 CADASIL patients without clinical signs of parkinsonism (C+P-; 2 males, age:54,55). Brain MRI was performed in all subjects. Results: in C+P+ patients I123-FP-CIT scan showed abnormal low values of striatal uptake: in 3/4 bilaterally and highly significant (C.I.:>97%) and in 1/4 in the left putamen. Heart I123-MIBG uptake was normal. The I123-FP-CIT study at follow-up was stable although the patient showed a severe worsening of clinical status. In C+P- striatal I123- FP-CIT SPECT was normal. Conclusions: conflicting with some literature data, all of our CADASIL patients with parkinsonism show striatal I123-FP-CIT abnormal uptake, severe (3/4) or slight (1/4), but in 3/4 patients myocardial I123-MIBG scans rule out PD. It's unclear if the high frequency of abnormal I123-FP-CIT in our patients correlates to microvascular putaminal/nigrostriatal damage or/and functional features (deafferentation) of cortical/subcortical vascular lesions.

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Cardiac MIBG in the differential diagnosis of Parkinson's disease and multiple system atrophy. Predictive ability of different quantitative parameters.

T. Amrani, E. Ramos-Moreno, S. Sanz-Viedma, S. Ortega-Lozano, M. Martinez del Valle-Torres, J. Jimenez-Hoyuela Garcia; University Hospital "Virgen de la Victoria", Malaga, SPAIN.

AIM: Assess which of the different parameters extracted from quantitative analysis of myocardial innervation with I-123 MIBG study, have higher predictive power to discriminate between Parkinson's Disease (PD) and multiple system atrophy (MSA). **MATERIAL AND METHODS:** This includes 14 patients with clinical diagnosis of probable MSA (11 MSA type P and 3 MSA type C, mean age: 65.64 ± 8.9) and 19 PD (64.74 ± 10.3) according the established criteria for each entity. Chest planar images are made at 20 minutes (early) and 120 minutes (late) and using ROIs, index are calculated: myocardial/mediastinum (M/M: average myocardial counts / average mediastinum count), early and late. Also determines the rate of washing by the expression (W/O: average early myocardial counts- average late myocardial counts / average early myocardial accounts.) From these parameters are performed ROC curve analysis. **RESULTS:** The average value of various indexes analyzed showed: **M/M:** PD:1.27 ± 0.25, MSA: 1.71 ± 0.38 (p = 0.00); **M/MI:** PD: 1.16 ± 0.20, MSA: 1.66 ± 0.43 (p = 0.00); **W/O:** PD: 0.299 ± 0.08, MSA: 0.293 ± 0.12

($p > 0.05$). The ROC curve analysis shows: **Index M/Me**: Az: 0.842 (95% CI: 0.673–0.945). Optimal cutoff 1.38, sensitivity (S): 78.9%, specificity (Sp): 78.6%, LR +: 3.68. **Index M/MI**: Az: 0.859 (95% CI: 0.694–0.954). Optimal cut point: 1.24 (S: 78.9%, Sp: 85.7%, LR +: 5.53). **W/O**: Az: 0.532 (95% CI: 0.351–0.707). Optimum cut point: 0.39 (S: 94.7%; Sp: 35.7%, LR +: 1.47). **CONCLUSIONS**: The quantitative parameter, extracted from the myocardial innervation study, which brings better performance to discriminate between PD and MSA is the index myocardium / mediastinum late.

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Usefulness of ^{123}I -IBZM SPECT in treatment assessment of Parkinson-Plus Disease.

P. Liévano, M. González, L. De la Cueva, M. Añafios, P. Navarro, E. Arroyo, M. Sangros, T. Baringo, M. D. Abós; Hospital Universitario Miguel Servet, Zaragoza, SPAIN.

Objectives: Parkinson-Plus Disease (PP) is frequently accompanied by denervation of both pre and post-synaptic dopaminergic pathways and therefore patients are L-DOPA resistant in most cases, something important in clinical practice due to identify the specific pharmacological treatment. The main objective of this study is to determine the diagnostic implications of ^{123}I -IBZM SPECT in the treatment assessment for movement disorders suggestive of PP. **Material and methods**: A retrospective analysis of ^{123}I -IBZM SPECT studies from 21 patients, 6 patients with a previous ^{123}I -FP-CIT SPECT, referred from the movement disorders unit in our hospital, between December-2008 to April-2010 was done. According to diagnostic suspicion, they were distributed into 3 groups: 16 patients had atypical symptoms with diagnostic of PP (2 showed no response to standard therapy), 3 had diagnostic suspicion of Multiple system atrophy (MSA) and 2 of Progressive supranuclear palsy (PSP). **Results**: ^{123}I -IBZM SPECT was informed as pathological in 5 from 16 patients with suspicion of PP (4 previous ^{123}I -FP-CIT SPECT abnormal). In group with suspicion of MSA, two were informed as uncertain and one as normal. In PSP both were normal.

Diagnostic suspicion	Nº patients	^{123}I -IBZM SPECT	^{123}I -FP-CIT SPECT
Parkinson-Plus Disease	16	11 Normal	1 Normal
		1 Abnormal	1 Abnormal
		4 Abnormal	4 Abnormal
AMS	3	1 uncertain	
		1 Normal	
PSP	2	2 uncertain	
		2 Normal	

Conclusions: ^{123}I -IBZM SPECT has a great value to establish differential diagnosis between pre and post-synaptic dopaminergic disturbance. In our experience, the study with ^{123}I -IBZM SPECT is useful in the clinical practice because it provides diagnostic information with implications for the treatment of patients with suspicion of PP. Except for uncertain studies results, in all patients ^{123}I -IBZM SPECT has contributed to select or change a specific pharmacological treatment.

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$^{99\text{m}}\text{Tc}$ TRODAT-1 SPECT in patients with delayed neuropsychiatric syndromes after CO intoxication

W. Huang¹, S. Chen¹, C. Cheng¹, K. Ma², L. Shen³; ¹Tri-Service General Hospital, Taipei, TAIWAN, ²National Defense Medical Center, Taipei, TAIWAN, ³Institute of Nuclear Energy Research, Taoyuan, TAIWAN.

Objectives: Carbon monoxide (CO) can induce delayed neuropsychiatric syndrome (DNS) that usually unpredictable in the acute stage yet result in major morbidity of victims. We observed changes of $^{99\text{m}}\text{Tc}$ -TRODAT-1 brain SPECT in CO intoxicated patients complicated with DNS and correlated with those found in brain MRI, biochemical data and clinical manifestations. **Methods**: Twenty-one CO intoxicated patients (9 women and 12 men; aged 20 - 68 yr) with DNS without prior neurological disorders were analyzed. SPECT commenced 3 h after 740 MBq of $^{99\text{m}}\text{Tc}$ -TRODAT-1 intravenous injection, using a dual-headed camera equipped with ultra-high resolution fan-beam collimators (Hawkeye, GE, WI, USA). Visual inspection and semi-quantitative measurements i.e. specific uptake ratios (SUR) were calculated by subtracting the mean counts per pixel in the occipital cortices (as background) from the mean counts per pixel in the whole striatum and dividing the result by the mean counts per pixel in the background. Results were compared with corresponding MRI, initial carboxyhemoglobin (COHb, %) and patient parkinsonian symptoms. **Results**: Over 80% of patients revealed abnormal striatal (ST) SUR of $^{99\text{m}}\text{Tc}$ -TRODAT-1 compared to the age-matched controls. The values significantly dropped in those with concomitant necrosis of globus pallidus on MRI than those with negative results (right ST, 1.65 ± 0.53 vs. 2.47 ± 0.24 ; and left ST, 1.61 ± 0.53 vs. 2.59 ± 0.20 ; $p < 0.01$ respectively). The basal ganglia damaged by CO poisoning showed evenly distributed as reflected by equally decreased mean SUR and visual inspection on bilateral ST (1.87 ± 0.59 , right vs. 1.87 ± 0.63 , left; $p > 0.05$). Notably, little overlap of SUR was found between patients with positive and negative MRI findings. Changes of ST $^{99\text{m}}\text{Tc}$ -TRODAT-1 uptake by either visual inspection or SUR measurements appear correlated with clinical parkinsonism manifestations. The averaged SURs tended to be correlated with serum COHb(%). The averaged TRODAT-1 SUR in post-hyperbaric oxygen therapy (HBO) however, showed no significant change compared to the pre-HBO group (right ST: 1.85 ± 0.55 vs. 1.92 ± 0.54 ; and left ST: 1.86 ± 0.59 vs. 2.06 ± 0.53 ; $p > 0.05$, respectively). One out of the 4 negative MRI patients showed parkinsonism with abnormal TRODAT-1 uptake. **Conclusions**: $^{99\text{m}}\text{Tc}$ -TRODAT-1 SPECT may reflect ST damage from CO poisoning with DNS which is characterized by bilateral involvement and well correlated with MRI.

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Oncology Basic Science: Preclinical Imaging

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Evaluation of $^{99\text{m}}\text{Tc}$ Labelled Bombesin on Human Prostate Cancer Xenograft

Z. Yu¹, H. J. K. Ananias², W. Helfrich³, R. A. J. O. Dieckx¹, X. Chen⁴, I. J. de Jong², F. Wang⁵, P. H. Elsinga¹; ¹Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS, ²Department of Urology, University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS, ³Surgical Research Laboratory, University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS, ⁴Molecular Imaging Program at Stanford (MIPS), Department of Radiology and Bio-X Program, Stanford University School of Medicine, Stanford, CA, UNITED STATES, ⁵Medical Isotopes Research Center, Peking University, Peking, CHINA.

Introduction. SPECT (single photon emission computed tomography) is widely used for cancer diagnosis. But the shortage of suitable radiotracer limits the clinical use of SPECT for prostate cancer. BN (Bombesin)-like peptides have very high binding affinity for the gastrin-releasing peptide (GRP) receptor which has proved to be highly expressed on prostate cancer. In this study, we synthesized a new radiotracer $^{99\text{m}}\text{Tc}$ (HYNIC-Aca-BN(7-14))(Tricine)(TPPTS) for SPECT imaging of GRP receptor expressing prostate cancer. **Methods**. HYNIC-Aca-BN(7-14), Aca-BN(7-14) were studied *in vitro* for their binding affinity with GRP-R using PC-3 cells. The full sequence of the bombesin peptide(1-14) was set as a standard. $^{99\text{m}}\text{Tc}$ (HYNIC-Aca-BN(7-14))(Tricine)(TPPTS) was synthesized as described previously^[1]. The internalization and efflux properties of the respective radioligands were tested *in vitro*. The biodistribution profiles and the imaging characteristics were determined in athymic mice bearing human PC-3 xenografts. **Results**. The $^{99\text{m}}\text{Tc}$ -HYNIC-Aca-BN(7-14) has high radiochemical yield and purity after purification. The IC_{50} of HYNIC-Aca-BN(7-14) was 12.8 ± 1.4 nM. The attachment of HYNIC group seems to reduce the GRP binding affinity of Aca-BN(7-14). In general, $^{99\text{m}}\text{Tc}$ -HYNIC-Aca-BN(7-14) had a rapid clearance, predominantly through the renal route. In the biodistribution study a relatively high uptake of $^{99\text{m}}\text{Tc}$ -HYNIC-Aca-BN(7-14) (2.24 ± 0.64 %ID/g) in human PC-3 xenografts was found at 0.5 h pi with a steady decrease over the 4 h study period. Generally, tumour-to-normal tissues ratio increased over time because of the long retention time of the radiotracer in tumour. The significant reduction of uptake on tumour at *in vivo* blocking experiments indicate that uptake of radiotracer was GRPR-mediated. And the pancreas also shows high GRPR expressing. Prostate cancer xenograft is clearly visualized from the SPECT imaging with high tumour-to-background contrast 4 hours after injection of the tracer. Preinjection of excess HYNIC-ABN result in a significant reduction in the tumour uptake also can be easily read from the images. **Conclusion**: The present study indicated that $^{99\text{m}}\text{Tc}$ (HYNIC-Aca-BN(7-14))(Tricine)(TPPTS) is a suitable tracer for *in vivo* tumour targeting. Work is in progress to implement this radiotracer for clinical studies. **References** [1]. Shi J, Jia B, Liu Z, Yang Z, Yu Z, Chen K et al. *Bioconjugate Chem.* 2008; 19, 1170-1178 This research was made possible by a financial contribution from CTMM, project PCMM, project number 030-203.

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Preclinical PET visualisation of adoptive immune cell therapy of EBV-lymphoma using human NOR-epinephrine transporter gene-modified lymphocytes

M. Doubrovin, E. Doubrovina, M. Moroz, I. Riviere, I. Serganova, R. Blasberg, R. O'Reilly; Memorial Sloan-Kettering Cancer Center, New York, NY, UNITED STATES.

Background: We previously demonstrated feasibility of reporter gene imaging with PET and ^{124}I -MIBG non-invasive quantitative monitoring of cytotoxic T-cells (CTLs) *in vivo* bearing hNET transgene. In this preclinical study, we test this clinically applicable imaging paradigm under conditions simulating adoptive immune cell therapy in patients. **Methods**: The hNET reporter gene was cloned into a clinical grade SFG pseudotyped MoMLV retroviral backbone, packaged in PG-13 retroviral producer cell line and was used to transfect EBV-specific T cells. Following the future clinical protocol, EBV-specific T cells were pre-generated from a normal donor by stimulation with autologous EBV-transformed B-cells, as we previously described. Based on expression of LNGFR, a selection gene in the same retroviral cassette, reporter-gene expressing cells (CTL-NIN) were selected by FACS sorting, characterized for cytotoxicity and frozen for long-term storage. Initially, ^{124}I -MIBG uptake was evaluated in the CTL-NIN retrieved from liquid nitrogen storage according to GMP requirements. In the preclinical study, upon thawing, prior to adoptive transfer, CTLs were injected in doses from 10^5 to 10^7 to the EBV-BLCL xenograft tumor model bearing NOD-SCID mice systemically in one set and locally in the tumors in the other. ^{124}I -MIBG was administered systemically in the dose of 100 $\mu\text{Ci}/\text{mouse}$. MicroPET imaging of the animals 4, 24 hours and 7 days post-injection, with post-mortem *ex-vivo* radioactivity measurements were performed. **Results**: CTL-NINs were produced according to GMP procedures appeared to have >90% reporter gene expression post-sorting with improved specificity to EBV-BLCL targets (35% with 10:1 E:T ratio). Storage and thawing decreased their cytotoxicity (25%) and ^{124}I -MIBG uptake (217 ml/g, compared to 330 ml/g pre-freezing). *In vivo* microPET imaging confirmed our ability to detect 10^5 ^{124}I -MIBG *in vivo* labeled CTL-NIN distributed in a 1 cm^3 tumor volume, which appeared persisting at the tumor site without significant migration out regardless of tumor HLA-specificity. Systemically administered CTL-hNET targeted HLA-matched EBV-associated malignancies and were visualized at doses as low as 10^5 per mouse. **Conclusions**: hNET transduced CTLs produced and prepared for adoptive immune cell transfer according to a clinical protocol that preserves their anti-EBV specificity and functionality, can be labeled with ^{124}I -MIBG *in vivo* and imaged by PET in the quantity corresponding to clinically applicable.

P357**Influence of Animal Handling and Image Reconstruction on ¹⁸F-DG Biodistribution in BALB/c Mice using PET**

H. C. Groen, S. C. Berndsen, S. E. Pool, E. P. Krenning, M. de Jong, ErasmusMC, Rotterdam, NETHERLANDS.

Aim Obtaining dynamic parameters of in-vivo tracer-distribution is becoming more important for studying and optimizing targeted imaging and therapy. The aim of this study was to determine optimal animal handling and image reconstruction to study the biodistribution of ¹⁸F-DG in mice using dynamic scans. **Materials & methods** 30 experiments were performed using 6 mice; each mouse was used in 5 different setups (see table). On average 7.4±0.4 MBq ¹⁸F-DG was administered per experiment. Mice were anesthetized using 2.5% isoflurane and scanned until 90 min after ip. injection using a Siemens Inveon animal PET scanner. Images were reconstructed using FBP or OSEM3D with standard settings for noise reduction, voxel size and iterations. Group 3 served as reference; this group was found to give the best results after ip. injection at 30°C by Fueger et al. in 2006. For analysis, acquisition data obtained between 60–90 min post injection were reconstructed. **Results** Between groups biodistribution varied largely (preliminary data, see table). Compared to group 3, all groups showed increased heart and brown fat uptake, with less brain and kidney uptake. Muscle and brown fat uptake were higher when animals were awake during administration (applied for easier injection, group 2 and 4). Due to the intra peritoneal administration method, group 3 showed additional inhomogeneous abdominal radioactivity, potential hampering assessment of metastasis in tumor bearing mice. OSEM3D reconstruction resulted in less image noise and reconstruction artifacts. The overall quantification was comparable for both reconstructions, although there was a strong trend of lower SUV values for heart, kidney and brown fat uptake after OSEM3D.

	Heart	Brain	Kidney	Muscle	Brown fat
Group 1 Fasted [#] , pre-warmed [#] , iv. cannula (iso)	2.2±0.4	1.4±0.1	1.6±0.2	0.5±0.1	0.6±0.03
Group 2 Fasted [#] , pre-warmed [#] , iv. needle (awake)	1.7±0.2	1.4±0.3	1.0±0.1	1.6±0.1	1.2±0.2
Group 3 Fasted [#] , pre-warmed [#] , ip. (awake)	1.0±0.2	2.0±0.3	2.4±0.4	0.5±0.1	0.5±0.1
Group 4 60 min awake after iv. needle (awake)	3.3±0.4	0.8±0.1	0.5±0.1	1.3±0.2	3.9±0.6
Group 5 Pre-warmed [#] , iv. cannula (iso)	4.5±1.1	1.1±0.1	1.7±0.1	0.6±0.2	0.6±0.1

Table 1: Average±SEM SUV values (4 per group) scanned at 36–38°C under 2.5% isoflurane (iso) and FBP image reconstruction. [#]overnight; [#]30°C

Conclusion Depending on the region of interest, animal handling should be adjusted such that maximal contrast is achieved between the target and surrounding tissue activity. Although the results between filters were in general comparable, further research has to be performed to validate the quantification by either FBP or OSEM3D reconstructions.

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Oncology Basic Science: Tumor Biology**P358****A new tumor neovasculature imaging tracer: radioiodine labeled small peptide**

R. Wang, M. Yu, X. Lu; Department of Nuclear Medicine, Peking University First Hospital, Beijing, CHINA.

Objective: In vivo imaging of specific molecular marks in intact tumor neovasculature would have great value and applications in founding tumor earlier and monitoring its plandromes. Although a variety of peptide have been designed, to image tumor angiogenesis, few can be applied in clinical trial. Tripeptide sequence motif Arg-Arg-Leu(RRL) can bind to tumor-derived endothelial cells. The purpose of this study was to redesign and synthesize A new tumor neovasculature imaging tracer for tumor neovasculature imaging. **Methods:** The 10-mer RRL peptide(Tyr-Cys-Gly-Gly-Arg-Arg-Leu-Gly-Gly-Cys-NH₂) and the control peptide(Tyr-Cys-Gly-Gly-Gly-Gly-Gly-Gly-Cys-NH₂) were assembled by the solid phase method and added an amino-terminal Tyrosine to facilitate radioniodination. The radiolabelling yield was measured by ITLC-SG thin-layer chromatography developed by acetone. The purified radioiodine labeled RRL peptide Tyr-Cys-Gly-Gly-Arg-Arg-Leu-Gly-Gly-Cys-NH₂ was put in human blood serum at 37°C for 24 h, and radiochemical purities were checked at 1, 2, 4, 8 and 24 h. Animal biodistribution experiments and SPECT imaging were carried out in 4–6 week old BALB/c nude mice implanted with PC3 human prostate carcinoma. BALB/c nude mice bearing human prostate carcinoma were injected intravenously with 0.74MBq ¹³¹I labeled RRL peptide or ¹³¹I labeled control peptide. The animals were anesthetized and dissected at 1, 6, and 24 h after injection of the ¹³¹I labeled peptides. Heart, liver, spleen, lung, kidney, stomach, intestines, bladder, bone, muscle, blood and tumor tissues were removed and weighed. The radioactivity in the tissues was measured using a γ counter. Results are expressed as the percentage injected dose per gram of tissue (%ID/g). Each value represents the mean and SD of three animals. **Results:** The crude product after purification yielded a main peak containing 99.56% end product by HPLC. The ¹³¹I labeling rate of RRL was approximately 60% and radiochemical purity was 96.5%. The radiochemical purity of the labeled compound remained 90.3% at 24 hours in human blood serum at 37°C. We performed in vivo SPECT imaging to determine the specific uptake of radioiodinated RRL in prostate carcinoma nude mice model. There is an intense accumulation of ¹³¹I-RRL in tumor tissue at 24 hours after administration via tail vein, whereas no such trend was found in other tissues and control agent group. **Conclusion:** This new molecular trace agent can be used to image and monitor tumor

neovasculature in vivo as a noninvasive imaging methods. **[Key words]** Tumor angiogenesis; Molecular marks; Peptide; Prostate carcinoma; Animal

P359**Experimental study on Antihuman Tumor-derived IgG light chain antibody (4E9) for Tumor Imaging in HeLa MR Xenografts**

R. Wang, P. Yan, C. Zhang, F. Guo, M. Yu, L. Kang, Y. Cui; Department of Nuclear Medicine, Peking University First Hospital, Beijing, CHINA.

Introduction: Human tumors from epithelial origin produce IgG. IgG contributes to cancer initiation in the precancerous stage when epithelial cells are actively proliferating. Tumor-derived IgG light chain genes have the identical sequence and high expression in many cancer cells. The study is to radiiodinate antihuman tumor-derived IgG light chain monoclonal antibody (4E9) and evaluate its biodistribution and imaging in nude mice bearing tumor for researching the potentiality in targeted therapy of human cancers. **Methods:** 4E9 was labeled with ¹³¹I by Chloramine-T method and purified with Sephadex G-25 column. BALB/c nude mice were inoculated with HeLa MR cells in the right fold inguen. ¹³¹I-4E9 was injected intravenously via tail vein for biodistribution study and SPECT imaging at 3h, 6h, 24h, 48h, and 72h. IgG2b was used as a contrast. All data were analyzed by the statistic software of SPSS13.0. **Results:** The labeling efficiency of ¹³¹I-4E9 reached 89.9±4.72% (n=4), the specific activity was up to 1.26MBq/μg, and the radiochemical purity was 98.1±1.24% (n=4). The radiochemical purities of ¹³¹I-4E9 kept highly stable (>90%) at 4 °C and 37 °C in human serum within 72 hr. At different time phases post-injection, ¹³¹I-4E9 and ¹³¹I-IgG2b mainly accumulated in liver and kidney. ¹³¹I-4E9 removed from heart, lung, kidney, stomach, muscle and blood faster than ¹³¹I-IgG2b (P<0.05). There was significant difference between T/N ratio of ¹³¹I-4E9 and ¹³¹I-IgG2b in heart and blood (¹³¹I-4E9 > ¹³¹I-IgG2b, P<0.05). Tumor/Muscle and Tumor/Blood ratio of ¹³¹I-4E9 reached to 8.89±3.72 (n=3) and 1.42±0.373 (n=3) respectively. In animal imaging, ¹³¹I-4E9 was more clearly imaged after 24h. **Conclusion:** This study provided the evidence that antihuman tumor-derived IgG light chain monoclonal antibody (4E9) could be a potential radiopharmaceutical for studies on cancer targeted imaging and therapy in new approach to blockade tumor-derived IgG. **Key works** antihuman tumor-derived IgG light chain monoclonal antibody (4E9); radioiodinate; tumor imaging.

P360**Max SUV 18F-FDG-PET Values And Somatic Mutations In The EGFR Gene In Patients With Lung Adenocarcinoma.**

A. Ruibal, A. Vázquez Boquete, I. Abdulkader, M. Garrido, A. Sánchez-Salmón, J. Cameselle-Teijeiro, L. León; Complejo Hospitalario Universitario de Santiago de Compostela., Santiago de Compostela, SPAIN.

We already know that around ten percent of patients with non-small-cell lung cancer (NSCLC) have tumors with somatic mutations in the gene for epidermal growth factor receptor (EGFR) and approximately 70% of these tumors show significant regression when treated with EGFR tyrosine kinase inhibitors. Last year we described a correlation between EGFR expression and maximum standardized uptake value of 18F-FDG-PET (maxSUV) in squamous cell lung carcinomas (Current Radiopharmaceuticals 2009; 2: 175). We have now studied the behavior of maxSUV in relation to the existence of genetic alterations in EGFR in patients with lung adenocarcinoma. Our study group included 48 recently diagnosed lung adenocarcinoma patients (17 females; aged: 27–74; 58.5±/–11.9 and 31 males; aged 45–88; 65.4±/–11.3; p:0.064). EGFR gene alterations were studied using the Beckman Coulter CEQ8000 and a microdissector Leica AS LMD. The PET image was acquired for staging 60 minutes after administration of 18F-FDG in a PET Advanced System (GE). The maxSUV was considered as the uptake of the region of interest (ROI) in relation to the injected dose and body weight. MaxSUV values were higher in males (range: 2.9–36.8; 13.6±/–8.8) than in females (range: 2.6–20.4; 10.7±/–4.8) with no statistically significant differences. 8 patients (16.7%; 5 females and 3 males) showed alterations in the EGFR gene (4 deletions in exon 19 (maxSUV: 8.8, 15.9, 13.9 and 12.7), 2 mutations in exon 21 (maxSUV: 7.4 and 4), 1 mutation in exon 20 (maxSUV: V774M)(7.3) and 1 mutation in exon 18 (Q70Astop); maxSUV 6.7). There were no differences in maxSUV related with to the patient gender. Likewise, statistically significant differences were not observed between patients with (range: 2.6–36.8; 13.2±/–8.1; median 12.5) or without (range: 4–15.9; 9.6±/–4.1; median 8.1) EGFR gene alterations. Nevertheless, maxSUV values in patients with deletions (12.9±/–2.9; range: 8.8–15.9) were higher than those observed in patients with mutations in the EGFR gene (6.3±/–1.6; range: 4–7.4). MaxSUV values higher than 7.5 were observed in 0/4 patients with mutations vs 4/4 patients with deletions in the EGFR gene (p: 0.012). Although, preliminary due to the reduced number of cases, our findings, led us to the following: 1) the presence of mutations, but not deletions, in the EGFR gene is associated with lower maxSUV-18F-FDG values; 2) The high maxSUV values observed in the patients with deletions in exon 19 could reflect increased tumor metabolism and a better response to tyrosine kinase inhibitors.

P361**Assessing metabolic activity of cancer stem cells during differentiation with [¹⁸F]FDG**C. M. F. Gomes¹, S. R. M. Neves¹, A. O. G. Lopes¹, A. do Carmo², A. J. Abrunhosa³, M. Botelho¹; ¹Institute of Biophysics/Biomathematics - IBILI - FMUC, Coimbra, PORTUGAL, ²Center for Neurosciences and Cell Biology - CNC, Coimbra, PORTUGAL, ³Institute for Nuclear Sciences Applied to Health - ICNAS, Coimbra, PORTUGAL.

Aim: The cancer stem cell (CSC) theory proposes a hierarchical organization within the tumor in which a small subset of stem-like cells is responsible for sustaining tumor growth and differentiation. These cells divide asymmetrically, producing an identical progenitor and a more differentiated cell, which in subsequent divisions generates the cellular heterogeneity of the tumor. The existence of CSCs has important therapeutic implications, since these cells are referred to be more resistant to conventional therapies compared with their more differentiated progeny. The main goal of this study was to evaluate the metabolic activity of CSCs during their differentiation using [¹⁸F]FDG and to correlate the obtained results with the cell cycle progression

and growth rate. **Methods:** A CSC population was isolated from a human osteosarcoma cell line (MNNG/HOS) using a sphere-culture system. This stressful growth conditions (serum starvation and anchorage independence) select for primitive clonogenic cells possessing attributes of stem and progenitor cells by eliminating the differentiated ones that are unable to survive under such circumstances. After 7 days, the spherical clones formed were cultured in serum-containing medium and allowed to grow in adherent conditions until acquiring a phenotype similar to the original MNNG/HOS cells. As cells reach the confluency, cultures were harvested and passaged to new flasks for further expansion and differentiation. The metabolic activity of spherical and adherent cells with 1st, 4th, 6th and 15th passages was assessed based on cellular uptake of [¹⁸F]FDG. Cell-cycle progression of CSCs and adherent cells was analyzed by flow cytometry. **Results:** After transferring to adherent growth conditions, CSCs start to expand from the sphere acquiring gradually spindle-shaped morphology similar to the original monolayer. CSCs proliferate at a slower growth rate compared with MNNG/HOS cells. The uptake of [¹⁸F]FDG in CSCs was 3.4±0.3% and start increasing progressively with the number of passages in adherent conditions (1st:2.5±0.1%; 3rd:10.6±0.2%; 6th:12.85±0.81%). After the 6th passage [¹⁸F]FDG uptake was similar to that of established MNNG/HOS cell line (%/10⁶cells=12.5±1.4). Cell cycle analysis revealed that CSCs contain lower percentage of cells in G2/M phase in comparison with more differentiated 15th passage and MNNG/HOS cells with 19.9% and 22.2%, respectively. **Conclusions:** The metabolic activity of cancer-stem like cells during differentiation varies and can be monitored with [¹⁸F]FDG. The differential uptake of [¹⁸F]FDG that was observed during the de-differentiation/differentiation process of MNNG/HOS cells revealed that [¹⁸F]FDG uptake is cell cycle-dependent and varies with the proliferative potential of cells.

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Oncology Basic Science: Animal Models

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Detection of Primary Tumor and Metastasis In a New Animal Model Using MiniPET-II

G. Trencsényi¹, I. Lajtos¹, J. Molnar², Z. T. Krasznai³, L. Balkay¹, M. Emri¹, P. Kertai⁴, L. Galuska¹, T. Marian¹; ¹University of Debrecen, Medical and Health Science Centre, Department of Nuclear Medicine, Debrecen, HUNGARY, ²Institute of Nuclear Research of the Hungarian Academy of Sciences, Debrecen, HUNGARY, ³University of Debrecen, Medical and Health Science Centre, Department of Obstetrics and Gynecology, Debrecen, HUNGARY, ⁴University of Debrecen, Medical and Health Science Centre, Department of Preventive Medicine and Public Health, Debrecen, HUNGARY.

Aim: Earlier examinations showed that there is connection between the lymphatics of the renal capsule and the parathyroid lymph nodes (PLN) in rats. We wished to prove with MiniPET-II, whole body autoradiography and organ distribution examinations by using 18FDG, that rat hepatocarcinoma (He/De), mesoblastic nephroma (Ne/De) and myelomonocytic leukemia (My1/De) cells give metastasis to the PLN. **Materials and methods:** 106 He/De, Ne/De and My1/De cells were placed under the left renal capsule by surgical procedure. Two weeks after implantation, control and tumor-bearing rats were anaesthetized and 18FDG (15.0 MBq) was injected into the tail vein. Forty minutes after the administration of 18FDG we used a small animal PET scanner (MiniPET-II, Department of Nuclear Medicine, Debrecen) to visualize the primary tumor and the metastasis. The MiniPET-II consists of 12 detector modules in one ring with LYSO scintillator crystal blocks and position sensitive photomultiplier tubes. For the whole-body autoradiography 60 µm thick cryostat sections (Leica CM 3600 cryomicrotome) were cut in the sagittal plane from the embedded animals. Sections were exposed to phosphor imaging plates. For organ-distribution different tissues were removed and their activities were measured with a gamma counter and the differential absorption ratio (DAR) was determined. **Results:** Autoradiographic experiments revealed that the radioactivity of the tumor and the PLN surpassed that of other organs. By taking the pixel intensity of resting striated muscle as one unit, the relative pixel intensities were: 14.23±2.6 in He/De tumor, 10.82±2 in PLN, 5.36±0.7 in kidney, 2.35±0.2 in blood and 1.57±0.4 in liver. In two other tumor models (Ne/De, My1/De) distribution patterns of radioactivity similar to that of He/De was observed. By taking the relative intensities from the MiniPET-II images the majority of the radioactivity was accumulated in the primary tumors and in the PLN. The DAR values also showed significant uptake in tumorous tissues. **Conclusion:** Our experiments have shown that tumor cells implanted under the capsule of the kidney generate metastases in the PLN. From the autoradiography, MiniPET-II and tissue distribution experiments, we concluded that He/De, Ne/De and My1/De tumors grown under the capsule of kidney represent a significant metastatic burden manifested primarily in parathyroid lymph nodes. The renal capsule-parathyroid lymph node complex seems to be suitable for the isolated in vivo examination of metastatic development and for the detailed analysis of secondary tumors.

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Oncology Basic Science: New & Innovative

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Auger-electrons emitting 5-Iod-4'-thio-2'-desoxyuridine (I-125-ITdU) for Endo-Radio-Therapy (ERT) of Multiple Myeloma

A. Morgenroth¹, C. Dinger², B. Zlatopolskiy², E. Al Moman¹, T. Kull², S. N. Reske²; ¹Clinic of Nuclear Medicine Aachen, Aachen, GERMANY, ²Clinic of Nuclear Medicine Ulm, Ulm, GERMANY.

Introduction: Multiple Myeloma (MM) is a malignancy of terminally differentiated B lymphocytes, characterised by accumulation of plasma cells in the bone marrow. Despite advances in treatment, MM remains an incurable disease. The phenotypic heterogeneity of myeloma cells is associated with their proliferative activity and resistance to apoptosis. The cytokine mediated

increased proliferation of MM cells represents an attractive target for a therapy using Auger-electrons emitting I-125-ITdU. The uptake and induction of apoptosis in U266 as a model for immature plasma cells, and two MM.1 cell lines representing drug sensitive and resistant mature cells were investigated. **Material and Methods:** Phenotypic analysis was investigated using FACS. The uptake and DNA incorporation of I-125-ITdU (50kBq/well) were assessed after 48 and 96h using gamma counter. Effect of IL6 on proliferation was determined by PI staining. Apoptotic cells were identified using Annexin-V. Additionally, effect on cleavage of Caspase 3 and PARP was visualized by western blot. **Results:** The phenotypic analysis indicated immature character of CD38⁺CD45⁺CD138⁺ U266 cells. The MM1.S and MM1.R showed expression pattern of terminally differentiated plasma cells with high expression of CD38 and CD138 and marginally CD45. The highest uptake was observed in U266 (12.8±0.9% and 8.9±0.5%, at 48 and 96h respectively). For terminally differentiated MM1.S and MM1.R the uptake reached 5.3±0.3% and 5.1±0.2% after 48h, and 2.8±0.1% and 2.5±0.1% after 96h, respectively. Correspondingly, the highest incorporation rate into the DNA was observed in U266 (58.2±5.1% and 61.3±5.8% of internalized activity at 48 and 96h, respectively). For the MM1.S, 25.2±3.2% after 48h and 28.4±3.5% after 96h of incubation was stable incorporated. In MM1.R, only 10.1±1.1% at 48h and 11.9±0.9% at 96h was determined as DNA associated. Incubation of IL6 sensitive MM1 cells with this cytokine led to increased proliferation rate (44.2±2.1% vs. 78.0±3.6% for MM1.S and 35.2±2.2% vs. 58.9±3.3% for MM1.R). This effect was only weakly pronounced in U266 (< 2%). Strong activation of Caspase 3 and PARP cleavage was detected independently on IL6 stimulation, correlating to high rates of apoptosis visualised by Annexin-V staining. **Conclusion:** I-125 labelled ITdU induces apoptosis in immature and terminally differentiated malignant plasma cells. Thus it overcomes IL6 mediated growth, survival and drug resistance in MM cells. This study demonstrates the potential of Auger-electrons emitters for therapy of Multiple Myeloma, providing preclinical rationale for the development of a novel treatment option. Project supported by Deutsche Jose Carreras Leukämie-Stiftung (grant DiCLS R 08/21v).

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Oncology Basic Science: Miscellaneous

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MICROPET vs. PET-CT EX-VIVO imaging of human tumor surgical samples after in-vivo 18-FDG injection

E. Prieto, J. M. Martí-Climent, M. J. García-Velloso, I. Peñuelas, J. L. Hernández, P. Garrastachu, I. Domínguez, G. Quincoces, J. Pardo, J. A. Richter; Clínica Universidad de Navarra, Pamplona, SPAIN.

The limited spatial resolution of clinical PET tomographs complicates the analysis small or heterogeneous tumors. This study investigates the use of a small animal PET scanner as a novel technique for characterization of ¹⁸F-DG uptake in surgical samples. The investigation of tumor samples ex-vivo can provide interesting results that will be useful in the future for a precise analysis of tumors in-vivo with PET. The objective of this study is to correlate ¹⁸F-DG uptake of tumor surgical samples measured ex-vivo in a clinical PET-CT and in a small animal PET scanner. **Methods** Twenty-three patients with cancer considered suitable candidates for surgery were included (4 breast, 13 colorectal and 6 prostate cancer). Each surgical sample was extracted after intravenous injection of 376.4±58.7 MBq of ¹⁸F-FDG and studied in a Biograph-2 PET-CT, with spatial resolution of 8.6 mm in clinical conditions for acquisition and reconstruction. Then, each sample was acquired on a Philips MOSAIC small animal PET scanner (MicroPET), with a spatial resolution of 2.6 mm. Maximum SUV (SUV_{max}) of the tumor was assessed. Two corrections were applied to correlate values between both tomographs: 1) A cross calibration factor to account for possible differences in their calibration. This factor was assessed from a 6 cm diameter phantom acquired in both tomographs, yielding a value of 0.85. 2) A smoothing filter to make both images equivalent in terms of resolution. The FWHM of the filter used was 8.2 mm (FWHM_{filter} = (FWHM_{PET-CT} - FWHM_{MicroPET})^{1/2}). Statistical analysis was carried out with the nonparametric Wilcoxon signed rank test for paired data (SPSS). **Results** SUV_{max} (median [range]) of the surgical samples at MicroPET were 20.4 [6.4-59.6], greater than SUV_{max} measured ex-vivo at PET-CT: 8.6 [2.2-32.0] (p<0.01). The smoothing filter was applied over MicroPET images, yielding SUV_{max} values of 11.3 [3.1-40.2]. After the application of the cross calibration factor, no statistical differences were found between both scanners PET-CT and MicroPET (p=0.35). **Conclusion** This study has proven the correlation, when correction factors are considered, between SUV_{max} of surgical samples measured ex-vivo with two different tomographs (PET-CT and MicroPET). This is the first step for the utilization of a small animal PET scanner for detailed characterization of human tumors.

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Retrospective observational comparison of 18FDG-PET/CT and whole body diffusion weighted MRI with background body signal suppression (MR-DWIBS) in malignant tumours.

A. Niccoli Asabella, F. luele, M. Fanelli, G. Rubini; Nuclear Medicine Unit, University of Bari, Bari, ITALY.

Aim: to assess the overall diagnostic accuracy of whole-body MR-DWIBS compared to 18FDG-PET/CT, considered the reference standard of whole body tumour imaging modalities, in a series of consecutive patients with malignant tumour. **Methods:** 14 patients diagnosed with a malignant tumour over a four-month period were enrolled in this retrospective, observational study. The PET/CT and MR-DWIBS images were reviewed, in double blind, by a nuclear medicine physician and radiologists with 4 years experience. Lesion size, SUV and ADC were measured and calculated for each lesion. **Results:** The qualitative analysis of MR-DWIBS and 18FDG-PET/CT showed that one patient was negative at both techniques. MR-DWIBS was positive in 13 patients, 9 of whom were positive and 4 negative at 18FDG-PET/CT, respectively. 94 lesions were identified by MR-DWIBS and 68 by 18FDG-PET/CT, a significant discordance was found. The correlation between SUV and ADC of the lesions positive at both techniques was not statistically significant. The mean difference between the lesion size in 18FDG-PET/CT and MR-DWIBS was not statistically significant. No correlation was found between glucose metabolism and water motion. **Conclusions:** The results of this observational, retrospective study show that MR-DWIBS may be used to evaluate localization of parenchymal neoplasms but is less efficacious in characterizing

lymphnode and skeletal lesions. 18FDG-PET/CT remains the best whole-body technique to identify lymphnode and skeletal lesions. 18FDG-PET/CT limit is identifying tumours with low glucose metabolism as in mucinous neoplasms. MR-DWIBS evaluation must be integrated with morphological images in order to increase the diagnostic accuracy of MR.

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FDG uptake in Brown Adipose Tissue - A brief report on brown fat with FDG uptake mechanisms and quantitative analysis using dual-time-point FDG PET CT.

B. E. Akkas¹, D. Gokaslan², L. Guner², N. I. Karabacak²; ¹Ankara Oncology Research and Training Hospital, Ankara, TURKEY, ²Gazi University Medical Faculty Department of Nuclear Medicine, Ankara, TURKEY.

Aim: Brown adipose tissue (BAT) is a potential source of false-positive findings on [¹⁸F] FDG PET. In this report, we discussed the [¹⁸F] FDG uptake mechanisms in BAT and aimed to determine if dual time point PET imaging help the differentiation of BAT from malign lesions. **Method:** Patients with dual-time-point PET/CT scans were reviewed retrospectively and 31 cases (11 males, 20 females, age: 28.6 ± 9.7) having hypermetabolic BAT were included for this study. [¹⁸F] FDG uptake in BAT was quantitatively analyzed by maximum standardized uptake values (SUVmax), average percent change in SUVmax of BAT between early and delayed images was calculated. **Results:** Initial PET/CT scans were acquired 60 minutes after i.v. injection of F18-FDG, delayed images were obtained 76 ± 20 min (mean ± SD) after the initial scan. Compared to the initial scans, [¹⁸F] FDG uptakes in BAT in delayed images were higher in 26 of the patients, lower in one patient. In terms of body regions, [¹⁸F] FDG uptake increased in 80.6 %, remained unchanged in 5.5 % and decreased in 13.9 % of the body regions. Mean percent increase of [¹⁸F] FDG uptake in 29 BAT regions was 69 ± 25 %, mean percent change in SUVmax including all BAT regions was 19.8 % ± 19.1, (p: 0.0001). **Conclusion:** In this brief report, we observed that on dual time point PET imaging, physiologic FDG uptake in brown adipose tissue increases over time mimicking malignancy and this increase correlates with the time interval between the PET scans. Today, fusion PET/CT provides the unique advantage to give anatomical information and CT component contributes the specificity of PET/CT imaging. But it must be kept in mind that by dual time point imaging, the observed uptake phenomenon of FDG in BAT may indeed lead to misdiagnosis in cases where the appearance of BAT is atypical.

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Oncology Clinical Science: Brain

P367

^{99m}Tc-Tetrofosmin uptake is not influenced by glioma's multidrug resistance phenotype.

G. A. Alexiou, S. Tsiouris, A. Goussia, A. Kyritsis, S. Voulgaris, A. Fotopoulos; University Hospital of Ioannina Greece, IOANNINA, GREECE.

Objective: Multidrug resistance (MDR) remains a major obstacle to successful chemotherapeutic treatment of cancer. Various genes have been implicated; among them *MDR1* and *MRPs*. The proteins encoded by these genes are transmembrane proteins and act as ATP-dependent drug efflux pumps. Several chemotherapeutic agents are a substrate and therefore their accumulation is prevented. Furthermore, some lipophilic cationic radiopharmaceuticals are also a substrate of *MDR1* and *MRPs* mediated transport; among them, technetium-99-tetrofosmin (^{99m}Tc-TF), a single photon emission computed tomography tracer. In the present study we evaluated *in vivo* whether ^{99m}Tc-TF uptake is influenced by the multidrug resistance profile of gliomas. **Material and Methods:** Eighteen patients (10 male, 8 female, mean age 53.5±7 years) with histologically confirmed glioma were included in the study. There were 13 glioblastoma multiforme cases, 2 anaplastic astrocytomas, 2 anaplastic oligodendrogliomas and 1 low grade astrocytoma. Brain SPECT by ^{99m}Tc-TF was performed within a week prior to surgical excision and the expression of *MRP5* was assessed by immunohistochemistry. Radiotracer accumulation was assessed by a semiquantitative method of image analysis, calculating the lesion-to-normal (L/N) uptake ratio. **Results:** The tracer uptake ranged from faint to profound (mean L/N=8.2, range 1.8-20). The *MRP5* expression ranged from 0-45%. Using spearman's rho analysis we found no correlation between tracer uptake (L/N) and *MRP5* expression (p=0.21, r=0.538). **Conclusion:** The present data suggest that ^{99m}Tc-TF uptake is not influenced by glioma's multidrug resistance phenotype. Thus, ^{99m}Tc-TF constitutes a suitable radiotracer for imaging gliomas.

P368

The Efficacy of Dual-Time-Point 18F-FDG PET Imaging for Grading of Brain Tumors

D. Kim, C. Kim, S. Park, S. Jung, W. Kim; Wonkwang University School of Medicine, Iksan, Jeollabuk-do, KOREA, REPUBLIC OF.

Several studies have explored the usefulness of dual-time-point 18F-FDG positron emission tomography imaging (DTPI) in improving detection of brain metastases and tumors outside the brain, distinguishing malignant from benign. In the same manner, DTPI may show better performance to grade of brain tumors. **Methods:** Twenty-two lesions of eighteen consecutive patients with primary or metastatic brain tumor were included prospectively. DTPI was performed and analyzed using maximum standardized uptake values (SUVmax), mean standardized uptake values within isocontour at 70% of maximum pixel values (SUViso) and retention index (RI) for each lesions. **Results:** SUVmax and SUViso of the delayed image were more efficient than those of early image to classify lesions by the grade of tumors (Table 1 and 2). The RI of SUVmax and SUViso were not significant to classify lesions. **Conclusion:** DTPI may be a better imaging method to grade the brain tumor than early imaging only. **Table 1.** Standardized uptake values and retention indices according to the grade of brain tumor

Grade of tumor	SUVmax1	SUVmax2*	maxRI	SUViso1	SUViso2*	isoRI
Grade I (n=6)	5.1±1.8	6.3±2.2	24.3±21.5	5.0±1.6	5.7±1.8	14.4±19.8
Grade II (n=2)	4.2±2.2	5.0±2.5	21.1±3.5	2.3±0.3	3.0±0.8	27.3±19.1
Grade III (n=3)	6.1±1.6	8.1±2.3	33.9±8.4	5.8±0.5	8.1±0.8	38.5±11.6
Grade IV (n=8)	7.7±3.0	10.0±3.4	33.0±17.0	6.5±2.4	8.3±2.6	30.4±12.7
Grade V (n=3)	8.3±3.3	10.1±3.7	23.9±17.5	6.3±2.6	7.6±2.7	21.8±10.5

* statistically significant (p<0.05); SUVmax1, maximum standardized uptake values on the early image; SUVmax2, maximum standardized uptake values on the delayed image; maxRI, retention index of maximum standardized uptake values; SUViso1, mean standardized uptake values within isocontour at 70% of maximum pixel values on the early image; SUViso2, mean standardized uptake values within isocontour at 70% of maximum pixel values on the delayed image; maxRI, retention index of mean standardized uptake values within isocontour at 70% of maximum pixel values. **Table 2.** Standardized uptake values and retention indices of grade I-II and grade III-IV

	Grade I-II (n=8)	Grade III-IV (n=11)	p-value
SUVmax1	4.9±1.8	7.2±2.8	.035*
SUVmax2	6.0±2.2	9.5±3.1	.010*
maxRI	23.5±18.3	33.2±14.7	.186
SUViso1	4.3±1.8	6.3±2.0	.083
SUViso2	5.0±2.0	8.3±2.2	.006*
isoRI	17.6±19.2	32.6±11.3	.083

* statistically significant (p<0.05).

P369

The incremental added value of including the head in F18-FDG PET/CT imaging for cancer patients

A. G. Abdelmalik, R. Muzaffar, M. Altinyay, N. C. Nguyen, M. M. Osman; St. Louis University Hospital, Saint Louis, MO, UNITED STATES.

Objective: To assess the added value of scanning the head in addition to the routinely used field of view (skull base to mid thigh) by retrospectively evaluating true whole body (TWB) FDG PET/CT of cancer patients for any incidental findings in the brain/scalp. **Methods:** We retrospectively reviewed the reports of TWB PET/CT of 500 consecutive cancer patients above the age of 50 (mean age 62). PET/CT abnormalities in the brain/scalp were tabulated whether they were incidental or known based on previously available data. Findings were correlated with pathology, other imaging studies (MRI and/or CT), and clinical follow up. **Results:** 78 of 500 patients (15.6%) had findings in the brain/scalp. Of those, 52 (10.4%) were known. Of the remaining 26 patients (5.2%); follow up data was not available in 11 patients; and abnormalities were confirmed in 15 patients (3%). Out of those 15 patients; 9 were confirmed metastatic (8 lung and 1 mucocoeperidermoid carcinoma of the floor of the mouth), and 6 were benign (2 pituitary adenoma, 1 lipoma of scalp, 1 neurosarcooidosis, 1 infarction, and 1 recurrent Schwannoma). The incidental finding of brain metastasis changed the management in 8 out of the 9 patients (89%) and staging in 4 patients (44%). **Conclusion:** Including the head in the field of view on PET/CT offers additional benefit to cancer patients, as detection of additional metastasis in these patients had significant impact on patient management and provided more accurate staging.

P370

NPV of 11C-Methionine PET/CT after radical therapy in patients with glioblastoma

C. Nanni, S. Nicolini, V. Ambrosini, F. Lodi, C. Pettinato, P. Castellucci, G. Montini, V. Allegri, S. Fanti; Ospedale S.Orsola Malpighi, Bologna, ITALY.

Objectives: 11C-Methionine PET is an accurate imaging modality to evaluate patients affected by glioblastoma, giving prognostic information at diagnosis and an early detection of recurrence during the follow up. However, in literature it is not specified which is the prognostic value of a negative 11C-Methionine PET after the first line treatment in patients affected by glioblastoma. **Aim** of this study was to evaluate the prognostic value of a negative 11C-Methionine PET after the first line treatment in patients affected by glioblastoma. **Methods:** 33 patients radically treated for glioblastoma were enrolled (13 F, 20 M, mean age 50.5, 10 patients grade 4, 11 patients grade 3, 12 patients grade 2). They underwent a 11C-Methionine PET 3 to 6 months after the first line treatment. Those who had a positive PET were subsequently treated again, while those who had a negative PET were followed up over time with repetitive 11C-Methionine PET scans carried out approximately every 6 months at he beginning, and then every year, with up to 9 scans. Mean follow up was 24,3 months. **Results:** 23/33 patients turned out to have a positive PET scan, while 10/33 were negative. Among negative patients, 4/10 (40%) had a disease relapse highlighted by a follow up PET scan on average 8 months after the first negative PET. 6/10 patients (60%), on the contrary, remained negative for a long time. Their mean follow up was 66 months. All relapsed patients had a grade 4 glioblastoma, while non-relapsed patients had a grade 2 glioblastoma in 1 case, grade 3 in 4 cases and grade 4 in 1 case. **Conclusions:** Although preliminary, these data show that a negative post treatment 11C-Methionine PET is a strong predictor for a long disease free survival in patients with low grade glioblastoma. If these results will be confirmed, in those patients the follow up could be less strict. This is not true for patients affected by the more aggressive grade 4 glioblastoma, who need to be frequently controlled to pick up an eventual early disease relapse.

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O-(2-[F-18]-fluoroethyl)-L-tyrosine PET and MRI in diagnosis of cerebral glioma and metastases

M. Marx, U. Lützen, M. Zuhayra, K. Kötz, M. Lürken, E. Henze; Klinik für Nuklearmedizin, Universitätsklinikum Schleswig-Holstein Campus Kiel, Kiel, GERMANY.

Aim: After introduction of an improved automated synthesis method for O-2-[F-18]-fluoroethyl)-L-tyrosine (F-18-FET) with increased radiochemical yield, specific activity and chemical purity we investigated the outcome in clinical practice for the diagnosis of cerebral gliomas, especially if their recurrence was suspected. **Materials and Methods:** 15 FET PET examinations were performed in 14 patients (5 male and 9 female, aged 21- 69 years, mean 46 years). Ten patients suffered from cerebral glioma (glioblastoma WHO Grade IV n=4; astrocytoma n= 5, WHO Grade III n=4, and WHO Grade II n=1; oligodendroglioma WHO Grade III n=1). Two patients had brain metastases (breast and lung cancer n=1 each); in two patients a cerebral glioma was suspected. The patients were treated by surgery (n=10), radiotherapy (n=7), and chemotherapy (n=3). Suspicious MRI findings led to a dynamic FET PET taking 40 minutes after administration of 100 - 380 MBq F-18-FET, an ACCEL PET scanner (Siemens, Germany) was used. In all patients standardized uptake values (SUVs) and tumor-to-brain ratios were obtained. In 13 patients fusion of PET and MRI was made. **Results:** In all patients abnormal MRI signals with contrast-enhancing lesions were observed. 9 of 14 patients (64%) showed a visual F-18-FET uptake [SUVmax 1,6 -4,1; tumor-to-brain ratio 1,6 - 3,9; in 3 patients the lesions presented hot spot kinetics with an early peak followed by a decrease of activity as a sign of high-grading glioma]; match findings with conclusive results in MRT, FET tumor-brain ratio and kinetics predicting tumor recurrence were achieved. In 5 of 14 examinations (36%) no increased F-18-FET uptake was noted [SUVmax 1,1 - 1,5; tumor-to-brain ratio 1,1 - 1,7], in this mismatch findings with suspicious MRI lesions and missing F-18-FET uptake a recurrence of glioma, tumor residuals, or suspected cerebral glioma seemed to be improbable. **Conclusion:** In patients with cerebral glioma PET scans were performed with O-2-[F-18]-fluoroethyl)-L-tyrosine (F-18-FET) produced by an improved and simplified synthesis method. The new procedure rendered reliable results even in detecting the recurrence of high-grade cerebral gliomas.

P372

Brain tumour imaging with 2-[¹⁸F]fluoroethylcholine PET-CT: comparison with magnetic resonance spectroscopy.

A. Filice¹, R. Sghedoni², M. Casali¹, A. Fraternali¹, M. Roncali¹, M. Asti¹, G. De Berti³, M. Di Paolo¹, A. Versari¹, D. Salvo¹, ¹Nuclear Medicine-Santa Maria Nuova Hospital, Reggio Emilia, ITALY, ²Medical Physics Dept-Santa Maria Nuova Hospital, Reggio Emilia, ITALY, ³Neuroradiology-Imaging-Department, Santa Maria Nuova Hospital, Reggio Emilia, ITALY.

Objectives: 2-[¹⁸F]-fluorodeoxyglucose (¹⁸FDG) is the most widely used radiopharmaceutical in positron emission tomography (PET) during the routine practice of oncologic disease. However, imaging of brain tumors with ¹⁸FDG is limited because of the relatively high uptake of this radiotracer in the grey matter. The aim of this study was to assess the clinical potential of 2-[¹⁸F]-fluoroethylcholine PET-CT (¹⁸FECH/PET-CT) in the diagnosis of brain tumors compared with the findings of magnetic resonance spectroscopy (MRS) as a reference standard. **Methods:** Ten consecutive patients were evaluated by ¹⁸FECH and MRS between November 2008 and October 2009. Four of these patients were excluded from the study because of a time lag greater than two months between the two examinations and for changes in clinical conditions. The other six patients, suspected of having brain tumours or relapse after radiotherapy, had undergone to ¹⁸FECH/PET-CT and MR according to the standard protocol and to single voxel spectroscopy scan (voxel volume 1.5x1.5x1.5 cm³) on the neoplastic and healthy tissue. Relative quantification of choline was calculated as the ratio between the areas related to choline and creatine peaks respectively (Cho/Cr). Cho/Cr values were compared with the mean standard uptake value (SUV) measured in ¹⁸FECH/PET-CT examinations in the same position of the MRS voxel. **Results:** in the neoplastic regions SUV and Cho/Cr showed a high correlation (r²=0.92). After a follow up of two years we can conclude that both ¹⁸FECH/PET-CT and MRS correctly identified relapses after radiotherapy and the tumor grade in four patients. In one patient, rightly evaluated by MRS, ¹⁸FECH/PET-CT wrongly classified an inflammatory area as a relapse. In another patient, MRS did not manage to discriminate between low and high-grade gliomas, conversely, the tumor grade was correctly differentiated by using ¹⁸FECH/PET-CT. **Conclusions:** In our experience, the combination of ¹⁸FECH/PET-CT and MRS imaging showed a higher accuracy than the single diagnostic examination for identified gliomas grade and relapses. Due to the low number of patients undergone to this study, further comparison in a higher survey is needed for more reliable conclusions.

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Oncology Clinical Science: Head & Neck

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Interest of 3'-deoxy-3'-[18F]-fluorothymidine (FLT) Positron Emission Tomography in glioma volume delineation : a preliminary multimodal image-guided biopsy study

P. Fernandez, S. Eimer, E. Gimbert, A. Doussau, P. Monteil, G. Penchet, P. Perez, D. Vimont, T. Tourdias, S. Ledure, M. Allard, H. Loiseau; CHU Pellegrin Bordeaux, Bordeaux, FRANCE.

AIM : determination of the ability of 3'-deoxy-3'- [18F]-fluorothymidine (FLT) to image cellular proliferation using positron emission tomography (PET) in comparison to malignancy parameters obtained from multiple multimodal image-guided brain biopsies. **MATERIALS AND METHODS:** seven patients (median age = 63.4y, range : 51-75) with a supratentorial malignant glioma that required a surgery were imaged preoperatively with PET after the administration of 350 ± 50 MBq of [¹⁸F]-FLT. Volume FLT were delineated from standardized uptake value (SUV) calculation. MRI volumes were delineated from a gadolinium enhanced T1-weighted sequence. PET and MRI matched and mismatched volumes were superimposed on MRI neuronavigation image with different colors. Before the opening of dura mater, different specimens were obtained from the different matched and mismatched PET and MRI volumes. Histopathological malignancy parameters (MIB-1 proliferative index (PI), cellular atypies, mitose number, necrosis, endothelial hyperplasia) and the final pathological diagnosis of malignant glioma (grade 3 or 4) were rated blindly and compared to imaging data. **RESULTS :** a total of 66 biopsies (median = 10 / patient, range 7-12) were studied : 10 samples from PET negative-MRI positive regions, 27 from PET positive-MRI negative regions, 22 from PET positive-MRI positive regions and 7 from PET

negative-MRI negative regions (access way to tumor in non functional area). Fifty six percents of 27 PET+/MRI- samples and 91 % of 22 PET+/MRI+ samples corresponded to grade 3 or 4. All 10 samples from MRI+/PET- were grade 4, including 9 from tumour center and 1 from tumour margin. Three PET-/MRI- samples out of 7, issued from 3 different patients were malignant. In a patient-based analysis, at least one PET+/MRI- sample was diagnosed as grade 3 or 4 in 6 patients among 7. Data from histopathological parameters showed that PI is ≤ 15% in 37.5 % of 48 malignant samples. Calculation of PET imaging performances showed a positive predictive value of 56 % for mismatched PET positive volumes. **CONCLUSIONS :** FLT PET seems to be a cellular proliferation marker which may be able to detect malignant tissue in MRI-negative volumes in more than half samples from mismatched PET positive volumes. It may therefore be useful to better identify the margin of malignant gliomas for planning radiotherapy and detect tumoral recurrence in association with MRI. Moreover, the histopathological proliferative index seems not to be sufficient for tumor grading since third of malignant samples showed IP ≤ 15%.

P374

¹⁸F-FAMT uptake correlates tumor proliferative activity in oral squamous cell carcinoma; Comparative study with ¹⁸F-FDG PET and immunohistochemistry

G. Miyashita¹, T. Higuchi², N. Oriuchi², Y. Arisaka², T. Ishikita², H. Hanaoka³, H. Tominaga⁴, M. Miyakubo¹, A. Negishi¹, S. Yokoo¹, K. Endo²; ¹Department of Stomatology and Oral Surgery, Gunma University Graduate School of Medicine, Showamachi Maebashi, Gunma, JAPAN, ²Department of Diagnostic Radiology and Nuclear Medicine, Gunma University Graduate School of Medicine, Showamachi Maebashi, Gunma, JAPAN, ³Department of Bioimaging Information Analysis, Gunma University Graduate School of Medicine, Showamachi Maebashi, Gunma, JAPAN, ⁴Department of Molecular Imaging, Gunma University Graduate School of Medicine, Showamachi Maebashi, Gunma, JAPAN.

Aim L-3-[¹⁸F]-fluoro-α-methyl tyrosine (FAMT) is transported into cancer cells by L-type amino acid transporter 1 (LAT1) . The purpose of the present study is to correlate the uptake of FAMT and FDG with the cellular proliferative activity measured by the Ki-67 labeling index (Ki-67 LI) in oral squamous cell carcinoma (OSCC). **Materials and Methods** Twenty five patients with OSCC were enrolled in this study. Both FAMT-PET and FDG-PET were performed within four weeks before surgery in all cases. The uptake of FAMT and FDG was compared by the semiquantitative analysis with maximal standardized uptake values (SUVmax) of the primary tumors. Ki-67 LI of the tumors were analyzed by immunohistochemical staining, and correlated with the clinicopathologic variables and the uptake of PET tracers. **Results** For the primary tumor detection, FAMT-PET exhibited a sensitivity of 84% whereas the sensitivity of FDG-PET was 88%. In all visible lesions, mean FDG uptake determined by average SUVmax was 9.7 (range, 4.2-15.9) and mean FAMT uptake was 3.5 (range, 1.3-8.5). The SUVmax of FAMT correlated better with Ki-67 LI (r=0.878, p<0.001) than that of FDG (r=0.643, p<0.001). **Conclusions** Uptake of FAMT correlated with cellular proliferation of OSCC. FAMT-PET may be a useful procedure to evaluate tumor proliferation of OSCC as compared to FDG.

P375

64Cu-at-sm pet/ct and 18f-fdg pet/ct in patients with h&n cancer candidate to radiotherapy: preliminary results.

C. Nanni, I. Grassi, G. Cicoria, V. Ambrosini, A. Cecconi, P. Castellucci, G. Montini, V. Allegri, C. Pettinato, E. Barbieri, S. Fanti; Ospedale S. Orsola Malpighi, Bologna, ITALY.

Purpose: to highlight hypoxic areas within the primary tumour and/or lymph nodal metastasis with 64Cu-at-sm pet/ct and to correlate its uptake with the event free survival after IMRT in pts affected by h&n cancer. Secondary aim is to compare 64Cu-at-sm pet/ct to fdg pet/ct, which is routinely used in our institution to draw the target volume. **Material and method:** so far, 5 pts with h&n cancer have been enrolled (mean age 60,4 yo; 3M 2F). All pts underwent an 18f-fdg pet/ct (carried out with standard technique) before therapy to stage the disease and define the gross tumour volume (GTV). Within 2 wks, they underwent also a 64Cu-at-sm pet/ct to highlight the hypoxic areas in the neoplastic lesions. 185 to 555 MBq of 64Cu-at-sm were injected iv. Images were acquired after 2h (early acquisition) and 16h (late acquisition) on a dedicated scanner (GE, Discovery STE) to eventually observe a tracer re-distribution. SUV max was calculated both for FDG and atsm. After this diagnostic flow chart, the pts were treated with IMRT on the basis of fdg pet/ct and clinical follow up was started. **Results:** all the pts presented and increased uptake of fdg and atsm, showing highly proliferative and hypoxic tumours. The following table shows the results of imaging procedures.

PT	GENDER	PRIMARY TOMOUR	FDG PET/CT	SUV		SUV	
				MAX FDG	ATSM PET/CT	MAX ATSM	MAX ATSM
1	M	82	2 left lc ln	15	1 lc ln	2	2
2	M	54	Left oropharinx and left lc ln	8	Left oropharinx and left lc ln. Peripheral redistribution in late images	2,3	2,3
3	F	64	Left tonsil	26	Left tonsil	1,7	3,9
4	M	57	Left tonsil and multiple ln	8	Left tonsil and 2 ln	6,8	6,1
5	F	45	Left tonsil	12	Left tonsil	0,2,77	2
MEAN		60,4		13,8			3,26

64Cu atsm presented a biodistribution equivalent or inferior to fdg and the SUV max tended to increase in late acquisitions. 1 month after therapy pt 1 died. Pt 2 did not obtain a complete response at fdg pet/ct after therapy. The other pts are currently in treatment and data about the eventual disease recurrence will be available in the next months. **Conclusions:** So far, 64Cu atsm

pet/ct did not change the radiotherapy plan. Despite that, 2 pts/5 with atsm uptake presented a persistence of disease. A wider population of pts (especially with negative atsm pet/ct) is needed to understand whether atsm uptake is a prognostic factor or not, and to clarify if adding a boost of dose in atsm positive areas may change pts prognosis. This study is ongoing.

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Radio-guided methods of sentinel lymph node identification in laryngeal and laryngopharyngeal cancers

E. A. Cherdynceva, V. A. Novikov, V. I. Chernov, I. G. Sinilkina, O. V. Cheremisina, S. Y. Chizhevskaya; Cancer Research Institute, Tomsk, RUSSIAN FEDERATION.

Lymphogenic spread of cancer influences not only on survival rates but also on the choice of treatment method. Complete lymph node visualization is difficult to perform and the problem concerning the extent of surgery on lymphatic nodes is still controversial. In view of the development of sentinel lymph node conception, the techniques of lymphoscintigraphy and intraoperative gamma-detection of regional lymphatic structures are actively designed. The purpose of the study was to analyze radio-guided techniques for detection of sentinel lymph nodes (SLNs) in patients with laryngeal and laryngopharyngeal cancers. **Materials and Methods:** The study included 17 patients with squamous cell laryngeal cancer (2 patients with T1, 4 with T2, 10 with T3 and 1 patient with T4) and 2 patients with laryngopharyngeal cancer (1 patient with T2 and 1 patient with T4). The median age of the patients was 58.7 years (range: 41 to 73). Sentinel lymph nodes were examined in all patients prior to surgery. To precisely localize SLNs, radioactive tracer ^{99m}Tc -Nanocis at a dose of 80 MBq was injected peritumorally during conventional fibrolaryngoscopy using 0.6–0.7 diameter needles. Single photon emission computed tomography (SPECT) was performed 20 minutes, 2 and 18 hours after radiotracer injection. During surgery, a gamma-probe was used to identify SLNs in the operating wound. Lymph nodes with increased radiotracer uptake were removed for subsequent histological examination. All patients with metastatic SLNs underwent neck lymphodissection. **Results:** SPECT revealed 1 (14 patients) to 3 (2 patient) SLNs. A total number of visualized SLNs was 22. The analysis of SLNs localization showed that 8 lymph nodes were identified in the upper third of jugular vein (level IIA), 1 in the middle third of jugular vein (level III), 1 in the lower third of jugular vein (IV), 4 in the area of prelaryngeal lymph nodes (VI) (4), 3 in paratracheal lymph nodes (VI) and 5 in paralaryngeal lymph nodes (VI). Histological study of SLNs showed metastatic involvement in 2 patients, inflammatory infiltration in 7, sinus histiocytosis and fibrosis in 4 and normal lymphatic tissue in 9 patients. One patient with SLN metastasis had no additional regional lymph node metastases. Metastases in both SLN and remaining regional lymph nodes were detected in 1 case. **Conclusion:** Radio-guided SLN detection is a promising technique in the assessment of the extent of surgery for patients with laryngeal and laryngopharyngeal cancers.

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Diagnostic capability of C-11 methionine PET for parotid gland cancer

S. Toubaru¹, K. Yoshikawa¹, S. Ohashi¹, M. Hasebe¹, H. Ishikawa¹, K. Sagou¹, K. Tamura¹, K. Tanimoto¹, S. Kandatsu¹, J. Mizoe², T. Fukumura¹, T. Saga¹, K. Kawaguchi³, Y. Hamada³, T. Kamada¹; ¹National Institute of Radiological Sciences, Chiba, JAPAN, ²Fondazione Centro Nazionale Adroterapia Oncologica, Milano, ITALY, ³First Dept. of Oral & Maxillofacial Surgery, Tsurumi University, Yokohama, JAPAN.

[PURPOSE] Many head and neck cancers show relatively high accumulation of C-11 methionine (MET) by PET, but normal parotid gland also accumulates MET at some level. Therefore it sometimes is very important to distinguish cancer accumulation from physiological accumulation in parotid gland. In this study, primary parotid cancers localized in parotid gland were evaluated by MET-PET or PET/CT for detectability and diagnostic ability. [MATERIALS AND METHODS] We reviewed MET-PET and PET/CT images of primary parotid cancer from May 1995 to May 2009, and picked 44 patients up with cancer localized in parotid gland. There were 32 pretherapeutic and 12 postoperative recurrent cases. Fifteen cases were adenoid cystic carcinomas, 12 cases were adenocarcinoma, 4 cases were mucoepidermoid carcinoma and 13 cases were others. All cases were confirmed by pathology. The accumulation of tumor was compared to contralateral normal parotid gland using TNR (tumor to normal tissue ratio). There were 40 cases that we could confirm the existence of normal parotid gland tissue around the tumor by MRI, we evaluated the ability of MET-PET and PET/CT for visually detecting the tumor boundary in surrounding normal parotid tissue. [RESULTS] Average TNR of MET accumulation was 7.3 (1.5–28.1) in parotid gland cancer, and 4.3 (1.1–10.0) in contralateral normal parotid gland. The average TNR of parotid gland cancer was significantly greater than that of contralateral normal parotid gland ([Unsupported Character - 検]; [Unsupported Character - 定]; [Unsupported Character - 法]); $p=0.0001$). The boundary of tumor surrounded by normal parotid tissue was visually detected in 28 cases out of 40 cases (70%). The tumor activity of MET was higher than surrounding normal tissue activity in 26 cases, and was lower in 2 cases. Tumor was totally included within normal parotid tissue in 4 cases, and was protruded from normal parotid tissue in 22 cases. Assuming that the contralateral parotid glands were true negative tissue, we calculated the diagnostic capability of MET for parotid gland tumor. Sensitivity, specificity and accuracy for malignancy of parotid gland tumor using 4.9 as cutoff value were 65.9%, 70.5% and 68.2%, respectively. [Conclusion] The average MET accumulation of parotid gland cancer was significantly greater than that of contralateral normal parotid gland. Parotid gland cancer was able to distinguish visually from surrounding normal parotid tissue in 70% of the cases.

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Comparison of 18F-FDG PET/CT and facial CT in restaging in patients with oral cavity cancer

A. Chong¹, J. Kim¹, S. Yoo¹, J. Oh¹, J. Ha¹, H. Oh², H. Bom¹, H. Song¹; ¹The Department of Nuclear Medicine of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF, ²The Department of Oral and

Maxillofacial Surgery of Chonnam National University Hospital, Gwangju, KOREA, REPUBLIC OF.

Purpose: We compared the usefulness of F-18 FDG PET/CT and facial CT in restaging of oral cavity cancer patients who underwent operation. Method: F-18 FDG PET/CT (PET) studies for restaging in 28 oral cavity cancer patients who underwent operation were included. In all of the cases, facial CT was done within one month from PET. Diagnostic accuracy in restaging was compared with facial CT. Confirmation of result was done by pathologic evaluation, clinical follow-up (with or without radiologic evaluation). Result: Further evaluation for PET and CT result were done by pathologic evaluation in 13 cases, by follow-up with radiologic evaluation in 5 cases and by clinical follow up by 10 cases. Among total 28 cases, final confirmation was normal (12), benign disease (8) and locoregional recurrence (6) and distant metastasis (2). In detecting recurrence, sensitivity, specificity, PPV, NPV of PET were 87.5%, 60.0%, 46.7% and 92.3%. In CT, sensitivity, specificity, PPV, NPV of CT were 75.0%, 70.0%, 50.0% and 87.5%. Diagnostic accuracy showed no statistically significant differences in both test (PET 67.9%. CT 71.4%). Comparison of ROC curve revealed statistically insignificant differences between two test ($p=0.41$). However, only PET detected distant metastasis in two cases. The diagnostic accuracy between locations showed no differences between PET and CT. Conclusion: In restaging oral cavity cancer after operation, PET showed similar diagnostic capacity with facial CT in locoregional metastasis. However, PET had additional advantage in detecting distant metastasis. So we can conclude that PET can be good substitute for facial CT in restaging of oral cavity cancer.

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FDG-PET/CT in assessment of residual or recurrent head and neck cancer after chemoradiotherapy.

M. J. Garcia-Velloso, C. Vigil, J. Alcalde, I. Dominguez, M. Moreno, J. Lopez-Picazo, J. Richter; Clinica Universidad de Navarra, PAMPLONA, SPAIN.

AIM: The goal of this study was to evaluate 2 fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT) for the detection of residual or recurrent disease after definitive chemoradiation therapy in head and neck cancer. METHODS AND MATERIALS: Posttreatment FDG-PET/CT and contrast-enhanced CT were performed in 30 patients, 24 male and 6 female, on average 4 months (range, 1 to 27 months) after completing definitive radiation therapy. FDG-PET/CT was visually analysed for the entire patient group and classified as negative or positive for residual disease. For the quantitative evaluation of FDG uptake, standardised uptake values (SUV) with an uptake period of 50 min were used. Pathologic findings and clinical follow-up served as the reference standard. RESULTS: Squamous-cell carcinoma was the most common tumour (28 patients, 93%). Follow-up data were available for all 30 patients (median, 16 months). Mean SUVmax in true positive for the primary site was 6.23 and for cervical disease was 3.77. FDG-PET/CT detected residual or recurrent disease with a sensitivity of 92%, a specificity of 76.5%, a positive predictive value (PPV) of 75%, and a negative predictive value (NPV) of 93% respectively, compared with 54%, 82%, 70%, and 70% for contrast-enhanced CT. The accuracy of FDG-PET/CT was 83%, compared with 70% for CT. The false-negative FDG-PET/CT result occurred 3 months after treatment and all the false-positive ($n = 4$ mean SUVmax=3.55) occurred between 3 and 5 months after treatment. CONCLUSIONS: FDG-PET/CT excelled by a higher specificity, negative predictive value and overall diagnostic performance than CT imaging. The metabolic-anatomic information from FDG-PET/CT is highly effective in evaluating patients for recurrent head and neck tumours. These results support a potential clinical role of FDG-PET/CT in the assessment of therapy response after definitive radiation therapy.

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Prognostic value of 18F-FDG-PET in patients with suspected recurrence of head and neck cancer

R. Fernández López, A. Gómez Torres, I. Borrego Dorado, R. Vázquez Albertino, F. Esteban Ortega, P. Gómez Camarero, R. Álvarez Pérez, I. Tirado Zamora, A. Menoyo Bueno, J. Cuenca Cuenca; HHUU Virgen del Rocío, Seville, SPAIN.

AIM: The purpose of this study was to establish the prognostic value of ^{18}F -FDG-PET in patients with suspected recurrence of head and neck cancer. MATERIALS AND METHODS Fifty-three consecutive patients (7 women/46 men) with suspected recurrence of head and neck cancer were studied prospectively with a minimum follow-up of 1 year (mean: 18.54 months). ^{18}F -FDG-PET was performed in all these patients between June 2007 and March 2009. PET results were proved with histology (21 patients) and/or clinical and imaging follow-up (32 patients) as reference standard. Reasons for requesting the PET were inconclusive morphological techniques in 29 patients and clinical suspicion of recurrence in 24. Maximum SUV (SUVmax) values have been correlated with clinical outcome to determine the cut-off level with predictive value. RESULTS PET scan was negative in 20 patients and positive in 33 with an average SUVmax of 7.57 (range: 18.4–1.9). Two cases were false positive. The disease-free survival rate after 1 year in patients with negative PET was 100% (20/20) compared to 45.45% (15/33) in patients with positive PET. The overall survival rate in the latest clinical follow-up in patients with negative PET scan was 94.73% (19/20) as opposed to 72.72% (24/33) in patients with pathological PET scan. Additionally, PET detected second primary tumors in 8 patients (4 lung cancer, 1 uterus cancer, 1 renal cancer, 1 colon cancer and 1 adenomatous polyp of colon). PET results modified the therapeutic approach in 47/53 patients (88.68%). CONCLUSIONS ^{18}F -FDG-PET imaging is an excellent technique for detecting recurrences in patients with suspected recurrence of head and neck cancer and has an important clinical impact by modifying the therapeutic approach in a high percentage of them. This imaging modality is able to predict those patients who have an unfavourable prognosis and may play an essential role in managing patients with suspected recurrence of head and neck cancer.

P381**PET/CT in the detection of local recurrence of head and neck carcinoma.**

R. Czepczyński¹, M. Popko², M. Wierzbicka², W. Szyfter², J. Sowiński²,
¹Poznan University of Medical Sciences, Euromedic Diagnostics, Poznań, POLAND, ²Poznan University of Medical Sciences, Poznań, POLAND.

Introduction. The diagnosis of local recurrence is difficult in patients with head and neck carcinoma due to surgery- and radiation-related morphologic changes. PET with 18F-FDG allows to differentiate malignant and benign tissue in majority of tumours. The aim of the study was to evaluate the utility of PET/CT using 18F-FDG in detection of local recurrence. Material and methods. Patients with head and neck cancer suspected of local recurrence based on clinical examination or other imaging modalities, were qualified to the study. The study group consisted of 55 subjects (42 male and 13 female), aged 25 - 80 years. The primary location of the tumour was: oral cavity (15), larynx (15), palatine tonsils (8), pharynx (6), salivary glands (6), nasal cavity (5). All the patients underwent PET/CT with 18F-FDG using Discovery STE scanner (General Electric) at least 3 months after surgery or radiotherapy. The standard parameters were: injected activity - 5 MBq/kg, uptake time - 60 min. The results of PET/CT were verified by clinical examination and ultrasonography in all patients, and contrast-enhanced CT or/and MR in majority of them. In positive PET/CT cases all metabolically active foci were verified histopathologically (biopsy or surgery). Negative cases were followed-up for 6-18 months after PET/CT. Results. In 29 patients PET/CT was positive. The recurrence was confirmed with other methods, incl. histopathology in 22 cases (true-positive). In 7 patients, the false-positive findings were verified as inflammatory or oedematous lesions without evidence of malignant tissue. In the remaining 26 cases, the scan was negative. In one of them, recurrence was diagnosed histopathologically only (false-negative). The statistical parameters were as follows: sensitivity 95.6%, specificity 78.1%, PPV 75.8%, NPV 96.2%. Independently of the findings in the head and neck region, distant metastases were detected in 5 patients (lungs and bone). Conclusion. PET/CT using 18F-FDG is a very sensitive tool for the detection of recurrence of head and neck carcinoma. Specificity of the method is slightly limited due to the local inflammatory processes.

P35 — Monday, October 11, 2010, 16:00 — 16:30, Hall Z

Oncology Clinical Science: Thyroid**P382****Amifostine protection of radioiodine side effects on salivary glands: a prospective, randomized and double-blind study**

J. P. Almeida¹, D. N. Viviani², R. B. Barra², M. Marone³, E. T. Rocha², E. T. da Silva⁴, M. Foschini⁵, A. L. Carvalho⁵, S. M. Moriguchi², L. P. Kowalski¹,
¹Department of Head and Neck Surgery and Otorhinolaryngology, Hospital A. C. Camargo, Sao Paulo, BRAZIL, ²Department of Nuclear Medicine, Barretos Cancer Hospital, Barretos, BRAZIL, ³Department of Nuclear Medicine, Hospital Samaritano de São Paulo, Sao Paulo, BRAZIL, ⁴Department of Physics in Nuclear Medicine, AmorimTinois Graphic Computer, Campinas, BRAZIL, ⁵Department of Epidemiology and Statistics, Research Support Center, Barretos Cancer, Barretos, BRAZIL.

Background: Radioactive Iodine Therapy (RIT) has many side effects on salivary glands. This randomized, double-blind study aims to describe the protection effects of amifostine on salivary glands in patients submitted to RIT as treatment to well-differentiated thyroid carcinomas. **Methods:** Thirty patients were randomized to receive 200 mg/m² of subcutaneous amifostine or saline solution as placebo before receiving radioactive iodine. Patients were evaluated with salivary gland scintigraphy, sialometry and subjective questions before and 3 months after RIT to investigate the efficacy of amifostine to protect salivary glands. **Results:** There were no differences between groups in all variables before treatment. During RIT, amifostine neither decreased the incidence of sialadenitis related to I-131, but it was able to decrease the mean time of sialadenitis related to I-131 from 6.27 days to 3.5 days (P = .02). Three months after RIT there were no differences of parotid/submandibular uptake pre-stimulus between. Values of parotid constant of excretion of -1.69%/min versus -5.03%/min in amifostine and placebo groups, respectively, show a diminished excretion function of parotid in both groups 3 months after RIT, higher in placebo but with no significant difference (P = .86). The values of submandibular constant of excretion of 1.51 %/min versus 1.99 %/min (P = .91) in amifostine and placebo groups, respectively, show that submandibular glands maintain the excretion function better than parotid glands after RIT. **Conclusions:** 200 mg/m² of subcutaneous amifostine was not able to protect salivary glands of acute side effects of RIT. More studies are needed to determine the safe and effective dose of amifostine in thyroid cancer patients.

P383**Investigation of non-functioning metastases from thyroid cancer with sestamibi-99m and iodine-131 whole body scan: comparative methodology assessment.**

M. C. P. Gonçalves¹, M. J. Santos¹, S. M. Moriguchi¹, A. L. Carvalho², M. I. P. Simões¹, N. Onari³, E. T. Rocha³,
¹Department of Nuclear Medicine, Barretos Cancer Hospital, Barretos, BRAZIL, ²Department of Surgical Oncology, Barretos Cancer Hospital, Barretos, BRAZIL, ³Department of Radiology, Barretos Cancer Hospital, Barretos, BRAZIL.

Our aim was to evaluate the reproducibility of the findings of whole body scan (WBS) with 99mTc-sestamibi compared to the conventional method using post therapy iodine-131 WBS, in differentiated thyroid carcinoma (DTC) and to assess the inter-observer reproducibility by three nuclear physician to classify such studies. We studied prospectively 68 patients who underwent total thyroidectomy for DTC, and that were referred for radioiodine therapy. They were divided

into two different groups: the first one with those that were submitted to thyroidectomy less than one year without any prior radioiodine therapy (MIBI-I), and subjects with active disease (MIBI-II). The sample was made up of 56 and 12 subjects, respectively. Overall, 42 subjects had Tg > 2ng/ml while 45 had TgAc > 10IU/ml. Calculations of kappa values for PCI-131I in MIBI-I showed agreement level among the physicians of at least moderate in the bone compartment and at least strong in the cervical lymph nodes, lungs and mediastinum; moreover, PCI-99mTc sestamibi agreement was at least moderate in lymph nodes and regular in cervical and mediastinal compartment, without agreement in the lung. However, when analyzing kappa values for the sestamibi-99mTc WBS in MIBI-II it was found that there was at least regular agreement rate among all compartments, while assessing inter-instrument reproducibility it was observed that agreement rate in both groups (MIBI-I e MIBI-II) was regular and strong, respectively. Besides, specificity and negative predictive value (NPV) were high in discriminating not ill patients in comparison to consensus sestamibi-99mTc WBS. The reproducibilities of the 99mTc-sestamibi WBS for post therapy 131I WBS showed that there was agreement by chance in group MIBI-I, though, all positive 99mTc-sestamibi WBS were positive after 131I therapy as well. In spite of the regular agreement rate in the MIBI-II group, the objective of the study was reached. It is interesting to add that 25% of patients with active disease were positive in the sestamibi-99mTc WBS and negative in post therapy 131I WBS, in other words, this group did not benefit from the therapy proposal. Sestamibi-99mTc WBS did not prove to be a reproducible method. The inter-instrument assessment showed high specificity and high NPV in the groups and helped to identify those patients who did not benefit from therapy with iodine-131.

P384**Tg developing in a pregnant patient with metastatic papillary thyroid carcinoma**

J. Gessler, C. Happel, W. T. Kranert, M. Middendorp, F. Grünwald; Hospital of the Johann-Wolfgang Goethe University, Frankfurt / Main, GERMANY.

Aim: Retrospective analysis of the thyroglobulin (Tg) level in a patient with metastatic PTC during pregnancy. **Methods:** A 31-year-old patient suffering from PTC (pT2 pN1 M1) with multifocal pulmonary metastases, first diagnosed at the age of 22, underwent eight radioiodine therapies within two years (age of 22 to 24 years) and two I-131 whole-body scintigraphies for diagnostic purposes after thyroidectomy. The cumulative activity was 53,531 MBq and the calculated dose 3.3 Gy according to IRCP. At the age of 29 years (one year after the last radioiodine administration) the patient became pregnant. The Tg level was determined in regular intervals: before pregnancy every 2 to 4 months, during pregnancy every 8 weeks, and 6 weeks after delivery. Moreover, the Tg level in the chorblood was determined (4 samples). **Results:** In the year before pregnancy the Tg had a mean value of 0.36 ng/ml (0.36 ng/ml 36 weeks before pregnancy, 0.3 ng/ml 24 weeks before pregnancy and 0.55 ng/ml 12 weeks before pregnancy). During pregnancy the Tg increased from 0.23 ng/ml to 1.7 ng/ml (0.74 ng/ml 16th week, 1.08 ng/ml 26th week and 1.75 ng/ml 38th week). Four weeks after delivery Tg decreased to 0.23 ng/ml within the normal range. The Tg values in the four samples of the chorblood ranged from 37.31 to 40.01 ng/ml. A retrospective analysis of the Tg course in 5 patients who conceived after complete remission due to surgical and radioiodine treatment showed no significant changes. The Tg value in the chorblood was consistent with the value in literature (44.61 +/- 23.84 ng/ml). **Discussion:** The reference value of Tg in patients after thyroid ablation (< 1 ng/ml) was exceeded during pregnancy and normalized four weeks after delivery. The increased Tg during pregnancy is probably attributed to a passover from fetal Tg to the maternal circulation.

P385**Nasolacrimal Duct Obstruction as a Complication of Iodine-131 Therapy in Patients with Thyroid Cancer**

A. Fard-Esfahani, S. Farzanefer, B. Fallahi, D. Beiki, M. Eftekhari, M. Saghari, A. Emamiardakani, M. Majidi; Research Institute for Nuclear Medicine, Tehran, IRAN, ISLAMIC REPUBLIC OF.

Aim: I-131 has been widely used in treatment of differentiated thyroid carcinoma for almost 70 years. During this period many complications such as sialadenitis and lacrimal gland dysfunction have been established. This study argues a new complication "symptomatic or asymptomatic nasolacrimal duct obstruction". **Materials and Methods:** 81 patients (162 eyes) treated with more than 100 mCi I-131 were categorized in 4 groups based on received cumulative dose and were evaluated in a historical cohort study. In addition 17 (34 eyes) age and sex matched persons were selected as control group. Using dacryoscintigraphy, patients and control group were evaluated for partial or complete nasolacrimal duct obstruction. The data on different groups of patients were compared with the data of control group. Fisher exact and Mann-Whitney U tests were applied for analyses of categorical and numeric variables, respectively. The analyses were considered significant with p<0.05. **Results:** 18% of exposed eyes (29 out of 162) and 9% of control eyes (3 out of 34) had evidences of nasolacrimal duct obstruction on the scan images. Among the patients treated with less than 300 mCi of I-131, 12.8% (5 out of 39) had asymptomatic nasolacrimal duct obstruction and 2.6% (1 out of 39) had symptomatic obstruction. These values for patients treated with more than 300 mCi were 19% (8 out of 42) and 35.7% (15 out of 42), respectively. Mean cumulative I-131 dose that lead to nasolacrimal duct obstruction was 429±264 mCi. This value was 273±173 mCi for the patients without obstruction (p<0.05). **Conclusion:** This study confirms nasolacrimal duct obstruction as a complication of I-131 therapy. The symptomatic form of this complication occurs mainly in cumulative dose more than 300 mCi.

P386**Assessment of Variables Associated with the Post-surgical Radioiodine Ablation of Thyroid Remnants**

A. Akgun, O. Omur, F. Hatipoglu, H. Uz, Z. Ozcan, H. Ozkılıç; Ege University Medical Faculty, Izmir, TURKEY.

Aim: Postsurgical ablative therapy with radioiodine (RAI) is an essential part of therapeutic management in patients with differentiated thyroid carcinoma (DTC). While higher success rates have been expected in patients receiving high dose activity, poor ablation rate may also be noted in a minority of patients. In this study it was aimed to compare the therapeutic efficacy of initial

RAI ablation with high doses of RAI and to investigate the possible factors that may affect the ablation rate. **Methods:** A total of 385 patients with DTC were included. The age range was 21–76 and the female/male ratio was 314/71. There were 331 papillary, 48 follicular and 6 mixed carcinomas. All patients underwent total or near/total thyroidectomy followed by RAI ablation for the remnant tissue. Following surgery, all patients received ablative therapy with a mean dose of 11.2 ± 3.2 mCi. The criteria for successful ablative therapy was defined as no uptake in the thyroid bed on the first diagnostic I-131 WBS and a thyroglobulin (Tg) value < 2 ng/ml at 6 months after therapy. Possible variables that may affect ablation rate such as age, sex, tumor histology, size, disease confined to the thyroid gland, the presence of local or distant invasion, TNM stage, preablative FT4 and Tg level and I-131 dose were investigated. **Results:** Successful ablation according to our criteria was obtained in % 84.9 patients. Diagnostic I-131 WBS and low Tg level were both in agreement in 327/385 patients. There were 25 WBS (+) Tg (-), 23 WBS (-) (Tg+) and 10 WBS (+) Tg (+) patients. Statistical analyses showed no relation between ablation success and age, sex, preablative FT4 level, tumor histology, tumor size or TNM stage ($p > 0.05$). Univariate analysis showed significant association of ablation success with preablative Tg level, disease confined to the thyroid gland and ablative I-131 dose ($p < 0.05$). Multivariate analysis demonstrated that the preablative Tg level was the only significant predictor of success (OR=1.06; 95% CI=1.04–1.09) **Conclusion:** Despite the use of high dose RAI treatment, ablation failure may be noted in a small sub-group of patients. Among the variables associated with ablation success rate, preablative Tg level appeared the most significant predictor. In addition to the preablative Tg level, ablative therapy dose and the disease confined to the thyroid gland are significantly related with ablation success.

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Scintigraphic assessment of thyroid remnants in the postoperative follow-up of patients with well differentiated thyroid carcinoma with 99mTc pertechnetate

M. P. Yaneva, A. Botushanova, M. Marovska; Medical University, Plovdiv, BULGARIA.

Aim: In the postoperative phase of patients with proven well differentiated thyroid carcinoma is important to know what is the amount of thyroid tissue left after the operation. Sometimes I-131 for diagnostic purposes is missing and at the same time it is important what will be the next treatment procedure for the patient. **Material and method:** 157 operated patients with well differentiated thyroid carcinoma were included in our study- 129 female and 28 male, mean age 48.4 yrs and range 21–83 years after total thyroidectomy and off L-Thyroxine therapy. Radionuclide studies are performed on SPECT cameras Siemens DIACAM and Siemens Symbia E, dual heads. The patients are injected intravenous with 99mTc-pertechnetate in dose of 74MBq. Static images were acquired for 5min, 20 minutes post administration of the radionuclide. The detector put on anterior position/AP/. Location of residual parenchyma is determined by the fossa jugularis and operational scarring. **Results:** Of 157 patients surveyed, 151 registered the presence of residual thyroid tissue. In the rest 6 we did not find any residual parenchyma. They were examined as a control study with I-131-I. Only 1 patient has proven to be with a small residue. The data show that thyroid scintigraphy with 99mTc pertechnetate is reliable method for rapid and early diagnosis of residual parenchyma after a total thyroidectomy. Put into practice allows it to determine therapeutic behaviour in these patients on time. **Conclusion:** Scintigraphy with 99mTc-pertechnetate is of particular importance in critical condition with irregular supply of I-131-I.

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Correlation of Incidental Thyroid Findings Using ^{18}F -FDG PET/CT in Oncological Patients without Known Thyroid Cancer

A. Prieto Soriano, G. Salazar Andía, L. Lapeña Gutiérrez, R. C. Delgado-Bolton, M. N. Cabrera Martín, A. Ortega Candil, C. González Roiz, M. P. Fierro Alanís, J. Cardona Arboniés, M. García García-Esquinas, J. L. Carreras Delgado; Hospital Clínico San Carlos, Universidad Complutense, Madrid, SPAIN.

Aims: Evaluate the impact of thyroid findings using ^{18}F -FDG PET/CT in oncological patients without known thyroid cancer. **Materials and methods:** A retrospective study was carried out on a series of cases. The patients correspond to Hospital Clínico San Carlos area. We reviewed 1320 ^{18}F -FDG PET/CT studies, which had been carried out between December 2008 and December 2009. Inclusion criteria were: (a) patients who did not have previous history of thyroid cancer; (b) and/or who presented findings on CT (solid nodules, cystic, goitre, etc.). We included 55 patients (43 female, 12 male, aged between 34 and 93, average age 68.5). These were divided into 2 groups: Group A: patients with known benign thyroid disease (12 patients). Group B: patients without known benign thyroid disease (43 patients). In each group it was determined if the findings observed in ^{18}F -FDG PET/CT were then correlated with other diagnostic methods (fine-needle aspiration, other imaging techniques or/and tests). **Results:** Of the 12 patients in Group A, in 6 patients the findings observed in ^{18}F -FDG PET/CT were correlated with other diagnostic methods, and all the findings suggested benign tumors, while 2 were doubtful. Of the 43 patients in Group B, in 21 patients the findings in ^{18}F -FDG PET/CT were correlated. Of these, 3 were diagnosed as thyroid cancer or metastasis of thyroid cancer (5.5% of the cases of the cohort of 55 patients). In these 3 patients, ^{18}F -FDG PET/CT suggested malignant disease in all; 2 were cases of unknown primary tumors and 1 was cancer of the penis. In the remaining 18 patients in Group B, the correlations suggested benign disease in 12 and was doubtful in 4. **Conclusions:** The incidental thyroid findings in ^{18}F -FDG PET/CT in oncological patients without known thyroid cancer have evidenced malignant thyroid disease in 5.5% of the cases in our study. This indicates additional diagnostic tests are necessary to confirm the diagnosis.

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Incidental Detection of ^{18}F -FDG Thyroid Uptake: The Risk of Malignancy

J. Correia, P. Lapa, A. Albuquerque, R. Macedo, R. Silva, H. Fernandes, G. Costa, J. Pedroso de Lima; Servico de Medicina Nuclear - Hospitais da Universidade de Coimbra, Coimbra, PORTUGAL.

Aim: The widespread use of whole body ^{18}F -FDG PET/CT into clinical practice facilitates the detection of incidental thyroid lesions. It is known that a percentage of these lesions is associated with cancer. The purpose of this study was to determine the prevalence rate and malignancy risk of incidental thyroid FDG uptake revealed on ^{18}F -FDG PET/CT imaging for non-thyroid disease, in patients studied in our department during a 6 years period. **Material and Methods:** The 7714 ^{18}F -FDG PET/CT examinations performed for a non-thyroid disease in our department from January 2004 to January 2010 were retrospectively reviewed. Thyroid incidentalomas were identified. The uptake pattern of ^{18}F -FDG was visually classified as focal or diffuse. Obtained data was correlated with histology and clinical follow up. SUVmax values were obtained for focal lesions and statistically compared between groups (malignant versus benign). **Results:** Of the 7714 reviewed scans, unexpected thyroid findings were detected in 145 (104 women and 41 men, mean age 62 years) corresponding to a prevalence of incidentalomas of 1.9%. Thyroid focal uptake was seen in 120 of the 145 cases (82.8%) and a diffuse uptake pattern in 25 patients (17.2%). Among the 120 patients with focal thyroid lesions histopathologic information was obtained in 28 patients (23.3%). Malignant involvement of the thyroid was confirmed in 9 patients (mean SUVmax: 16.9 ± 16.0): 5 primary tumors (4 papillary carcinoma and 1 less differentiated cancer) and 4 metastases; the remaining 18 cases corresponded to benign lesions (mean SUV max: 5.2 ± 2.4). The thyroid malignancy risk for the focal FDG uptake pattern was 32.1%. Thyroid functional assays (TSH and auto-antibodies) and/or ultrasound were performed in 10 (40%) of the 25 patients with diffuse uptake pattern, 8 showed chronic thyroiditis and the other two had nodular goiter. The overlap between maximum SUV values of malignant and benign thyroid lesions didn't allow the definition of a cut-off value for malignancy. **Conclusions:** In our experience, the prevalence of thyroid ^{18}F -FDG uptake incidentally detected during whole body ^{18}F -FDG PET scan is 1.9%. Malignancy was histologically proven in 32.1% of the patients who underwent fine needle aspiration. A diffuse thyroid uptake pattern was associated with benign conditions. On an individual patient basis SUVmax cannot differentiate benign from malignant lesions. Therefore we suggest that any focal thyroid incidentaloma detected on a ^{18}F -FDG PET/CT should be carefully evaluated because of a significant risk of cancer.

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131I treatment for thyroid cancer in patients under haemodialysis (HD)

G. C. Magri¹, A. De Agostini², E. Movili³, S. V. Gabanelli⁴, G. Merli⁵, C. A. Rodella², F. Caobelli⁴, G. Jeannin³, R. Zubani⁶, R. Giubbini⁵; ¹Dpt of Nuclear Medicine Spedali Civili, Brescia, ITALY, ²Medical Physics, Spedali Civili, Brescia, ITALY, ³Division and Chair of Nephrology, University of, Brescia, ITALY, ⁴Chair of Nuclear Medicine University of, Brescia, ITALY, ⁵Chair of Nuclear Medicine University of, Brescia, ITALY, ⁶Division and Chair of Nephrology, University of, Brescia, ITALY.

OBJECTIVES: The extensive use of neck ultrasound in HD pts in view of a kidney transplant (TX), in an area of endemic goitre allows the detection of an increasing number of thyroid cancers. The demonstration of complete remission is essential to readmit pts to a TX program (after 3 years negative follow up) So the number of Pts who need 131I treatments is increasing as well. **Aim** of this study is to review the feasibility and the results of this treatment **METHODS:** 4 pts aging 47 to 68 years operated for thyroid cancer (3 papillary, 1 follicular) have been treated with 131I after total thyroidectomy during the year 2009. A standard activity of 3.7 GBq of 131I after Thyrogen® 0.9 mg X 2 was administered After radioiodine administration they underwent HD in the therapy section of the department of nuclear medicine, assisted by a trained nurse of HD dpt at 2nd and 4th days. A post therapy scintigraphy was obtained after the 2nd HD. For each patient radiation exposure rate was evaluated before and after each dialysis treatment; the adsorbed dose of the HD nurses was also recorded **RESULTS:** a) clinical After Thyrogen® no adverse reaction was observed; in all the pts TSH values increased > 100 mU/l. Thyroglobulin (Tg) value significantly increased in 1 pt (8 to 64 ng/ml); in two remained undetectable also after stimulation; finally in the last one was not reliable because of high anti Tg antibodies level. At the scan 5 days after iodine administration no patient demonstrated I31 uptake out of the thyroid remnant. At the follow up after 6 months, during thyroid replacement therapy no clinical or biochemical evidence of disease was seen. For 2 of them the 1 year follow up is available; no increase of Tg after thyrogen was seen and renal TX can be reconsidered b) dosimetry The average drop in Pt exposure was about 50 % after each HD; All the pts could be discharged 5 days (2 HD) after I31 according to Italian rules on radiation protection. The absorbed dose for HD nurses was negligible. In 2 pts the adsorbed dose for the bone marrow was calculated and resulted less than 1 Gy. **CONCLUSIONS:** 131I for thyroid cancer in HD pts is safe both for pts and the staff, effective and mandatory also in low risk patients to be readmitted to the transplantation program.

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Clinical significance of pathological thyroid FDG uptake

C. Paniagua Correa, M. A. Balsa Breton, M. P. Garcia Alonso, A. Mendoza Paulini, A. Mariana Monguia, S. I. Vasques Tineo, A. Ortega Valle, L. Castillejos Rodriguez, J. Panizo Alcaniz, F. J. Penin Gonzalez, C. Pey Illera; Hospital Universitario de Getafe. Medicina Nuclear, Getafe (Madrid), SPAIN.

Introduction: The normal thyroid FDG uptake is generally absent or minimal and mild diffuse uptake can be a normal variant. Greater degrees of diffuse uptake are seen in Grave's Disease and Chronic Thyroiditis. Focal uptake is non-specific and can be seen in both benign and malignant nodules. **Objective:** To determinate the prevalence and clinical relevance of incidental focal or diffuse thyroid ^{18}F -FDG uptake in patients with known cancer. **Methods:** We retrospectively reviewed 665 cases of FDG-PET/CT performed at our institution between May/2.009 and February/2.010. Incidental focal or diffuse thyroid FDG uptake was found in 21 patients without known thyroid cancer (16 female and 5 male) with a mean age of 60.23 years (34–83). **Results:** The prevalence of pathological FDG thyroid uptake was 3, 15% (21/665). *) 7/21 (33, 33%) had diffuse uptake, of which 4 had prior diagnosis of thyroid disease: 3 subclinical primary hypothyroidism and 1 multinodular goiter. All these patients continued with their clinical, laboratory and ultrasound controls. *) 14/21 (66, 66%) had focal uptake, two of them with previous known thyroid disease (multinodular goiter). The diagnosis was performed by FNA (fine-needle aspiration) or post surgery in 4/14: in 2 cases papillary thyroid cancer was histologically confirmed (2/14: 14.28%) with SUV values of 2.76 and 3.89, respectively. In 2

benignity was confirmed (SUV of 8.3, and 2.33, respectively). There was overlapping of the lesion's SUV between the benign and malignant cases. The remaining patients (10/14) didn't have histological confirmation of their thyroid lesion because no specific biopsy site was visualized on CT or sonographic images. 4/10 patients continue in follow-up with their endocrinologist. 1/10 PET/CT study, requested for initial lymphoma staging, showed severe focal FDG uptake that disappeared after treatment, that's why we relate this finding with metabolic activity of its underlying disease. We have no data of 5/10 patients from other hospitals. Conclusion: Our data support the importance of characterizing incidental pathological thyroid uptake, mainly in focal lesions, because we found malignant disease in 14, 28% of focal uptake, and show similar prevalence with other studies (3, 15%). The SUV values vary too much (from 2 to 8, 5), so focal uptake in the thyroid requires further workup because malignancy cannot be excluded on SUV alone.

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Are the increased/asymmetric thyroid FDG uptakes, incidentally found during Total Body PET (incidentalomas), potential predictors of thyroid malignancy, if compared to histological findings?

M. Rudoni¹, G. Sacchetti¹, C. Baiocco¹, R. Boldorini², P. Neri³, R. Matheoud⁴, F. Pia⁵, E. Inglese¹, ¹Nuclear Medicine Dept. AOU Maggiore della Carità, Novara, ITALY, ²Histo Pathology Dept. AOU Maggiore della Carità, Novara, ITALY, ³Radiology Dept. AOU Maggiore della Carità, Novara, ITALY, ⁴Medical Physics Dept. AOU Maggiore della Carità, Novara, ITALY, ⁵Head & Neck Dept. AOU Maggiore della Carità, Novara, ITALY.

Aim: In 1%-2% of pts submitted to ¹⁸F-DG-PET/CT for non-thyroid clinical indications, we found unexpected abnormal thyroid uptake (thyroid incidentalomas). The aim of this study was to determine if these abnormalities corresponded to unknown focal sites of thyroid malignancy. Materials: In 39 pts with abnormal thyroid FDG uptake, taken from the PET diagnostic workup of the last two years, was clinically possible a complete thyroid evaluation. After informed consent all pts were submitted to ultrasonography, ^{99m}Tc-scintigraphy and ultrasound-guided fine-needle cytology (FNAC). Final pathologic diagnoses were compared with ¹⁸F-DG-PET/CT findings. Results: A single focal FDG abnormal uptake was observed in 32/39 pts (94.8%); multiple focal sites of abnormal uptake were found in 5 pts and a diffuse and inhomogeneous increased FDG uptake was found in only 2 pts. The mean SUV was 6.3. In 19/39 pts ultrasonography identified a single node coincident with the FDG focal uptake. In 17/39 pts the ultrasonic finding was multinodular goiter and in 3 pts the ultrasound scanning of the thyroid was nodule-free. The nuclear scan was available in 29 pts and in 14/29 pts a "cold nodule" was found, coincident with the FDG focal uptake (48.3%). The other scintigraphic findings were: "hot nodules" in 3/29 pts (10.3%); inhomogeneous ^{99m}Tc uptake in 7/29 pts (24.1%) and "normal distribution" of the tracer in 5/29 pts (17.2%). The ultrasound-guided FNAC was available in 37 pts and performed accordingly to the ¹⁸F-DG-PET/CT findings, with the following results: in 14/37 pts the cytology was suspected for malignant lesion; 2 lesions were suggestive of Hurtle's cell type, both confirmed as papillary carcinoma at histology; 4 cytologies were suspected to be follicular carcinoma, 2 confirmed at histology and the other 2 were found to be medullary cancer; 7 cytologies were suspected to be papillary carcinoma, five of which confirmed at histology and one that is waiting for surgical intervention. Conclusions: In 36% of our pts the abnormal focal or diffuse thyroid uptake corresponded to cancer lesions. There were no significant differences between the non-neoplastic and neoplastic populations in terms of uptake intensity (expressed by the SUV), ultrasonographic and scintigraphic findings. Therefore these ¹⁸F-DG-PET/CT incidentalomas require a complete diagnostic thyroid evaluation by scintigraphy, ultrasonography and FNAC, irrespective of the SUV value, because at least one third of these pts have a thyroid cancer. The appearance in multinodular goiters of one or more hypermetabolic (FDG-PET) nodes, provides a useful guide for a "guided" biopsy.

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Clinical Impact of Positron Emission Tomography with 18F-Fluorodeoxyglucose (18-FDG-PET) in patients with suspected recurrence of differentiated thyroid cancer (DTC).

A. Santiago-Chinchilla¹, M. A. Muros¹, H. Palacios-Gerona¹, C. Ramos-Font¹, M. Moreno-Caballero¹, M. Navarro-Pelayo-Láinez¹, T. Muros², Á. Ramírez-Navarro¹, J. M. Llamas-Elvira¹; ¹Servicio de Medicina Nuclear. Hospital Universitario Virgen de las Nieves, Granada, SPAIN, ²Servicio de Endocrinología. Hospital Universitario Virgen de las Nieves, Granada, SPAIN.

Aim: To evaluate the clinical impact of 18-FDG-PET in patients with suspected recurrence of differentiated thyroid carcinoma (DTC). Material and methods: 24 patients with DTC (14 papillary, 8 follicular, 2 mixed) under recurrence (increased thyroglobulin antibodies, or positive US) suspicion were referred to our department for radioiodine treatment. 18-FDG-PET studies were acquired on a Siemens ECAT EXACT 47 tomograph and iterative OSEM reconstruction (2 iterations, 8 subset) was used for processing. In the follow up analysis other imaging techniques, analytical determinations and treatment were take in consideration. Results: 14 patients had positive FDG PET study. Of these, 8 were referred for surgery, confirming the presence of disease in 7. All of them have favourable clinical evolution with a decrease or undetectable level of thyroglobulin. 1 patient had radiotherapy, 1 received radioiodine and 1 was derived for chemotherapy treatment. 3 patients remain untreated. 10 patients had a negative PET study, in 3 patients disease was not confirmed by the follow-up and serum thyroglobulin levels evolution, 5 continue with no evidence of disease and positive thyroglobulin and and 2 false-negative results were demonstrated after surgery. The results of the FDG-PET studies modified the therapeutic approach in 13 patients (54%). Results of the US and FDG-PET studies were discordant in 8 patients, where FDG-PET detected more lesions than US. Conclusions: 18-FDG-PET is a useful tool in patients with suspected recurrence of differentiated thyroid cancer (DTC). In our series 18-FDG-PET changed treatment in 54% of patients under suspicion of recurrence.

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Negative Predictive Value of Positron Emission Tomography with 18-Fluorodeoxyglucose(18-FDG-PET) in patients with suspicion of recurrence of differentiated thyroid cancer(CDT).

A. Santiago-Chinchilla¹, M. A. Muros¹, M. Navarro-Pelayo-Láinez¹, C. Ramos-Font¹, H. Palacios-Gerona¹, M. Moreno-Caballero¹, E. Torres-Vela², S. Cespedes-Más³, C. García-Calvente³, J. M. Llamas-Elvira¹; ¹Servicio de Medicina Nuclear. Hospital Universitario Virgen de las Nieves, Granada, SPAIN, ²Servicio de Endocrinología. Hospital Universitario San Cecilio, Granada, SPAIN, ³Servicio de Endocrinología. Hospital Universitario Virgen de las Nieves, Granada, SPAIN.

Objective: To assess the negative predictive value of 18-FDG-PET in patients with suspicion of recurrence of CDT. Methods: 18-FDG-PET were performed in 20 patients with CDT (17 papillary, 2 follicular, 1 combined) submitted to Nuclear Medicine for suspected recurrence by positive thyroglobulin levels (14 patients) or positive ultrasound (6 patients). In 20 patients the results of 18-FDG-PET were negative. The 18-FDG-PET were acquired on a Siemens ECAT EXACT tomograph 47 and OSEM iterative reconstruction (2 iterations, 8 subset). We studied disease-free interval (average), the results of conventional imaging techniques (ICTs) and Tg values during the follow-up. Results: 20 patients were studied for suspected recurrence and were negative in 18-FDG-PET study. We considerer three groups: 1) 6 patients with positive ultrasound and negative Tg (less than 1 ng / ml): 5 patients remain free of disease and negative Tg levels (mean follow-up = 33, 1 months) and 1 patient was found to be a false negative in a new PET-CT study. 2) 7 patients with Tg levels of ≤ 10 ng / ml: All of them remain with Tg levels below 10 ng / ml and no evidence of disease in other ICT (mean follow-up = 29 , 7 months . 3) 7 patients with Tg > 10 ng / ml : 4 patients remain without evidence of disease in other ICT and decreasing Tg levels (mean follow-up = 55 , 9 months) . 3 patients were false negative in 18-FDG-PET demonstrated by Tg increase and / or surgery of lesions. Conclusions: -Between 20 patients studied by suspected recurrence and 18-FDG-PET negative study, 16 patients remain free of disease (NPV = 80%) during the follow-up (mean follow-up =39,5 months). -Negative 18-FDG-PET study could be an indicative of a good outcome of patients allowing a conservative attitude during follow-up.

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Role of FDG-PET/CT in positive serum Thyroglobulin and negative radioiodine scan in differentiated thyroid carcinoma patients. A single center preliminary experience.

I. Munir, M. K. Nawaz, Z. S. Farooqui, A. Murtaza, S. Muzhair, M. Saadullah, S. Sajid; Shaukat Khanum Memorial Cancer Hospital and Research center, Lahore, PAKISTAN.

Background: The prognosis of differentiated thyroid carcinoma (DTC) is favorable even in case of distant metastases if the malignant tissue has the capacity to concentrate I-131. Unfortunately in 10-30% of metastatic or recurrent thyroid carcinomas, the original cancer cells lose their ability to concentrate I-131 due to dedifferentiation to another type or unable to be picked up by I-131 scan due to poor resolution of gamma camera. Treatment of such patients presents a therapeutic dilemma since physician don't know weather such patients will gain any benefit from high dose radioiodine therapy or not. Therefore in these patients, localizing the tumor sites accurately may allow removal of the diseased tissue by surgical intervention. Aim: To establish the role of FDG-PET/CT in the management of patients with a clinical suspicion of recurrent or metastatic thyroid carcinoma with raising Tg levels and negative radioiodine scan at our center. Materials & Methods: Six treated patients of DTC(4 female, 2male; age range 24-60 years, mean 42 years)are included in the study. The histopathology revealed papillary carcinoma in all 6 patients. These patients had been previously treated with radioactive iodine in last 3 years following thyroid surgery. All patients have elevated serum thyroglobulin levels (Tg >10 ng/ml, range:110-1401ng/ml) were suspected of suffering from recurrent or metastatic disease. Whole-body Scanning after tracer dose of I-131 was performed at 48hr after the oral ingestion. All patients had failed to show any functioning thyroid tissue or metastatic lesion. FDG-PET/CT was performed with in a week of I-131 diagnostic scan after intravenous injection of 270-310MBq of FDG. Metabolically active lesions on the PET was subjected to biopsy for the histopathological confirmation of recurrent /metastatic disease. Results: FDG-PET was positive in all six I-131 whole body scan negative patients. In 2 patients metabolically active foci found in the thyroidectomy bed indicating recurrence. 2 had nodal metastases and two patients have nodal as well as lung metastases. 5/6 patients came positive for recurrence /metastatic on biopsy of metabolically active lesions on PET while in 1/6 patient biopsy of the metabolically active neck node shows reactive hyperplasia. The overall sensitivity and the positive predictive value Of FDG-PET were 100% and 83.33% respectively. Conclusions: FDG-PET is an excellent tool for detecting recurrent non-iodine avid DTC. This in turn, may lead to planning appropriate surgical intervention for the removal of tumor tissues or another dose of I-131 as the therapeutic option in these patients.

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The usefulness of FDG PET/CT in the routine follow-up of differentiated thyroid cancer

H. Lee, S. Lee, C. Hong, B. Song, S. Kang, S. Jeong, B. Ahn, J. Lee; Kyungpook National University Hospital, Daegu, KOREA, REPUBLIC OF.

Aim: The purpose of this study is to evaluate the clinical usefulness of FDG PET/CT in the routine follow-up of the patients with differentiated thyroid cancer (DTC) after total thyroidectomy and radioiodine ablation. Materials and methods: One hundred eighty-seven consecutive patients with previously treated DTC who underwent FDG PET/CT for follow-up were retrospectively reviewed (50.2±13.8 years, female 158, papillary thyroid cancer 181). All patients had received total thyroidectomy and radioiodine ablation at least 1 year before PET/CT scanning. TNM stage was I in 67, II in 3, III in 83 and IV in 34 patients. The measurement of serum Tg, TgAb and TSH, diagnostic radioiodine whole body scan (DxWBS) and neck ultrasonography (USG) were also performed regularly in all patients. Abnormal PET/CT findings were further assessed with histopathologic examinations or correlative imaging studies. Results: Eighteen patients (9.6%)

with suspicious FDG PET/CT findings confirmed as metastatic lesions by histopathologic examination in 7, subsequent post-treatment radioiodine WBS in 7 and follow-up imaging study in 4 patients. Sixteen out of 18 patients with metastatic foci were N1 and 12 patients were stage IV. Among 60 patients with Tg positive (off-Tg more than 2 ng/mL or on-Tg more than 1 ng/mL), DxWBS negative and USG negative, 10 patients (16.7%) with positive FDG PET/CT were diagnosed as metastatic lesions. Unexpected abnormal lesions on PET/CT were found in 7 patients (3.7%), which were proved as follows by histopathologic examination; 2 malignant lung cancer, 1 neurilemmoma, 1 fibroadenoma, 1 abdominal aortic aneurysm, 1 sarcoidosis and 1 pulmonary tuberculosis. Conclusion: FDG PET/CT might be helpful in the detection of unexpected secondary malignant or benign diseases as well as metastatic lesions in the follow-up of the patients with DTC.

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Bone marrow toxicity in radioiodine therapy of differentiated thyroid carcinoma with regard to pretherapeutic blood dosimetry with iodine-124: first versus multiple radioiodine therapy and TSH stimulation with recombinant thyrotropin versus thyroid hormone withdrawal

V. Hartung, W. Jentzen, L. Freudenberg, I. Binse, M. Hamami, A. Bockisch, A. Stahl; University Essen, Essen, GERMANY.

Aim: Bone marrow (BM) toxicity limits therapy of differentiated thyroid carcinoma (DTC) at high activities. BM toxicity after radioiodine therapy (RIT) of DTC was examined and correlated with pretherapeutic blood dosimetry using iodine-124 PET/CT, especially in comparison of following situations: first versus multiple RIT and TSH (thyroid stimulating hormone)-stimulation with recombinant thyrotropin (rTSH, Genzyme) versus thyroid hormone withdrawal. **Methods:** 176 patients with DTC received RIT with iodine-131 (3 to 20 GBq) and pre-therapeutic blood dosimetry with iodine-124. It was the blood dose compared per applied iodine-131 activity (in Gy/GBq) for patients with (i) first versus multiple RIT and (ii) TSH stimulation with recombinant TSH versus thyroid hormone withdrawal. In so far 52 patients the BM toxicity were correlated with the calculated blood dose (in Gy) for the situations (i) and (ii). Therefor sequential blood samples (hemograms) were obtained immediately before RIT, at 1, 2, 3-4 weeks, as well as at 3-4 and 6-12 months after RIT. **Results:** The blood dose per applied activity was at first RIT (n = 71) 0.06 versus 0.07 Gy/GBq in multiple RIT (n=105, p <0.05) and for TSH-stimulation with thyroid hormone withdrawal (n=105) 0.08 versus 0.06 Gy/GBq with recombinant TSH (n=62, p <0.05). The tumor stage was in the group of multiple RIT significantly higher than in first RIT. In all subgroups there was a correlation between calculated blood dose and percentage decrease for leucocytes, granulocytes and platelets within the first 3-4 weeks, and for lymphocytes within the first 2 days after RIT. At even low numbers in the subgroups, there were no significant differences for (i) or (ii). **Conclusions:** After RIT of differentiated thyroid carcinoma early effects on the white blood cell line and platelets are detectable and correlate well with the calculated blood dose, regardless of the number of completed RIT and type of TSH stimulation. These effects are temporary and are correlated with the pretherapeutically calculated blood doses (achieved by iodine-124 blood dosimetry). There was a significantly higher blood dose per applied activity in patients with multiple RIT (probably caused by higher tumor stages) and in patients with thyroid hormone withdrawal.

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RET expression and its correlation with clinicopathologic data in papillary thyroid carcinoma

A. Punda¹, D. Eterovic¹, V. Markovic¹, N. Kunac², V. Bedekovic³, M. Titilic⁴, M. Kotic⁵, L. Grandic⁶, V. Pesutic Pisac²; ¹Department of Nuclear Medicine, University Hospital Split, Split, CROATIA, ²Department of Pathology, University Hospital Split, Split, CROATIA, ³ENT Department, University Hospital Sisters of Charity, Zagreb, CROATIA, ⁴Department of Neurology, University Hospital Split, Split, CROATIA, ⁵ENT Department, University Hospital Split, Split, CROATIA, ⁶Department of Surgery, University Hospital Split, Split, CROATIA.

Purpose: The purpose of this study was to analyse possible prognostic value of RET mutation in papillary thyroid carcinoma. **Methods:** The present study included 180 patients operated for papillary thyroid carcinoma. The clinical and histopathologic characteristics were analysed. Paraffin sections of the selected histologic slides were cut again and immunohistochemically stained by the Clone 3F8 P (HIER) from Novocastra (Vision Bio Systems Europe, Newcastle upon Tyne, UK) monoclonal antibody to RET oncoprotein with clinical and histopathologic characteristics of this cancer subtype. **Results:** Univariate analysis indicated sex (p=0.01), histologic subtype (p=0.075) and capsular invasion (p=0.010) to be statistically significant predictors of lymph node metastases, whereas age (p=0.796), tumor size (p=0.556) and intraglandular dissemination (p=0.131) showed no such correlation. The presence of RET mutation (p=0.704) was not a statistically significant predictor of the tumor metastasizing potential. RET mutation (p=0.500) showed no statistically significant correlation with papillary thyroid carcinoma classified into prognostic groups according to clinicopathologic features either. RET mutation was detected in 30% of 180 papillary thyroid carcinomas, which is consistent with the classic distribution of sporadic cases. **Conclusion:** This is the first large study demonstrating that Chernobyl disaster and related radiation did not influence the increased prevalence of papillary carcinoma recorded in Croatia in the last decade.

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Sentinel node biopsy in medullary thyroid cancer: a pilot study

G. Manca¹, M. Puccini², G. Boni¹, M. Grosso¹, E. Borsò¹, E. Biggi¹, A. Lorenzoni¹, B. Dell'Anno¹, D. Volterrani¹, G. Mariani¹; ¹Regional Center of Nuclear Medicine, PISA, ITALY, ²Department of Surgery, PISA, ITALY.

Introduction: the extension of lymphadenectomy in medullary thyroid carcinoma (MTC) consists in laterocervical dissection on the basis of clinical or ultrasonographic involvement of lymph

nodes; however, prophylactic lymphadenectomy still represents the treatment of choice. We describe the sentinel lymph node (SLN) technique to evaluate the feasibility and potential role of this method in MTC. **Materials and methods:** four consecutive MTC patients underwent lymphoscintigraphy 2-6 hours before surgery, after intralesional injection of 99mTc-albumin nanocolloid (4-9 MBq in 0.1-0.3 ml) under ultrasonographic guidance. Immediately after intratumoral injection of the radiocolloid, dynamic scintigraphic acquisition and static images were recorded in the anterior and lateral views of the neck using a dual-head gamma camera equipped with LEHR collimators. To improve localization and definition of scintigraphic findings, a SPECT/CT study of the cervico-thoracic region was carried out at a later stage. Skin projections of SLN(s) were confirmed by external counting with the gamma-probe and were marked with indelible ink. Intraoperative SLN(s) biopsy was performed under intraoperative radioguidance using a hand-held gamma-probe. SLN(s) of the central compartment were not considered in this study as surgical excision with thyroid is part of the initial surgical treatment of MTC. After surgical removal of SLN(s), the surgeon excised the contiguous soft tissue, then performed thyroidectomy with generalized dissection of the central neck compartment, and finally laterocervical lymphadenectomy when necessary. **Results:** three out of 4 patients had no laterocervical involvement (clinically NO), one presented clinically evident metastases in the laterocervical compartment. In clinical NO cases lymphoscintigraphy was always able to identify at least one sentinel lymph node ipsilateral of tumor site, and in one case in a contralateral compartment. The ipsilateral lymph node resulted positive at histopathologic examination (micrometastases) in two cases, while the contralateral resulted inflammatory. In a clinically metastatic patient, the radiotracer revealed one contralateral lymph node, which was metastatic. The other contiguous lymph nodes examined resulted to be inflammatory (identified from a minimum of 3 to a maximum of 36). **Conclusion:** in our experience, SLN biopsy in MTC patients determined correct staging in three cases that otherwise would have been underestimated. Our study demonstrates the efficacy and accuracy of this technique, which could be used to revise the actual systems of staging, to determine whether prophylactic lymphadenectomy or compartment lymphadenectomy guided on the basis of positive SLN(s) might influence progression of the disease.

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Lymphatic mapping and sentinel lymph node biopsy in thyroid cancer

m. sabate, A. Garcia-Burillo, O. Gonzalez, C. Zafon, X. Serres, I. Roca, J. Castell; Hospital Universitario de Vall de Hebron, Barcelona, SPAIN.

Background: Lymphoscintigraphy with lymphatic mapping and sentinel lymph node (SLN) biopsy allow the detection of lymphatic spread. This technique can be applied to the management of differentiated thyroid carcinoma (DTC). **Objective:** - To validate the technique of SLN biopsy for the N staging of patients with DTC. - To value the SLN technique in the clinical management of DTC: Avoiding or not the central neck dissection (CND). Removing SLN at levels normally not included in the usual surgical strategy (central neck lymphadenectomy). In case of positive SLN, performing the lymphadenectomy of non usual lymphatic areas. - To value if these changes in the surgical management entail lower morbidity. - To compare these more accurate lymphatic staging with post-treatment ¹³¹I scintigraphy, and value if the new technique can allow a modification of the administered dose according to the known N staging. **Method:** Eight patients with PTC have been included in our study (5 female, median age 47.4 years). The injection technique consists in an intra-tumour injection (ultrasound guided) of 4 mCi of ^{99m}Tc-nanocolloid the day-before surgery. Surgery was carried-out according to the hospital's thyroid surgery protocol. Two hours after injection, planar (anterior and lateral) views of the neck are acquired, as well as SPECT-CT images (Hawk-Eye4, GE). The lymphatic drainage, including the number of SLN and their localization, is commented in detail with the surgeons. During surgery, after thyroidectomy, the SLN are localized and removed (using both the anatomic localization by SPECT-CT and the surgical gamma probe (Europrobe)). Then, the surgeon finishes the surgery with the lymphadenectomy decided by the committee in each case. The results of the SLN biopsy are compared to current staging methods (US and SPECT-CT at the seventh day after treatment with ¹³¹I). **Results:** Ninety-eight lymph-nodes were removed in total. Twenty-six of them were positive, of which nine were SLN. Sensitivity of SLN selective biopsy was 100%. There were no cases of positive nodes when SLNs were negative.

PATIENT	STAGING		MODIFICATION OF SURGICAL STRATEGY	MODIFICATION OF ¹³¹ I DOSE
	BY US	BY SLN		
1	Nx	N1	Yes (lateral SLNs)	Yes
2	Nx	N0	CND could have been avoided	No
3	Nx	N0	Yes (posterior compartment SLN)	No
4	Nx	N0	CND could have been avoided	No
5	N1	N1	No	No
6	Nx	N0	CND could have been avoided	No
7	N1	N1	No	No

Conclusions: Our preliminary results foresee an important clinical impact of the technique, consisting in changes of the surgical technique, decreasing surgery-specific morbidity (in 42.9% of the patients CND could have been avoided), and appraising lymph-nodes which would not have been routinely analyzed but which turned out to be metastatic (in our cases, in 14.3% of the patients). Furthermore, the ¹³¹I dose for therapeutic ablation was modified in 1 out of 7 cases (14.3%) of our cases as a result of the SLN technique (upstaging).

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Relationship between lemon sucking and salivary gland damage after radioiodine therapy for thyroid cancer

S. Yilmaz¹, L. Kabasakal¹, A. Dumlu², M. A. Elcin², I. Uslu¹; ¹Cerrapaşa Medical School Department Of Nuclear Medicine, Istanbul, TURKEY, ²Marmara Medical School Faculty Of Dentistry Department Of Oral Diagnosis, Istanbul, TURKEY.

INTRODUCTION: Radioactive iodine (I-131) targets the thyroid gland and has been proven to play an effective role in the treatment of differentiated papillary and follicular cancers.

Simultaneously, this radioisotope hones in on the salivary glands where it is concentrated and secreted into the saliva. Salivary gland impairment following high activity radioiodine therapy of differentiated thyroid cancer is a severe side effect. In this study we aimed to investigate the effect of using sialagogues after high dose radioactive iodine (RAI) on salivary gland in patients with differentiated thyroid cancer. **MATERIAL AND METHODS:** A total of forty-four patients (6 males (%14) and 38 (%86) females) undergoing RAI for thyroid remnant ablation were enrolled in the research with a mean age of 43.7 ± 11.3 (age ranges was 20-65). Patients were divided into 3 groups on the basis of lemon sucking after RAI ablation treatment. Group 1: Randomly selected 16 patients (%36) sucked lemon in the first day of RAI ablation. Group 2: who eat lemon in the second day of RAI ablation (13 patients, 30%) and group 3: who did not suck lemon (15 patients, %34). We performed sialometry and pH meter study at 3rd months of RAI administration. SPSS 15.0 was used for statistical analysis. **RESULTS:** The incidences of xerostomia in group A, group B, group C were 6%, 7% and %15 ($P > 0.005$) respectively. Oligosialia occurred in 5 patients in group A (31%), 6 patients in group B (46%) and 3 patients in group C (23%). Salivary gland dysfunction correlated well with the administered dose. **CONCLUSION:** The potential reduction of radiation absorbed dose to the salivary glands secondary to the use of lemon juice was observed. One proposed mechanism is that prevention of the ^{131}I sialadenitis may involve the use of sialogogic agents to hasten the transit time of the radioactive iodine through the salivary glands. An early start of sucking lemon may induce a significant decrease in salivary gland damage. This may help to increase patients' quality of life in differentiated thyroid cancer. Lemon eating should be advised after radioiodine therapy. However, studies are limited to delineate the efficacy of this approach.

P402

Incidental thyroid lesions identified by F18 FDG-PET/CT imaging

E. Özkan, N. O. Kucuk, G. Aras; Ankara University Medical Faculty, Department of Nuclear Medicine, Ankara, TURKEY.

Aim: To investigate the prevalence and the risk of malignancy of focal or diffuse thyroid incidentalomas found FDG-PET/CT and the diagnostic accuracy of low dose CT for differentiating benign from malignant thyroid lesions. **Methods:** From October 2006 to December 2009, 4500 patients (mean age, 54.8 ± 13.2 yrs) underwent F-18 FDG-PET/CT in our institution for suspected or known nonthyroid cancer. Patients who had incidental thyroid FDG uptake were retrospectively reviewed according to pattern of FDG uptake (focal-diffuse), SUV max, FNA and histopathology results. Noncontrast CT images were also evaluated in for size, attenuation, presence of calcification within thyroid lesion. **Results:** The prevalence of incidental thyroid FDG uptake (including both focal and diffuse lesions) was 3.2% (145 of 4500) on FDG-PET/CT, of which 72.4% (105/145) were focal and 27.6% (40/145) were diffuse. 27 patients with focal or diffuse FDG uptake underwent further evaluation. The cancer risk of incidentally found thyroid lesions on F-18 FDG PET/CT was 48% (13/27) and the cancer risks associated with focal FDG uptake 59.1% (13/22). The cancer risk associated with diffuse FDG uptake was not found. The maximum SUV of malignant thyroid lesions was significantly higher than that of benign lesions (17.8 ± 13.7 vs 6.1 ± 3.8 ; $p < 0.05$). There is no significant difference between the size of benign and malignant nodules on CT (16.2 ± 9.6 vs 15 ± 11.6 mm; $p > 0.05$). In malignant thyroid lesions, the presence of calcification and low attenuation CT pattern were higher than that of benign lesions (calcification 30.8% vs 7.1%; attenuation 84.6% vs 28.6%). **Conclusion:** The probability of malignancy of focal thyroid incidentalomas seen on F-18 FDG PET/CT is high. There is a significant difference in the SUVmax between the benign and malignant nodules. Low dose CT scan could be helpful for differentiating benign from malignant thyroid lesions.

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The retrospective analysis of SUV of lesions detected on 18F-FDG PET/CT in differentiated thyroid cancer

E. Ozkan, N. O. Kucuk, S. Lacin, G. Aras; Ankara University Medical Faculty, Department of Nuclear Medicine, Ankara, TURKEY.

Aim: Serum thyroglobulin (Tg) and anti-thyroglobulin (antiTg) are tumor markers that have been routinely used in clinical follow-up of patients with differentiated thyroid cancer. Recently 18F-FDG PET/CT is used to detect residue and recurrence in patients especially with ^{131}I wbs negative and high level of Tg and/or anti - Tg. The aim of this study is to retrospectively evaluate the SUV of lesions detected in patients with differentiated thyroid cancer those who were performed 18F-FDG PET/CT due to high Tg and/or anti - Tg levels and negative ^{131}I wbs. **METHODS:** 48 patients (43 thyroid papillary ca, 5 thyroid follicular ca) that 18F-FDG PET/CT performed due to high Tg and/or anti - Tg levels and negative ^{131}I wbs have been retrospectively analyzed. All PET/CT scans were performed to determine any residue/recurrence. SUVs of pathological uptakes of thyroid bed, distant metastasis, lymph nodes in neck and mediastinum have been separately calculated and mean values have been reached for respective calculated results. FDG avid lesions those which had operated were compared histopathologically; those which had not operated were compared in accordance with the occurrence of uptake in lesions after high dose ^{131}I therapy and clinical follow-up. **RESULTS:** Totally 60 pathological uptake (32 neck and mediastinum, 8 thyroid bed, 8 distant metastasis) were detected in these 48 patients with 18F-FDG PET/CT scan. 39/60 lesions were compared with histopathological findings. According to these findings 31/39 were revealed metastatic, 7/39 were reactive, 1/39 was granulomatous lymphadenitis. 12/60 lesions were evaluated with ^{131}I wbs which performed after high dose ^{131}I therapy. Since all lesions had ^{131}I uptake, these lesions were regarded as metastasis. 9/60 lesions were clinically followed. Mean values of Tg, anti - Tg and SUV were 931.75, 277.79 and 11.26 in metastatic lesions which detected in neck and mediastinum respectively; 19.22, 20.1 and 6.03 in reactive lesions respectively. All of the pathological 18F-FDG uptakes which seen in thyroid bed were revealed as thyroid cancer and mean Tg, anti - Tg and SUV were 301.67, 123.04 and 12.2 respectively. Tg, anti - Tg and SUV for distant metastasis were 4477.99, 616.65 and 16.3 respectively. **CONCLUSION:** SUV is extremely crucial in evaluation of patients with differentiated thyroid cancer. The malignity potential of uptakes especially in thyroid bed is high. In neck and mediastinum differentiation in SUV can be low between malign and non-malign lesions. In this situation, Tg and anti-Tg levels can be instructive to clinicians.

P404

The efficiency of Tc-99m MIBI scintigraphy for detecting

remnant thyroid tissue after thyroidectomy

B. Sonmez, I. Dogan, C. Yavruglu; Karadeniz Technical University, School of Medicine, Trabzon, TURKEY.

Aim: Tc-99m Perchnetate scintigraphy is commonly used to monitor remnant tissue of total / near total thyroidectomy patients. However, the intake of thyroxine should be avoided before at least 2 weeks from scintigraphy. Meanwhile unnecessary hypothyroid and regrowth of thyroid remnant can be observed. For evaluation of recurrence in patients with thyroid cancer, without thyroxine withdrawal, Tc-99m MIBI scintigraphy is used. However, the efficiency of Tc-99m MIBI scintigraphy in showing the remnant tissue was not studied. **Method:** 48 patients who had total or near total thyroidectomy were included to the present study (10 patients with multinodular goiter, 38 patients with thyroid cancer). All thyroidectomies were done at least 6 week before Tc-99m perchnetate / Tc-99m MIBI scintigraphy. TSH levels of the patients were determined. First, before thyroxine withdrawal, Tc-99m MIBI scintigraphy were obtained. Secondly, thyroxine was withdrawn along the 2 weeks and subsequently Tc-99m perchnetate scintigraphy were obtained. The amount of remnant tissue and activity intensity were analysed visually and quantitatively from the Tc-99m perchnetate and Tc-99m MIBI images. **Results:** The remnant tissue was detected in 45 patients (93.5%) with Tc-99m perchnetate scintigraphy and in 35 patients (72.9%) of those also imaged with Tc-99m MIBI scintigraphy. Neither Tc-99m perchnetate nor Tc-99m MIBI scintigraphy showed any remnant tissue in 3 patients (4.2%). In 19 of 35 patients, the amount of remnant tissue was found to be same in both imaging techniques. In the remaining 16 patients, the amount of remnant tissue with Tc-99m MIBI scintigraphy were less than that those of the Tc-99m perchnetate scintigraphy. The activity intensities in the remnant tissue obtained by Tc-99m MIBI images did not show a significant relationship neither with activity intensities obtained by Tc-99m perchnetate images ($p > 0.05$) nor with the TSH levels ($p > 0.05$). **Conclusion:** Preliminary data indicated that in some patients, the remnant tissue can be observed by Tc-99m MIBI imaging. However, detectability is not related to TSH levels and the amount of the remnant tissue imaged by Tc-99m perchnetate scintigraphy.

P405

Evaluation of the Effect of Acute Hypothyroidism on Kidney Functions by Using Double Serum Sampled GFR Measurement with ^{99m}Tc -DTPA in Thyroid Cancer Patients

B. Turgut, P. Kelkit, T. Erelcan; Cumhuriyet Univ. School of Medicine, Dept. of Nuclear Medicine, Sivas, TURKEY.

Aim: The aim of this study was to evaluate the effect of acute hypothyroidism formed prior to therapy/scanning on kidney by performing double serum sampled GFR measurement with ^{99m}Tc -DTPA. **Material&Methods:** The study was performed in thyroid cancer patients who consulted for treatment of I-131 or in patients who have consulted to have a whole body scanning with low-dose I-131. Totally 53 patients (49 female, 4 male, mean age: 44.40 ± 12.04 yrs) were included to the study. The double serum sampled GFR measurement with ^{99m}Tc -DTPA was practiced in all patients two times both in hypothyroid period and while using T4. Also; serum freeT3, freeT4, TSH, thyroglobulin, antithyroglobulin, creatinine, BUN, albumin and cystatin-C levels were measured. Again, GFR values measured by using ^{99m}Tc -DTPA was compared to other GFR values which were calculated with the formulas of "Cockcroft&Gault" (C&G) derived from creatinine and the "Modification of Diet in Renal Disease" (MDRD) with four and seven variables and the other formulas which were derived from the value of cystatin-C. **Results:** While, there was a significant difference between two periods for the levels of serum freeT3, freeT4, TSH, thyroglobulin, creatinine, and cystatin-C ($p < 0.05$), the difference was not significant for antithyroglobulin, BUN and albumin levels ($p > 0.05$). There was a significant difference between two periods for GFR values measured with ^{99m}Tc -DTPA and for the ones calculated with other formulas ($p < 0.05$). It was found that the GFR values of hypothyroid period which were measured with ^{99m}Tc -DTPA and calculated with other formulas like C&G, MDRD₍₇₎ and MDRD₍₄₎ (DTPA-GFR: 89.27 ± 28.61 , C&G: 98.67 ± 20.45 , MDRD₍₇₎: 83.23 ± 16.50 , MDRD₍₄₎: 77.45 ± 16.09 ml/min/1.73m², respectively) were lower than the values of T4 therapy period (DTPA-GFR: 111.22 ± 31.94 , C&G: 119.22 ± 24.57 , MDRD₍₇₎: 99.00 ± 21.52 , MDRD₍₄₎: 97.24 ± 22.39 ml/min/1.73m², respectively). When the GFR values derived by using Grubb, Larsson and Sjöström formulas among serum cystatin-C values were examined, GFR values of hypothyroid period (69.07 ± 15.83 , 90.93 ± 24.55 , 93.88 ± 20.24 ml/min/1.73m², respectively) were higher than the GFR values obtained in T4 therapy period (55.82 ± 14.04 , 70.69 ± 20.95 , 76.64 ± 18.89 ml/min/1.73m², respectively). **Conclusion:** Having examined the GFR values which were obtained during the hypothyroid period and while using T4, through the Bland-Altman analysis, we think that except the GFR values measured by ^{99m}Tc -DTPA, there is not a common and highly-adaptable formula to be used in both periods among the values which are obtained from other formulas. Therefore we think that it will be suitable to use the double serum sampled GFR measurement with ^{99m}Tc -DTPA in assessing the kidney functions for thyroid cancer patients in preparation for radioiodine scan/treatment.

P36 — Monday, October 11, 2010, 16:00 — 16:30, Hall Z

Oncology Clinical Science: Breast

P406

Lymph nodes visualisation before sentinel node biopsy in patients with breast cancer: to do or not to do?

S. N. Novikov, S. Kanaev, M. Girshovich, O. Zotova, A. Barbashov, L. Jukova, V. Semiglazov; N.N. Petrov Inst. Oncol., St. Petersburg, RUSSIAN FEDERATION.

Aim of the study: to evaluate the value of lymph-nodes (LN) visualisation before sentinel LN (SLN) biopsy in patients (pts) with breast cancer. **Material & Methods:** LN visualisation was performed before SLN biopsy in 89 consecutive primary pts with early breast cancer. Scintigraphic images were acquired 1-15, 30, 240 and 480-720 min after intratumoural injection of 75-150 MBq (0.5-1 ml) of ^{99m}Tc -nanocolloids ($d < 80$ nm). Delayed images (obtained 1-2 hr before operation) more precisely visualised hot nodes which can be detected by gamma probe

during biopsy. SLN were determined according to the following criteria: first appeared LN in the area, the only visualised LN, LN connected with tumour by the "the road of lymph flow". All other LN were considered as second-echelon nodes. **Results:** SLN were successfully visualised in 85 of 86 evaluated pts (98%). Axillary LN detected in 83 pts: in 38 (44.2%) pts it was the only region of lymph flow from tumour, in 45 (55.8%) cases - it was accompanied by drainage to internal mammary and/or sub-supraclavicular LN. In 3 pts all SLN were localised outside axillary region: subclavicular - in 1 and internal mammary - in 2 cases. Second echelon LN detected in 64 of 83 (77.1%) pts with "hot" nodes in the axillar. "Hot" nodes revealed in sub-supraclavicular region were SLN only in 4 of 34 (11.7%) cases. On the contrary, visualised internal mammary LN were considered SLN in all 27 (24.4%) observations. **Conclusion:** LN scintigraphy must be obligatory done before SLN biopsy in order to differentiate SLN from second echelon axillar LN (77.1% of cases) and because visualisation help to detect SLN outside the axillary region in 36.1% of pts.

P407

Sentinel Node Biopsy In Multifocal And Multicentric Breast Cancer Patients. Reliability of the Technique.

A. Benitez Segura¹, **M. Bajen Lazaro**¹, **P. Cecilia Notta**¹, **D. Ramal**¹, **J. Mora**¹, **A. Lopez-Ojeda**², **S. Pernas**², **L. Prieto**², **A. Petit**², **J. Martin-Comin**¹; ¹S. Medicina Nuclear - Hospital Universitari de Bellvitge-IDIBELL, L'Hospitalet de Llobregat, SPAIN, ²Unidad Funcional de Mama. Hospital Universitari de Bellvitge-ICO-IDIBELL, L'Hospitalet de Llobregat, SPAIN.

Aim: Asses the reliability of sentinel lymph node biopsy in patients with multifocal or multicentric breast cancer. **Methods:** In the period 2000-2008 sentinel node localization and biopsy was applied to 1651 breast cancer. 30 patients with multifocal (McBC) or multicentric breast cancer (MFBC), 14 with McBC and 16 with MFBC were selected for this study. Lymphoscintigraphy was performed with 55,5 - 111 MBq ^{99m}Tc-albumin nanocolloid the day before surgery. The injection was peri/ intratumoral when two nodules were present and it was performed periareolar when more than three nodules were present. Axillary lymphadenectomy was performed only in cases of non-surgical detection and positive sentinel node metastases. The scintigraphic and surgical sentinel node detection, the pathologic status of the sentinel node and other nodes in the axillary lymph node dissection in the cases it was done, and the axillary recurrence rate in patients with non metastatic SN at surgery was analyzed. The follow-up was 6 years (1 year-6 years). **Results:** In all patients at least one axillary sentinel node was detected by lymphoscintigraphy (scintigraphic detection 100%). Only 1 out of 30 patients surgical sentinel node detection was not possible (surgical detection rate 97%). This patient underwent axillary lymph node dissection that resulted negative for metastases. The sentinel node was positive in 11/30 cases (37%), 9 out of the 11 were McBC (82%). The sentinel node was negative in 19/30 cases (63%). In the group with no metastatic sentinel node no axillary recurrence has been detected in the follow-up period (1 year-6 year) **Conclusion:** Despite the controversy still present, the results of our experience support the reliability of the technique in this patient group.

P408

Comparison of Subareolar Injection Lymphoscintigraphy with the 1 Day and the 2 Day Protocol for the detection of Sentinel Lymph Nodes in Patients with Breast Cancer

J. Seok; College of Medicine, Chung-Ang University, Seoul, KOREA, REPUBLIC OF.

Objectives: Lymphoscintigraphy and sentinel node biopsy were used for the detection of axillary lymph node metastasis in breast cancer patients. We compared the results of subareolar injections on the day of surgery (1 day protocol) with injections the day before surgery (2 day protocol). **Methods:** This study included 508 breast cancer patients who underwent surgery between 2001 and 2009. For the 1 day protocol 0.8 ml of Tc-99m Tin-Colloid (37MBq) was injected in 269 in the subareolar region on the morning of the surgery. For the 2 day protocol 0.8 ml of Tc-99m Tin-Colloid (185MBq) was injected in 239 patients on the afternoon before surgery. Lymphoscintigraphy was performed in the supine position and sentinel node identification was performed by hand-held gamma probe during surgery. **Results:** Among 259 patients with the 1 day protocol, 248 cases (92.2%) were identified by sentinel node lymphoscintigraphy, and 249 cases (92.6%) were identified by gamma probe. Among the 239 patients, in the 2 day protocol, 218 cases (91.2%) had the sentinel node identified by lymphoscintigraphy, and 211 cases (88.3%) had the sentinel node identified by the gamma probe. There was no significant difference in the identification rate of the sentinel node between the 1 day and 2 day protocol by lymphoscintigraphy and the gamma probe. **Conclusions:** The results of the identification of the sentinel node according to 1 day or 2 day protocols showed no significant differences. Because the 2 day protocol allows for an adequate amount of time to perform the lymphoscintigraphy, it is a more useful protocol for the identification of sentinel nodes in patients with breast cancer.

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Comparison of the Efficiency for Tc-99m Tin-colloid and Tc-99m Phytate in Sentinel Node Detection in Breast Cancer Patients

J. Seok; College of Medicine, Chung-Ang University, Seoul, KOREA, REPUBLIC OF.

Objectives: Lymphoscintigraphy and sentinel node biopsy has become a standard method for detection of axillary lymph node metastasis in breast cancer patients, but the standard radiopharmaceutical was not prepared. About detection of axillary lymph node metastasis by lymphoscintigraphy and sentinel node biopsy in breast cancer patient, we compared the results of Tc-99m Tin-colloid and Tc-99m Phytate by subareolar injection. **Methods:** This study included 508 breast cancer patients who were performed operation during 2001-2009. Four hundred twelve patients was injected 0.8 ml of Tc-99m Tin-colloid (37-185 MBq) by subareolar injection. Ninety six patients was injected 0.8 ml of Tc-99m Phytate (37-185 MBq). Lymphoscintigraphy was performed in supine position and sentinel node localization was performed by hand-held gamma probe in operation. **Results:** Among 412 patients by Tc-99m Tin-colloid, 374 cases (90.8%) localized the sentinel node by lymphoscintigraphy, 367 cases (89.1%) localized by gamma probe. Among 96 patients by Tc-99m Phytate, 92 cases (95.8%) localized by lymphoscintigraphy, 93

cases (96.9%) localized by gamma probe. Detection rate by lymphoscintigraphy and gamma probe was superior for Tc-99m Phytate compared to that with Tc-99m Tin-colloid, with a statistically significant difference. ($p < 0.05$, $p < 0.05$) **Conclusions:** Tc-99m Phytate is a better choice for localization of sentinel node than Tc-99m Tin-colloid in breast cancer patients.

P410

Tumour related lymphatic mapping of multiple carcinomas within one breast: feasibility and first results

L. Vermeeren¹, **I. M. C. van der Ploeg**¹, **R. A. Valdés Olmos**¹, **C. E. Loo**¹, **L. Pereira Arias-Bouda**², **F. Smit**², **O. E. Nieweg**¹, **M. T. F. D. Vrancken Peeters**¹, **E. J. T. Rutgers**¹, **H. S. A. Oldenburg**¹; ¹Netherlands Cancer Institute, Amsterdam, NETHERLANDS, ²Rijnland Hospital, Leiderdorp, NETHERLANDS.

Aim: To evaluate the feasibility of lymphoscintigraphy and sentinel node biopsy in patients with multiple invasive tumours in one or more quadrants of the breast, and to investigate whether an intralesional injection of the radiopharmaceutical in each tumour yields additional sentinel nodes, compared to an intralesional injection in the largest tumour only. **Patients & methods:** Patients are currently being included after informed consent, in six centres in The Netherlands. After administration of 120 MBq ^{99m}Tc-technetium-nanocolloid (GE Healthcare) in the largest tumour, the lymphatic flow is studied with planar lymphoscintigraphy and SPECT/CT (SymbiaT, Siemens). Subsequently, an injection (80 MBq) followed by the exact same imaging is performed for the other tumour(s). Sentinel node biopsy is performed within 24 hours after the first injection, using a gamma-ray detection probe (Neoprobe, Johnson&Johnson), blue dye (Laboratoire Guerbet) and careful palpation of the axilla. **Results:** Fourteen patients, with a mean age of 55 years, have been included up till now. Nine patients had a multifocal tumour and 5 patients had multicentric lesions. In 79% of the patients, additional lymphatic drainage was depicted after the second and/or third injection. Visualisation of additional drainage was seen both in patients with multifocal and in patients with multicentric lesions. Comparison of planar images and SPECT/CT after consecutive injections enabled visualisation of the number and location of additional sentinel nodes (7 axillary, 2 infraclavicular, 5 internal mammary chain and 2 intramammary). All such additionally identified sentinel nodes could be harvested intraoperatively, except for two internal mammary nodes. The sentinel node biopsy was tumour-positive in 5 patients (36%). In one other patient, isolated tumour cells were found in both an axillary and an additionally found internal mammary chain sentinel node. Two patients with an involved node in the axilla that was visualised after the first injection had an additional involved node identified after the second injection. In none of the patients, the postoperative therapeutic regimen was changed on the basis of the additional sentinel node harvesting. **Conclusion:** Lymphatic mapping of multiple malignancies within one breast using separate consecutive intratumoural injections appears to be feasible. The high incidence of additional sentinel nodes draining from tumours other than the largest one, suggests that assessment of lymphatic drainage of each tumour separately may result in more reliable staging.

P411

The Number of Sentinel Lymph Node in Early Stage Breast Cancer

H. Bozkurt, **R. Bekiş,** **Y. Demir,** **A. Sevinç,** **B. Değirmenci;** Dokuz Eylül University, Izmir, TURKEY.

Introduction: Sentinel lymph node (SLN) can be described as the first lymph node which the primary tumour drains. Although this concept include single sentinel lymph node, in fact multiple sentinel lymph node may be detected by sentinel lymphoscintigraphy. On the other hand the main goal of sentinel lymph node biopsy (SLNB) is to determine the status of axilla in breast cancer with minimal invasive procedure. However increasing the number of SLNs constitute paradoxical result comparing with the aim of SLNB. The aim of our study is to investigate some clinical and technical factors has been accepted previously increasing the number of sentinel lymph node in early stage breast cancer. **Subjects and Methods:** Totally 228 patients (mean age 54.2±11.5) with early stage breast cancer (stage I-II) were accepted to perform sentinel lymphoscintigraphy. SLNs were detected in all patient by lymphoscintigraphy. SLNs number was recorded in each patients. Patients were divided two group according to having single and multiple SLNs. Then we compared two groups statistically with multichannel qi square test according to patient's age, histopathological subtypes of cancer, size of tumour, technique of injections, localization of injections, and operated previously. **Results:** Mean number of SLNs detected by lymphoscintigraphy was 1.5±0.6 (1-4). The first and second group constituted 55% (126/228) and 45% (102/228) of patients. There was no significantly difference between subgroups according to SLNs number.

N=228(Lymphoscintigraphy) Single SLN Multiple SLN χ^2 test P value ≤ 0.05

Age			0.2
Less than 40	16 (64%)	9 (36%)	
40-60	80 (58%)	59 (42%)	
More than 60	30 (47%)	34 (53%)	
Tumour types			0.2
Inv. Ductal	59 (55%)	48 (45%)	
Inv. Duc+inv. Lob	22 (54%)	19 (46%)	
Inv. Lobular	24 (58%)	17 (42%)	
DICS and LICs	5 (31%)	11 (69%)	
Others	16 (70%)	7 (30%)	
Tumour size			0.7
≤ 0.5 cm	7 (44%)	9 (56%)	
0.5<... ≤ 1 cm	17 (61%)	11 (39%)	
1<... ≤ 2 cm	36 (54%)	31 (46%)	
2 cm<...	66 (56%)	51 (44%)	

Injection technique		0.1
Intradermal	109(57%)	82 (43%)
Intradermal&peritumoural	17 (46%)	20 (54%)
Injection's location		0.076
Upper Outer Quadrant	88 (62%)	53 (38%)
Upper Inner Quadrant	10 (42%)	14 (58%)
Lower Outer Quadrant	11 (48%)	12 (52%)
Lower Inner Quadrant	9 (37%)	15 (63%)
Retroareolar	8 (50%)	8 (50%)
Breast operation		0.2
yes	93 (58%)	68 (42%)
no	33 (49%)	34 (51%)

Discussion: Increasing SLNs number with palpable tumour, intradermal injection technique and young age was reported in the literature previously. However in our study we didn't find any relationship between SLNs number and patient related factors as mentioned in the literature.

P412

Molecular Breast Imaging in Women Undergoing Neoadjuvant Therapy for Breast Cancer - A Pilot Study

D. L. Wahner-Roedler, J. C. Boughey, C. B. Hruska, R. W. Maxwell, C. L. Tortorelli, D. J. Rhodes, M. K. O'Connor; Mayo Clinic, Rochester, MN, UNITED STATES.

Introduction: Neoadjuvant therapy (NT) is increasingly used for operable breast cancer (BC). Accurate imaging to assess response to therapy is important for surgical planning. Molecular Breast Imaging (MBI) using ^{99m}Tc -sestamibi is able to detect small BCs. **Aims:** To document that MBI can assess response to NT in BC patients. **Methods:** Twenty newly diagnosed BC patients scheduled to undergo NT were enrolled. Patients underwent MBI prior to starting and after completion of NT prior to BC surgery. MBI was performed using a dedicated dual-head CZT-based gamma camera system after injection of 30 mCi ^{99m}Tc -sestamibi. **Results:** Mean age of patients: 51 years (range 38-76). Median pre-therapy tumor size as determined by conventional radiologic studies: 6.5 cm (range 1.8-14). In 3 patients post NT MBI was not obtained due to scheduling problems. **Pre-NT Imaging:** MBI correlated well with mammogram (MMG) in 12/20, with ultrasound (US) in 14/19, with Magnetic Resonance Imaging (MRI) in 17/18. In one patient, MBI and MRI detected a contralateral BC not seen on MMG. In cases where measurements differed, the MBI size was larger than MMG and US size, except in one case of inflammatory BC where the size on MBI was smaller than MRI. **Post-NT Imaging:** MMG was concordant with pathology in 6/10 (60%) (MMG overestimated lesion size in all discordant cases), US in 7/11 (64%), in 3 discordant cases pathology was negative while US still revealed disease, in the 4th case US was negative and pathology showed 2 foci of 1 mm disease. MRI and pathology were concordant in 3/7 patients (43%). In 3/4 discordant cases MRI revealed more disease than seen pathologically. In one discordant case MRI still revealed minimal enhancement and pathology showed no residual disease. MBI and pathology were concordant in 10/18 BCs (56%) in 17 patients. In 3/8 discordant cases MBI was negative while pathology revealed minimal residual disease (1-6 mm foci). Findings in the remaining 5/8 discordant cases were: 1) MBI near complete resolution; pathology 2.2 cm carcinoma; 2) MBI minimal uptake; pathology 1.2 cm cancer 3) MBI mild diffuse uptake; pathology no residual cancer, but flat epithelial atypia; 4) MBI focal uptake; pathology fibroadenoma with no residual BC; 5) MBI 7.5 cm residual lesion; pathology 12 cm inflammatory BC. **Conclusion:** This pilot study suggests that MBI can satisfactorily assess response to NT in BC patients and further evaluation is warranted.

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Usefulness of dual time images of Breast specific gamma camera imaging in patients with suspected or known breast cancer.

S. Yoon¹, M. Bae²; ¹Cheil General Hospital & Women's Cancer Center, Seoul, KOREA, REPUBLIC OF, ²Myongji Hospital, Seoul, KOREA, REPUBLIC OF.

purpose In our hospital, 303 cases were pathologically confirmed by only routine early images, the sensitivity and specificity of BSGI were 90% and 60% because of many false positive lesions such as fibroadenoma, intraductal papilloma etc. BSGI using Tc-99m MIBI showed lower specificity due to many benign lesions. In this study, we investigated the usefulness of dual time (early-delayed) image using breast specific gamma camera image for differentiation of benign and malignant breast lesions. **Methods** A total of 30 patients with any focal uptake on routine early image underwent delayed image using Tc-99m MIBI. **Standard** craniocaudal and mediolateral oblique images of both breasts were acquired using a breast specific high resolution gamma camera at 5 min after intravenous injection of 1,100 MBq Tc-99m MIBI. **Early images** were compared to delayed images. **More increased uptake on delayed images** were classified as abnormal findings suggesting malignancy. **the results** were compared with hisopathology. **Results** Recently we acquired dual time images in 30 patients. Among 30 breast lesions, 18 lesions were proved to be malignant. the sensitivity of BSGI using dual time images was 83 %. There were 3 false negative lesions on dual time BSGI. There was only 1 false positive lesion by fibroadenoma on dual time BSGI. The specificity of BSGI using dual time images was 91%. **conclusion** Although only small number of patients, BSGI using early-delayed dual time imaging showed more high specificity to detect breast cancer. Dual time images were very useful by decreasing many false positive interpretation if there was any focal uptake on routine early breast image. Further studies will be needed to define the role of dual time BSGI in large population.

P414

Preliminary Results of ^{18}F -FDG PET/CT Follow-up of Patients with Sentinel Node-Positive Breast Cancer after Axillary Nodal

Irradiation without Completion Axillary Dissection

Á. Sávolt¹, G. Péley², L. Tóth¹, Z. Mátra¹, F. Rényi-Vámos¹, C. Polgár¹, Z. Horváth¹, É. Szabó¹, K. Borbély¹; ¹Hungarian Institute of Oncology, Budapest, HUNGARY, ²Norfolk and Norwich University Hospital, Norwich, UNITED KINGDOM.

Purpose The National Institute of Oncology has just closed a randomized clinical phase III study. The OTOASOR (Optimal Treatment of the Axilla - Surgery or Radiotherapy) trial compared the result of the completion axillary lymph node dissection (ALND) and axillary nodal irradiation (ANI) without ALND in patients with early-stage breast cancer after positive sentinel lymph node biopsy (SLNB). In the investigational arm of the trial patients received 50 Gy ANI postoperatively without ALND. Actually we had information only about the sentinel lymph node (SLN) status, but the further nodal involvement remained unknown. Positron emission tomography combined with computed tomography (PET/CT) has been receiving increasing attention recently for restaging and follow-up of breast cancer. The aims of this study were to evaluate the therapeutic effect of the axillary nodal irradiation and to detect early axillary recurrences or residual diseases. **Patients and Methods** In year 2009, forty-five T1-2 SLNB positive patients were retrospectively selected from the investigational arm of the OTOASOR trial. All patients underwent surgery (breast-conserving or mastectomy) and SLNB, the SLN(s) were found positive and the patients received 50Gy ANI instead of completion ALND. Six months after the end of the radiotherapy, patients underwent ^{18}F -FDG PET/CT and mammography combined with breast and axillary ultrasound or breast MRI simultaneously. The findings of PET/CT, mammography and/or breast MRI were compared. **Results** Only 5 out of 45 patients had suspicious findings in the axillary tail on mammography combined with breast and axillary ultrasound. In those five patients PET/CT suggested locoregional residual disease in only one patient that was confirmed by core biopsy. In the remaining four cases both the PET/CT and the biopsy showed no evidence of malignancy. **Conclusions** Our preliminary data suggest that axillary nodal irradiation (ANI) without completion axillary lymph node dissection (ALND) does not increase the risk of recurrence of the sentinel positive patients. Furthermore, the results of our study demonstrate the benefit of ^{18}F -FDG PET/CT in the follow-up of breast cancer patients with positive SLN without ALND.

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Impact of ^{18}F -FDG PET/CT in suspected breast cancer recurrence

M. Razzouk-Cadet¹, B. Padovani², P. Azuar³, J. Mouroux⁴, S. Lao¹, P. Viau¹, P. Carrier⁵, M. Poudenx⁶, G. Paone¹, J. Darcourt¹; ¹Nuclear medicine CHU, Nice, FRANCE, ²Radiology CHU, Nice, FRANCE, ³Gynecology, Grasse, FRANCE, ⁴Thoracic Surgery CHU, Nice, FRANCE, ⁵Nuclear medicine, Toulon, FRANCE, ⁶Oncology CAL, Nice, FRANCE.

Aim: to evaluate retrospectively the impact of ^{18}F -FDG-PET/CT in the assessment and management of suspected recurrent breast cancer. **Materials and methods:** 62 patients (age between 40-80 years), treated for breast cancer and suspected for recurrence of breast cancer underwent whole-body FDG PET/CT, that was performed approximately 60 minutes following IV injection of 18 F-FDG. **Histological type** included invasive ductal carcinoma (n=54), invasive lobular carcinoma (n=5), 1 mixed lobular and ductal, 1 metachronous bilateral cancer (lobular and ductal), 1 malignant phylloid tumor). **PET/CT findings** were compared with results of additional imaging, pathology and follow-up. **The impact of FDG PET/CT images** on clinical management of patients was evaluated on the basis of clinical decisions obtained from patient files. 17 patients had elevated tumors markers in which 13 had elevated CA 15-3 and 4 elevated CA 125. **Results:** 42 patients (67,7%) had abnormal FDG-PET/CT and malignant results. The presence of metastatic disease was identified in 37 of them (59,6%) and the presence of another malignant disease in 5 of them (4 pulmonary neoplasms and 1 thyroid cancer). 29 of 37 patients with distant metastasis were treated by palliative systemic treatment (chemotherapy and/or hormoneotherapy, Herceptin) and unnecessary surgery was prevented. 9 of 37 patients were treated by surgery. 8 of 17 patients who had elevated tumors markers (47%) had positive FDG-PET/CT. 3 patients (4,8%) had false positive results: 1 benign pulmonary fibroma SUV-max 3,1; 1 Mycobacterium Avium infection (pulmonary bilateral nodules SUV-max 7,8) and 1 tuberculous adenitis (2 cm axillary adenopathy SUV-max 3,3). 3 patients (4,8%) had false negative results (8 mm intramammary malignant lesion detected on MRI; 8 mm hepatic lesion associated with a small sternal lytic lesion and disseminated bone metastasis from a lobular carcinoma with no FDG uptake). 14 patients (22,5%) had normal distribution of FDG without evidence of disease. **The sensitivity and specificity of FDG-PET/CT in patients with suspected recurrence breast cancer** were 93% and 82 % respectively. **Conclusion:** FDG-PET/CT is a useful technique in the evaluation of suspected recurrence in breast cancer and had impact on the management on patients in the decision-making of the therapeutic approach.

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Terminal ileum metastasis from breast cancer : Case report with F-18 FDG PET/CT

K. Chun¹, E. Kong¹, I. Cho¹, K. Won²; ¹Yeungnam University Hospital, Daegu, KOREA, REPUBLIC OF, ²Keimyung Medical Center, Daegu, KOREA, REPUBLIC OF.

Purpose: Although breast cancer most frequently metastasizes to the bone, lung, pleura, liver, adrenal glands and brain, it can also affect other organs such as the small bowel and ovaries, especially if the type of cancer is infiltrating and lobular. Solitary metastasis to terminal ileum with FDG PET/CT was not reported in breast cancer as far as our knowledge, especially in ductal carcinoma. We report a solitary terminal ileum metastasis from breast cancer with F-18 FDG PET/CT. **Subjects and Methods:** A 45-years-old female patient underwent breast conserving surgery due to bilateral invasive ductal cancer (Stage : T1N0M0) 2 years ago. She underwent F-18 FDG PET/CT for routine follow up. **Results:** Whole body FDG PET/CT image showed focal uptake with wall thickening (SUVmax = 5.7) in the terminal ileum and other sites were unremarkable. **PET/CT** suspect primary lesion in terminal ileum, including inflammation rather than metastasis. **Pathologic report** was metastatic adenocarcinoma from breast. **Conclusion:** Terminal ileum metastasis is very rare in invasive ductal breast cancer, but metastasis can be possible and considered when focal uptake is noted in the terminal ileum.

P417**SPECT with 99Tc MIBI in breast cancer detection and chemotherapy response prediction**

A. A. Titskaya, V. I. Chernov, E. M. Slonimskaya, I. G. Siniikin, R. V. Zelchan; Cancer Research Institute, Tomsk, RUSSIAN FEDERATION.

Purpose: To assess the role of SPECT with 99mTc-MIBI in breast cancer detection and chemotherapy response prediction. **Materials and methods:** Seventy breast cancer patients underwent SPECT with 99mTc-MIBI. SPECT studies were carried out 20 minutes and 2 hours after the injection of 370 MBq of 99mTc-MIBI using ECAM-180 gamma-camera (Siemens). Twenty seven patients received neoadjuvant chemotherapy. The images were quantitatively assessed using the tumor/background index (T/B) and retention index (RI). Indices were compared with clinical effect which was assessed by RECIST scale. **Results:** SPECT revealed breast lesions in 59 of the 61 patients (93.4%). In lesions smaller than 10 mm in size, abnormal radiotracer uptake in the breast was observed in 3 of the 5 patients, the minimum size of visualized lesion was 6 mm. Tumors greater than 10 mm in size were detected in 100% of cases. SPECT showed multicentric tumors in 6 of the 13 cases. SPECT visualized metastatic axillary lymph nodes in 31 of the 34 patients. Also lesions in pectoral (n=9), subclavian (n=5) and subscapular (n=2) lymph nodes were shown. SPECT sensitivity in detection of involved lymph nodes was 93.1%. Partial response was registered in 20 patients (n=20) and stable disease was observed in 7 patients. The tumor/background ratio (T/B) and retention index (RI) were the most useful indices in predicting response to breast cancer neoadjuvant chemotherapy. Pre-treatment T/B and RI parameters were lower in patients who positively responded to chemotherapy than those of patients with insignificant effect of chemotherapy (T/B: 3.5±1.7, RI: 0.1±0.3 versus T/B: 7.6±4.01, RI: 0.3±0.2). **Conclusion:** The data obtained indicate that SPECT has a high diagnostic significance in detection of primary breast cancer and it can be used in predicting chemotherapy effect.

P418**First clinical validation of a dedicated high-resolution PET for hanging breast**

T. S. Aukema¹, A. J. González², R. A. Valdés Olmos¹, C. Vroonland¹, W. V. Vogel¹, M. T. F. D. Vrancken Peeters¹, E. J. T. Rutgers¹, J. M. Benlloch³; ¹Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, Amsterdam, NETHERLANDS, ²GEM-IMAGING, Valencia, SPAIN, ³Instituto Fisica Corpuscular, Paterna, SPAIN.

Aim: The sensitivity of current FDG PET/CT scanners for the detection of primary breast cancer is suboptimal. A novel high-resolution breast PET scanner was developed to improve primary tumour detection and characterization. The aim of the current study was to validate this dedicated high-resolution breast PET in patients with stage II-III breast cancer in relation to the primary tumour. **Method:** 20 patients with invasive breast cancer > 3 cm and/or lymph node metastases received a baseline FDG PET/CT before neo-adjuvant chemotherapy. FDG-PET/CT was performed using a hybrid system (Gemini II, 16-slice CT), 60 minutes after administration of 18-240 MBq 18F-FDG intravenously. Subsequently, a scan was performed with the dedicated high-resolution breast PET (MAMMI, Oncovision) with the patient in prone position. The device uses a ring of 12 detector heads, one single and monolithic LYSO crystal per detector. The results of the dedicated breast PET were compared to the FDG PET/CT images. **Results:** In 19 patients (95%) the primary tumour was visualized by the dedicated breast PET. In 1 patient no primary tumour was visible on FDG PET/CT nor on the dedicated breast PET (nor on MRI), this patient had a large lymph node metastasis. The median distance from the pectoral muscle to the primary tumour was 18mm (range 10-52mm). The median size of the primary tumour was 36mm (range 21-76mm). Comparison of SUV values for therapy response is ongoing. **Conclusion:** The dedicated high-resolution breast PET is able to visualize breast carcinomas in nearly all stage II-III breast cancer patients. Due to the hanging breast position, tumours close to the pectoral muscle can also be visualized by this dedicated PET device.

P419**Sentinel lymph node biopsy in patients with high risk ductal carcinoma in situ**

J. Duch, M. Estorch, M. J. Quintana, C. Artigas, A. Flotats, V. Camacho, A. Fernandez, E. Lerma, I. Carrió; Hospital de la Santa Creu i Sant Pau, Barcelona, SPAIN.

Introduction: The role of sentinel lymph node biopsy (SLNB) in patients with ductal carcinoma in situ (DCIS) of the breast is still controversial. **Aim:** The aim of the present study was to evaluate the results of SLNB in high risk DCIS patients. **Material and methods:** We studied 55 patients with preoperative diagnosis of high risk DCIS. In our centre we usually perform SLNB in patients with DCIS who require mastectomy, have comedonecrosis or tumour size is > 4 cm. Intratumoral or subdermal injection of 111 MBq of 99mTc-nanocolloid was used for sentinel lymph node (SLN) identification. Intraoperative detection of SLN was performed by using a hand-held gammprobe. Injection of vital blue dye was not performed. All SLNs were sectioned serially and stained with hematoxylin and eosin. Immunohistochemical analysis was performed using a cytokeratin monoclonal antibody. **Results:** Histopathologic analysis of the specimens showed that 31 patients (56%) had a pure DCIS and 24 patients had an invasive carcinoma. In four cases no SLN was identified (SLN detection rate 93%). There were five patients with metastatic SLN (four micrometastases and one macrometastasis). Four of five patients with metastatic SLN had histologic demonstration of invasive carcinoma whereas only one patient had an histology of pure DCIS (this patient had a micrometastasis). **Conclusion:** The results of our study suggest that SLNB is feasible in high risk DCIS of the breast and may allow a better staging for these patients.

P420**Utility of FDG-PET in the evaluation of recurrence breast cancer. A comparison with CT imaging.**

A. Benítez, M. D. Albalá, R. Maza, P. I. Contreras, C. Pacheco, J. M. Latre; Unversitary Hospital Reina Sofia, Córdoba, SPAIN.

AIM: To analyze the utility of 18F-FDG-PET in the evaluation of patients with recurrence of breast cancer (suspected or confirmed) and to compare the FDG-PET findings with CT data. **MATERIAL & METHODS:** We performed a retrospectively analysis of 35 FDG-PET in 29 patients (age 37-81years) referred for: 1) early detection of recurrence in patients with progressive elevation of tumour markers or 2) re-staging in recurrent breast cancer. Simultaneously, a CT exploration was performed in all patients. We compared FDG-PET and CT findings in each patient and at the different anatomical regions. Results were confirmed by pathology when histological sampling was possible, by another conventional imaging modalities (bone scintigraphy, ultrasound) and/or by clinical follow-up to 12 months at least. **RESULTS:** Among the 35 studies performed, 11/35 FDG-PET and 9/35 CT resulted negative. We had 4/11 false negatives in FDG-PET, in 2 patients the recurrence was limited to the liver, and in the other 2 cases there were bone metastatic too. Otherwise, 5/9 CT studies were false negatives with lesions localized in pleura, adrenal glands, lymphatic nodes and skeleton. These 5 patients were referred to FDG-PET for progressive elevation of tumour markers and FDG-PET findings were the unique evidence of recurrence. Thus, the percentage of false negatives (PFN) was 36% for FDG-PET and 56% for CT. For anatomical regions, the Sensitivity (Sn) in lymphatic node and bone metastasis was 100% and 85% for FDG-PET and 62% and 36% for CT respectively. However, in liver lesions the Sn was 43% for FDG-PET and 100% for CT. The anatomical distribution of the lesions is resumed in the table.

LOCALIZATION	TOTAL	FDG-PET				CT			
		TP	FN	FP	TP	FN	FP		
SKELETAL SYSTEM	13	11	2		8	5			
LYMPHATIC NODES	14	14		1	5	9			
LIVER	7	3	4		7				
LUNG	4	3	1	1	4	1			
LOCAL RECURRENCE	1		1		1				
PLEURA	2	2			2				
ADRENAL GLANDS	1	1			1				

CONCLUSIONS: 1. FDG-PET has been shown to be helpful in staging recurrent breast cancer 2. FDG-PET has been shown to be helpful in the early detection of recurrence in patients with progressive elevation of serum tumour markers. 3. FDG-PET is a very useful technique in the evaluation of lymphatic and skeletal lesions 4. FDG-PET can't replace CT evaluation of liver lesions.

P421**Mixed invasive ductal associated with *in situ*, but not pure invasive breast carcinoma, correlates with increased neoangiogenesis, breast density, calcitonin gene related peptide positivity and cell proliferation seeking radiotracer ^{99m}Tc(V)DMSA uptake**

V. Papanoniu¹, A. Tsaroucha¹, P. Valsamaki², A. Fothiadaki¹, T. Karianos¹, A. Archontaki¹, S. Marinopoulos¹, V. Pappas¹, K. Syrgiannis¹, T. Liotsou¹, M. Sotiropoulou¹, S. Tsiouris³, A. Stipsanelli¹, C. Dimitrakakis¹, A. Antsaklis¹; ¹Alexandra University Hospital, Athens, GREECE, ²Pammakaristos Hospital, Athens, GREECE, ³Ioannina University Hospital, Ioannina, GREECE.

Aim: To assess neoangiogenesis in relation to breast density (BD), calcitonin gene related peptide (CGRP), cell proliferation seeking radiotracer ^{99m}Tc(V)DMSA uptake (SMM) in invasive ductal associated with extensive *in situ* carcinoma (DCIS + IDC) and in pure invasive breast carcinoma (IDC). **Methods:** 20 patients with histologically confirmed mixed DCIS + IDC (n=10) and pure IDC (n=10) were submitted preoperatively to mammography and scintimammography. The percentage of breast density (BD) and the percentage of tracer uptake (SMM) were calculated with computer assisted methods. CGRP and the number of newly formed blood vessels (NBV) were immunohistochemically assessed. NBV, BD, CGRP, and SMM were compared (t-test) between the two groups. Linear regression analysis was performed between NBV, BD, CGRP and SMM in both groups. **Results:** NBV, BD, CGRP and SMM were significantly higher in mixed DCIS + IDC as compared to pure IDC (32.1±10.4 vs 24.3±5 p=0.048, 35.2 ± 6.9 vs 25.6±10.7 p=0.028, 25.5±7.6 vs 17±7.8 p=0.024, 26.75±4.09 vs 11.34±8.5 p=0.0009). NBV was strongly correlated with BD and CGRP in the DCIS component of the mixed group (r=0.933 p<0.001, r=0.793 p<0.01 respectively). BD was also significantly correlated with CGRP and SMM in the DCIS component of the same group (r=0.974 p<0.001, r=0.728 p<0.05 respectively). In contrast, no significant correlation(NS) was found between NBV and BD, CGRP or between BD and CGRP, SMM in both the IDC component of mixed group and pure IDC group (r=0.388 NS, r=0.391 NS, r= - 0.597 NS, r= - 0.352 NS in the IDC component of mixed group; r=0.584 NS, r= 0.297 NS, r= - 0.574 NS, r= - 0.294 NS in pure IDC respectively). **Conclusion:** Mixed DCIS + IDC lesions exhibit significantly increased NBV, BD, CGRP and SMM values as compared to those of IDC lesions. The strong correlation between neoangiogenesis and the other parameters in the mixed group indicates that the mixed DCIS + IDC constitutes a strictly different entity from pure IDC, more aggressive and probably originates from the stroma through the CGRP pathway.

P422**Breast Cancer Relapse Rate after Sentinel Lymph Node Biopsy: Results of Lymphoscintigraphy at Royal Perth Hospital 2002-2006.**

R. G. Troedson, J. Tinning, A. Bechaz-Blake; Royal Perth Hospital, Perth, AUSTRALIA.

Purpose: This review aims to assess breast cancer lymphoscintigraphy in the first 5 years of this procedure at Royal Perth Hospital (Jan 2002 to Dec 2006). The aim of this review is to compare the rate of cancer relapse in patients who had sentinel lymph node biopsy (SLNB) with patients who had axillary lymph node dissection (ALND). **Methods:** Using the RPH Breast Clinic Database this audit reviewed the results and clinical information of patients with primary breast cancer presenting to RPH Breast Clinic in the period 2002-2006 who had lymphoscintigraphy. **Results:**

1259 patients presented to the RPH Breast Clinic with primary breast cancer from Jan 2002 to Dec 2006. 446/1259 (35%) patients had breast lymphoscintigraphy. Of these patients a sentinel node was seen in 303/446 patients (68%). The detection rate has improved over time and in 2007 the rate was: 98/107(92%) and in 2008:143/151 (95%). The average patient age was 57.8 years with a median of 58 and a range of 32-84. Ages were similar in ALND and SLNB groups. The average length of follow up post surgery was 199 weeks. There was a higher rate of clinical T2 tumours in the ALND group and lower rates for clinical T1 and TIS (in situ carcinoma) tumours. The rate of ALND was 123/446(28%) and the rate of SLNB was 323/446(72%). Visualisation of a sentinel node at lymphoscintigraphy did not increase the rate of SLNB and non visualisation did not result in an increased rate of ALND. Radiotherapy rates were similar in the two groups however the ALND group had higher rates of both adjuvant chemotherapy and hormonal therapy. The rates of local, regional, and distant recurrences combined were a) ALND group 10/123 (8.1%) b) SLNB group 9/323(2.8%) There was only one patient in the SLNB group who had an axillary relapse and this was combined with distant metastatic disease. No patient in the ALND group had an axillary nodal relapse. There were 1/123 (1%) contralateral new primary breast cancers in the ALND group and 8/323 (2.5%) in the SLNB group. Conclusion: In this patient group presenting with primary breast cancer the rate of relapse was lower in the group who had SLNB compared with those who had ALND (2.8% versus 8.1%.) The SLNB group had a higher rate of contralateral new breast cancers however (2.5% versus 1%) and this should be considered in follow up.

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Technical and clinical factors predicting delay or failure to localise sentinel lymph nodes in patients with breast cancer

M. Naji¹, W. Mok¹, N. Patel¹, S. Khan¹, Z. Win¹, W. Svensson², A. Al-Nahhas¹, ¹Hammersmith Hospital, London, UNITED KINGDOM, ²Charing Cross Hospital, London, UNITED KINGDOM.

Aim The aim of the study is to investigate the technical and clinical factors that could potentially predict delay or failure to localise sentinel lymph nodes (SLNs) in patients with breast cancer. **Methods** 131 patients with breast cancer and clinically negative axillary nodes underwent sentinel lymph node scintigraphy following single intra-dermal injection of ^{99m}Tc albumin nanocolloid from January 2008 to January 2009. Several technical and clinical variables including patient's age, tracer dose, injection volume, injection site, air tracking, blanching and presence of localisation wire, were evaluated retrospectively with the aim to investigate the impact of these factors on the localisation of SLNs. **Results** Sentinel node lymphoscintigraphy, in our institution, has a high sensitivity of 98% (128/131) in localising SLNs. Rapid visualisation of SLNs within 15 minutes of the injection was achieved in 82% (107/131). Our results suggest that lack of air tracking and poor blanching during injection seem to be associated with delay or failure to visualise SLNs (P=0.0017 and P=0.0001 respectively). Other variables (age, injected activity, injection volume, injection site and presence of localisation wire) do not significantly influence the visualisation of SLNs. **Conclusion** In our experience, lack of air tracking and poor blanching during injection could predict delay or failure to localise SLNs. Early recognition of these technical factors may help to speed up and improve the SLN detection rate by implementing techniques such as early massage in this group of patients. Our results also suggest that sentinel node scintigraphy is an effective study in the majority of cases with a very high sensitivity in visualising SLNs.

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Clinical utility of FDG-PET/CT in patients with suspected recurrence of breast cancer.

A. P. Caresia Aroztegui¹, C. Gámez Cenozo¹, M. Cortés Romera¹, J. J. Robles Barba¹, L. Rodríguez Bel¹, S. Rossi Seoane¹, F. Martínez Torrens², A. Urruticoechea Ribate³, F. Moreno Sala³, J. Gil Gil³, A. Benítez Segura⁴, ¹PET unit. Institut de Diagnòstic per la Imatge (IDI). Hospital Universitari de Bellvitge- IDIBELL., L'Hospitalet de Llobregat. Barcelona, SPAIN, ²Radiology Department. Hospital Universitari de Bellvitge-IDIBELL., L'Hospitalet de Llobregat. Barcelona, SPAIN. ³Oncology Department. Institut Català d'Oncologia (ICO)., L'Hospitalet de Llobregat. Barcelona, SPAIN, ⁴Nuclear Medicine Department. Hospital Universitari de Bellvitge-IDIBELL., L'Hospitalet de Llobregat. Barcelona, SPAIN.

OBJECTIVE: To evaluate the utility of PET/CT for restaging patients with suspected local or metastatic recurrence of breast cancer. **METHODS:** Forty-seven women (mean age 55 years, range 34-78 years) with suspected recurrence of breast cancer were included in our study. According to the indications for restaging, patients were divided in 3 different groups: Group 1 with elevated tumor markers (n=18), Group 2 with indeterminate lesions on other imaging studies (n=15) and Group 3 before surgical resection of local recurrence or solitary known metastases to exclude dissemination (n=14). All patients underwent a whole-body PET/CT with FDG. Follow-up was > 6 months. Changes in further management based on PET/CT were recorded. **RESULTS:** In group 1, PET/CT was useful in pinpointing recurrence in 12/18 patients (66%) with unexplained elevation of CA 15.3 and the other 6/18 patients did not show any further evidence of disease. In group 2, PET/CT showed FDG uptake in the indeterminate lesion in 8/15 patients (53%): all of them (8/8) proved to be malignant and in 6/8 patients other non suspected metastases (lung, bone and lymph nodes) were discovered. In 7/15 patients (47%) PET/CT was negative in the suspected area and no other findings were detected. In group 3, all the potentially resectable lesions were FDG-avid (14/14: 7 locoregional recurrence and 7 isolated distant metastases) but PET/CT demonstrated other unsuspected metastases in 4/14 patients (28%) mostly localized in bone and lymph nodes. Overall sensibility, specificity and accuracy for PET/CT were 96.9%, 86% and 93.7%, respectively. A second malignancy was detected by PET/CT in 2 patients (thyroid cancer and colorectal cancer) but 1 patient showed a non-FDG avid renal mass. PET/CT had an impact on the management in 31/47 patients (66%): 23/31 received chemotherapy for metastatic disease, 7/31 changed to watching and 1/31 (included in group 1) underwent surgical resection of an isolated axillary recurrence. **CONCLUSIONS:** PET/CT can improve restaging and alter therapeutic options in patients suspected to have breast cancer recurrence, primarily by demonstrating distant metastases occult at other imaging studies.

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Impact of PET/CT in treatment planning in breast cancer patients. Evaluation of therapy response by PET/CT.

F. Vlachou¹, R. Efthimiadou¹, L. Vlachou¹, D. Kechagias¹, A. Nikaki², N. Eftychiou², K. Dalianis¹, S. Merisoglu¹, J. Andreou¹, V. Prassopoulos¹; ¹D.T.C.A. Hygeia Department of PET/CT, Athens, GREECE, ²Saint Savvas Cancer Hospital Nuclear Medicine Department, Athens, GREECE.

AIM: This retrospective study was scheduled to examine the impact of PET/CT examination in treatment planning of patients suffering from locally recurrent, known or suspected metastatic breast cancer. Evaluation of therapy response with PET/CT was also examined. **METHODS:** 27 patients suffering from locally recurrent, known or suspected metastatic breast cancer underwent 54 PET/CT examinations, before and after therapy (follow up period 6-12 months). All patients had been evaluated pretreatment by conventional imaging and were referred for PET/CT examination for: better localization of tumor burden, treatment decision, baseline PET/CT for treatment response evaluation. All patients were restaged after therapy by PET examination, in comparison with anatomical imaging, and regarded as responders: negative post-therapy PET, or reduction of the number of the metastatic lesions or reduction of SUV of the existed lesions, and non responders: disease, as evaluated in pre therapeutic PET, either remained stable or progressed. **RESULTS:** PET/CT changed the treatment planning at 12/27 patients (44.4%). 4/12 had PET/CT negative while CT was positive or equivocal; 3/4 did not receive any treatment and remained stable during follow up period. The other one received chemotherapy, but not bisphosphonates (BPN), and presented having partial response at following CT examination. 4/12 received additional BPN, as they presented having osseous disease on PET. The last 4/12 patients, who received additional chemotherapy or radiotherapy (2 presented local recurrence), 2 had progressive disease present both on following PET/CT and CT; PET became negative for the other 2, while CT became negative for 1 and remained positive in 1. Of the rest 15 patients, whose treatment did not alter after PET/CT examination, clarified as responders 6 and non responders 9 based on PET results. On the other hand, based on CT results the responders were 7 and non responders 8. In 3 patients, who presented with progressive disease PET/CT revealed more metastatic lesions than CT in both pre and post therapy examinations, while there were 2 patients with progressive disease on PET whose CT was negative. **CONCLUSIONS:** PET/CT altered treatment planning in 44.4% of breast cancer patients with known or suspected metastatic disease. PET is more accurate than CT in evaluating possible local recurrence, as well as osseous metastasis, as PET can detect incipient tumor lesions. Therapy should be based on CT when multiple small lung nodules, but single small non metabolic pulmonary nodule on PET give the right to wait and watch.

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The Incidence and Predictive Factors of Sentinel Lymph Node Metastases in Early Stage Breast Cancer

H. Bozkurt, R. Bekiş, Y. Demir, A. Sevinç, B. Değirmenci, Dokuz Eylül University, Izmir, TURKEY.

Introduction: Radioguided sentinel lymph node biopsy (SLNB) has been performed routinely in many centre to evaluate axilla in early stage breast cancer instead of axillary dissection (AD). Although SLNB is accepted as a guide to show axillary status, the incidence and positive predictive factors of SLN metastases in early stage breast cancer is not evaluated as well as AD. The aim of our study is to investigate incidence and positive predictive factors of SLN metastases. **Subjects and materials:** Totally 225 patients (mean age 54.2±11) with early stage breast cancer confirmed by histopathologically underwent SLNB by using radioguided gamma probe. Pathological results of SLNB were recorded as positive and negative SLN metastases. Comparison SLN metastases was obtained statistically with multichannel χ^2 square test according to ages, tumour histopathology, tumour size and radiocolloid injection location. **Results:** SLN metastases rate was 37% (84/225). Micrometastasis was found 14 % (12/84) of SLN metastases. There was statistically significant difference between histopathologic and tumour size subgroups (p value was 0.009 and 0.006 respectively). SLN metastases rate was 49% and 43% respectively at invasive ductal plus invasive lobular and T2 tumour subgroups. However no statistically significant difference was found among age and injection location subgroups (p value was 0.1 and 0.1 respectively).

N=225	SLN metastases positive	SLN metastases negative	χ^2 test P value ≤ 0.05
Age			0.1
≤ 40	12 (48%)	13 (52%)	
40-60	54 (40%)	82 (60%)	
60 \leq	18 (28%)	46 (72%)	
Tumour types			0.009
Inv. Ductal	43 (41%)	61 (59%)	
Inv. Duct+inv. Lob	20 (49%)	21 (51%)	
Inv. Lobular	16 (39%)	25 (61%)	
DICS and LICs	1 (6%)	15 (94%)	
Others	4 (17%)	19 (83%)	
Tumour size			0.006
≤ 0.5 cm (T1a)	2 (12%)	14 (88%)	
0.5<... ≤ 1 cm (T1b)	6 (22%)	21 (78%)	
1<... ≤ 2 cm (T1c)	26 (40%)	39 (60%)	
2<... ≤ 5 cm (T2)	50 (43%)	67 (57%)	
Injection location			0.1
Upper outer quadrant	49 (35%)	89 (65%)	
Upper inner quadrant	7 (29%)	17 (71%)	
Lower outer quadrant	14 (61%)	9 (39%)	

Lower inner quadrant	9 (37%)	15 (63%)
Retroareolar	5 (31%)	11 (69%)

Discussion: In our study SLN metastases was mostly seen invasive ductal and invasive ductal plus invasive lobular subgroups. SLN metastases also increased with tumor size. This result is compatible with AD report. However our SLN metastases rate was higher than AD has been reported in the literature previously. SLN micrometastasis may explain this situation. The other results of our study is that radiocolloid injection location do not effect the SLN metastases rate.

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West of Scotland experience of F-18 FDG PET/CT imaging in Breast Cancer

S. Han¹, S. Leslie²; ¹West of Scotland PET Centre, Gartnavel General Hospital, Glasgow, UNITED KINGDOM, ²Glasgow University Medical School, Glasgow, UNITED KINGDOM.

Background: Breast cancer is the most common cancer in the UK. Accurate staging of breast cancer is crucial in deciding appropriate therapeutic modalities as well as for prognosis. Although breast cancer is not included in the UK PET/CT Board referral criteria 2009, PET/CT has been utilised in breast cancer when conventional staging is inconclusive. Aim: This study is to determine the diagnostic accuracy of F-18 FDG PET/CT in defining distant metastases and the impact on patient management in breast cancer. Methods: From radiology information system 43 consecutive patients (all women, mean age 57 years, range 30-85 years) who had FDG PET/CT reports mentioning breast lesions during January 2008-March 2010 were identified and retrospectively reviewed. 38/43 cases were for staging or restaging of known breast cancers (carcinoma 34, sarcoma 1, melanoma 2, lymphoma 1). 5/43 cases were patients with incidental FDG avid breast lesions seen in PET/CT scanning for other tumours (lung 4, oesophageal 1). PET/CT reports were compared with gold standard pathological staging in 14 cases (resection 6, biopsy 8), and clinical and imaging follow up (CT, MRI, isotope bone scan, PET/CT) in 29 cases. Results: Sensitivity, specificity and accuracy of PET/CT staging for distant metastases were 95%, 93% and 87% respectively (n=38). PET/CT changed the original stages of conventional imaging in 15/38 cases (42%): up-staged in 9 cases and down-staged in 7 cases. 3/38 cases were inconclusive (8%). PET/CT demonstrated true positive metastases in bones (8), distant nodes (6), lungs and pleura (3), liver (1) and left ventricle (1). PET/CT excluded metastases in lungs (3), mediastinal nodes (2), brain (1) and biliary tract (1). Among 5 cases with incidental FDG avid lesions 2 cases had breast biopsy (carcinoma 1, inflammatory 1). 3 cases had clinical and imaging follow up (1 breast metastasis responding to chemotherapy, 2 false positives). Overall the use of FDG PET/CT altered clinical management in 16/43 patients (32%). Conclusions: F-18 FDG PET/CT imaging is a useful addition to conventional imaging in the staging of advanced breast cancer. PET/CT can occasionally pick up occult breast tumour.

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Breast cancer: predictors of positive bone scintigraphy

S. Isgoren, E. Alkan Ciftci, M. Gur, G. Daglöz Gorur, M. A. Oc, H. Demir; Kocaeli University Department of Nuclear Medicine, Kocaeli, TURKEY.

Breast cancer is one of the most frequent types of cancer affecting women, which commonly metastasizes to bone. Bone scintigraphy is still the standard investigation for the evaluation of bone metastases. The aim of this study was to identify breast cancer patients at high risk for bone metastases. We retrospectively analyzed the data of 183 female breast cancer patients (mean age: 52±11 years) admitted to our unit for bone scintigraphy between 2008-2009. All patients mastectomy were followed by axillary dissection. Bone scintigraphic results of the patients were grouped as normal, equivocal and definite metastasis. Equivocal results were excluded and patients with normal and metastatic bone scintigraphy were analyzed. Age of patient, tumour histotype, diameter, grading, tumour multicentricity, axillary lymph nodal status, estrogen and progesterone receptor status statistically compared with bone scintigraphy results. Table 1 shows the personal and tumour characteristics of the patients and summarizes the correlation between bone scintigraphy results and patient characteristics. Patient age, tumour type (invasive ductal/ invasive lobular), tumour histopathological grade, tumor multicentricity, estrogen and progesterone receptor status, receiving RT and chemotherapy were not predictors of a positive bone scan. Patients with tumour diameter > 3 cm, positive axillary lymph node and number of lymph node > 3 were highly associated with a positive bone scan. The nodal ratio (NR) is the absolute number of metastatic nodes/number of nodes examined. Also, higher NR was predictive of a significantly higher incidence of bone involvement. In conclusion, tumour diameter, axillary lymph node status, number and ratio of involved axillary lymph node are predictors of a positive bone scan. Equivocal lesions on bone scans of patients with these characteristics should correlated with radiological methods.

Table 1: The personal and tumour characteristics of the patients

The characteristics of the patients			
Histopathological	Nodal and hormonal	Other	
Tm type	Nodal status	KT	
ILOB	25 Positive	94	Yes 93
IDUC	114 Negative	45	No 46
Tm grade	(+) LN number	RT	
1	40 0	45	Yes 53
2	72 1-3	57	No 86
3	27 >3	37	
Tm multicent.	Proges. resepe	Scintig.	
Yes	18 Positive	90	Normal 112
No	121 Negative (<=10)	49	Metastatic 27
Tm diameter	Estro. resepe		
≤ 3 cm	95 Positive	89	
> 3 cm	44 Negative (<=10)	50	

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Tumour Markers and Medical Imaging Devices: what is the prognostic significant in long-term follow-up?

L. Evangelista, A. Cervino, M. Gregianin, L. Vinante, G. Saladini, G. Sotti; Istituto Oncologico Veneto, Padova, ITALY.

Aim: the aim of this study was to assess the role of tumour markers, 18F-Fluorodeoxyglucose Positron Emission Computed Tomography/Computed Tomography (18F-FDG PET/CT) and Conventional Imaging (CI) in patients with breast cancer and suspected relapse of disease after primary treatment. Materials and Methods. We studied 115 females (mean age: 61±12 years) with previous breast cancer, already treated with surgery and adjuvant treatment, and with clinical and/or biochemical (tumour marker increase) suspect of disease relapse. All patients underwent CI with Computed Tomography (CT) and 18F-FDG PET/CT. In overall patients, the value of tumour marker CA 15.3 was compared to PET/CT and CT findings. The final diagnosis of recurrence was established by invasive and non-invasive (radiological or nuclear medicine) follow-up and it was compared with Ca15.3, CT and PET/CT. Univariate and multivariate analysis were used to identify the independent predictors of disease recurrence. Results: Of the overall patients, 43 (37%) showed tumour marker increase and 72 (63%) normal value. CT was negative in 39 (34%) patients and positive in 76 (66%) patients; whereas at PET/CT imaging, 48 (42%) patients showed negative findings and 67 (58%) positive findings for recurrence of disease. Of 43 (37%) patients with markers value increase, 23 patients had positive CT while 33 had positive PET/CT (53% vs. 77%, p<0.005). At the end of follow-up (mean time 12±1 months), the recurrence of disease occurred in 33/115 (29%) patients, of these latter 17 (52%) showed high levels of CA15.3. PET/CT predicted the relapse of disease in 28/33 (85%) patients, whereas CT imaging correctly identified 23/33 (70%) patients. At univariate analysis, recurrence of disease was significantly associated with high levels of tumour markers (H.R. 2.28, 95%CI 1.00-5.22, P<0.05) and positive PET/CT (H.R. 6.17, 95%CI 2.17-17.56, P<0.001), while on multivariate analysis only PET/CT findings (H.R. 5.49, 95%CI 1.88-16.01, P< 0.05) remained an independent predictor of disease relapse. Conclusions: FDG-PET/CT is more sensitive than CT and CA15.3 in the evaluation of relapse of disease. Thus, 18F-FDG PET/CT might be considered a complementary imaging technique during long-period follow-up in patients with breast cancer.

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Simultaneous detection of breast tumor resection margins and sentinel node biopsy using a high energy gamma probe

E. Biggi¹, G. Manca¹, A. Lorenzoni¹, E. Roncella², G. Boni¹, M. Grosso¹, S. Chiacchio¹, M. Ghilli², F. Betti¹, D. Volterrani¹, G. Mariani¹; ¹Regional Center of Nuclear Medicine, PISA, ITALY, ²Department of Surgery, Unit of Senology. University of Pisa, PISA, ITALY.

Introduction: breast-conserving surgery for selected patients with early infiltrating breast cancer has become the preferred method of treatment by intraoperative assessment of lesion margins and sentinel lymph node biopsy. Evaluation of margins represents an evolving feature of breast conserving surgery, as positive/close margins are associated with higher local post-surgical recurrence. 18F-FDG concentrates in cells with high metabolic rate, and represents an ideal radiotracer to identify neoplastic tissues. The most recent hand-held radiation probes can help localize 18F-FDG-avid areas intraoperatively by detecting high energy annihilation gamma rays or beta particles. Materials and methods: we describe the case of a 79-year-old woman with infiltrating cancer in the external upper-left breast quadrant. The patient had undergone 18F-FDG PET/CT which showed an area of glucose hypermetabolism corresponding to the mammary lesion. No other areas of pathological radiotracer uptake were found. Lymphoscintigraphy was performed the day before surgery, after intradermal injection of 99mTc-nanocolloid on the cutaneous projection of the mammary lesion. The lymphoscintigraphic images showed the presence of two different areas of uptake in the left axilla corresponding to sentinel nodes. Three hours before surgery, the patient underwent an i.v. injection of 200 MBq 18F-FDG. We used an innovative high energy gamma probe (Gammalocator DXI GF&E) to detect positron annihilation quanta. This electronic collimation probe with suppression of background energy is based on a multiple detector system which correlates the count rates of single units of detection thanks to elaborate algorithms, with a range overdrawn from 100 KeV to 1 MeV. Results: by measuring the radioactive counts of the lesion before surgery and considering the counts rate of the right clavicle as background, we found an in vivo target/background ratio of 20:1. We then re-evaluated the resection margins after external upper-left quadrantectomy. The counts ex vivo of the quadrantectomy margins and the resection bed were the same as those of the background. We then proceeded with the search for sentinel lymph nodes. By changing the energy window level, the nodes were found easily, even if with in vivo target/background ratio less than the one previously reported (10:1). Intraoperative histology showed presence of infiltrating breast cancer, margins free of neoplastic infiltration, and sentinel lymph nodes with micrometastases (the surgeon performed therefore axillary lymphoadenectomy). Conclusion: in our experience, the high energy gamma probe used for detection of lesion margins and sentinel lymph nodes can play an important role in breast-conserving surgery.

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Three-dimensional Reconstruction Based on Single Photon Emission Computerized Tomography (SPECT) of Sentinel Lymph Nodes and its Potential Use in Combination with Radioguided Surgery

M. D. Matovic¹, M. Jeremic¹, M. Vljakovic², M. Radovic³, D. Nikolic³, N. Filipovic²; ¹Clinical Centre Kragujevac, Kragujevac, SERBIA, ²Clinical Centre Nis, Nis, SERBIA, ³Faculty of Mechanical Engineering, Kragujevac, SERBIA.

Planar scintigraphy of sentinel lymph nodes (SLN) and radioguided surgery are increasingly used in many solid tumors, apart from being used as a standard procedure in breast carcinoma and malignant melanoma surgery. Based on the scan localization, the surgeon attempts to detect SLN intraoperatively, by means of collimated high sensitive thin probe detector, and an appropriate counting device. However, this is often not easy to do because of the superposition and influenced activity of surrounding tissue, as well as due to the relatively small size of SLN in

comparisson to other structures. We tried to improve preoperative diagnostics as well as intraoperative detection of SLNs by using three-dimensional reconstructions from previously conducted SPECT studies. Using the data from SPECT study, we made a 3-D reconstruction in order to obtain geometry and position of observed SLN. The coordinate transformation according to a global system was done for each scan of SPECT. This way, we got surfaces within the global coordinate system, which represent the projections of objects from different angles. The objects can be SLN, tumors or other anatomical structures of interest. Finally, an algorithm of the **Maximum Likelihood, Expectation Maximization (ML-EM)** type, obtained from a split system matrix reconstruction was implemented. As a result we got a 3-D image of SLN which the surgeon was able to see beside the operative field on the screen during the surgery. In addition, by using the above-mentioned data, we were able to make a physical model of the tumor region, adjacent SLN, patient's axilla, etc. All this was very useful for the surgeon during the surgery, as he was able to get a better understanding of the anatomical relations between the tumor, SLN and other relevant anatomical structures visible in the model, and compare them to those in operative field. This can generally increase the possibility of a faster intraoperative detection of SLN, its extirpation and ex-tempore pathohistological examination. Furthermore, we can contribute to reducing the total duration of the surgery, and ensure greater chances of detection and extirpation of the right SLN. Preliminary results all point to the fact that extensive research should be continued with the aim of improving the SLN diagnostics.

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Linking Overweight, Obesity, Invasive Breast Carcinoma and Gynecologic Cancers: A Retrospective Study from F18-FDG PET/CT Studies

B. Gunalp¹, C. Liman², S. Ince¹; ¹Gulhane Military Medical Academy and Faculty, Ankara, TURKEY, ²Pozitron Nuclear Imaging Center, Ankara, TURKEY.

Introduction: An increasing number of studies are finding that overweight and obese people are more likely to develop cancer of various kinds and tend to have more aggressive, higher grade cancers. **Aim:** We investigate relationships between overweight, obesity, diabetes mellitus and invasive breast and gynecologic cancers retrospectively from FDG-PET studies. **Patients and Methods:** Total 606 patients (345 Breast Ca, 159 Over Ca, 49 Endometrial Ca, 44 Cervix Ca, 6 Uterine sarcoma and 3 two primary carcinomas together) who referred to FDG-PET study for investigation of the metastatic focus included in this study. The women were classified according to their body mass index, or BMI, which is a measure of body fat based on height and weight. Women with BMIs below 25 are considered to be at a healthy weight, those with BMIs of 25-29 are designated overweight, and those with BMIs of 30 or above are considered clinically obese. **Results:** A strong correlation was found between breast carcinoma, over carcinoma, endometrial carcinoma, uterine sarcoma, two primary carcinoma together and BMI (LR=24,03; p=0,007) and fasting blood sugar >100 mg/dl. (LR:14,092; p=0.015). See Table. In this group of patients, 73% of metastatic carcinoma patients were overweight (34%) and obese (39%). **Conclusion:** This study clearly demonstrates that excess weight and increased glucose levels are strongly correlated with increased risk of invasive breast, over and endometrial cancers and uterine sarcomas and more aggressive disease with wide metastatic spread.

Distribution of patients according to BMIs and blood glucose levels

Type of Carcinoma	Age ± 2SD	Overweight+Obes	Fasting blood Sugar >100 mg/dl
Breast Ca (345 patients)	51±12	74,5% (257)	48,7% (168)
Over Ca (159 patients)	54±11	81% (129)	36,5% (58)
Endometrial Ca (49 patients)	59±11	81% (40)	51,1% (27)

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Comparison of Sentinel Lymph Node Biopsy with Routine Axillary Dissection in Early Stage Breast Cancer

Z. Tazeler, G. U. Vural, B. E. Akkas, U. Topal; Ankara Oncology Research and Training Hospital, Ankara, TURKEY.

Sentinel lymph node biopsy (SLNB) is a well established diagnostic tool for axillary staging of breast cancer and has many advantages in comparison with routine axillary lymph node dissection (ALND). The goal of this study is to evaluate the accuracy and predictive value of SLNB for assessing axillary involvement in patients with early stage breast cancer. **Method:** 81 patients with early stage (T1 and T2, Nx, M0) breast cancer were underwnt presurgical sentinel lymph node mapping (SLNM) with 6 peritumoral intradermal and 1 intraparenchymal injections of Tc99m nanocolloid. Dynamic anterior and lateral images were acquired and late planar images were obtained when no lymphatic drainage is seen. Then, all patients had SLNB guided by intraoperative gamma probe, blue dye and ALND. The results of SLNB were compared to ALND. **Results:** In 72 of 81 patients (89%) sentinel nodes were detected by lymphoscintigraphy. In 8 patients, no lymphatic drainage was detected and one patient had drainage only to the internal mammarian chain (IM). 8 of these 9 patients had outer quadrant tumors. Lymph nodes in the IM chain were detected in another 8 (10%) patients and metastases were present in 4. 1-6 (mean: 2 ± 1.5) lymph nodes per patient were resected surgically in SLNB. Both SLNB and ALND were negative for malignancy in 39 patients and positive in 18 patients. 6 patients had negative SLNB and positive ALND while 9 patients had positive SLNB despite negative ALND. The false negative rate of SLNB was 19 % (6/33).

	ALND (+)	ALND (-)	total
SLNB(+)	18	9	27
SLNB(-)	6	39	45
total	24	48	72

Conclusion: SLNB is established to be a reliable and efficient method in axillary staging in breast cancer patients. Nevertheless, the relatively higher false negative rate of this study may originate

from initial experiences of the medical centre. The detection of lymph nodes by gamma probe despite nondetectable lymphatic drainage in SLNM may indicate the limitation of planar imaging and signify the need for SPECT/CT. Preoperative lymphoscintigraphy must be performed in all patients with early stage breast cancer for the evaluation of unexpected lymphatic pathways since the detection of drainage towards the IM chain may provide additional information for radiotherapy planning.

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Our results in the sentinel lymph node biopsy technique in patients with breast cancer with and without previous nodulectomy.

A. Sainz-Esteban, P. García-Talavera, M. Gonzalez-Selma, R. Olmos, M. Ruiz, F. Gonzalez-Criado, A. Gomez-Lopez; Hospital Clínico Universitario de Valladolid, Valladolid, SPAIN.

AIM: The aim of the study was to report our experience with sentinel lymph node biopsy (SLNB). **MATERIAL AND METHODS:** The study included 74 women (mean age: 56.65 +/- 11.66 years old) and 75 breast lesions (1 patient had bilateral cancer). All of them had breast carcinoma clinically staged T1-2 N0 and underwent SLNB between November 2008 and December 2009. In 24 patients nodulectomy was performed before SLNB. Patients with tumour > 5 cm, multicentric, axillary involvement and previous lymphadenectomy, radio or chemotherapy were not included. After surgery the patients were histologically classified: 2 cases were Tis, 55 were T1 and 18 T2. Average tumour size was 16.42 +/- 7.7 mm. A lymphoscintigraphy was performed after peritumoral (45 patients with palpable tumour) or periareolar (30 patients with non palpable tumour or previous nodulectomy) injection of 74-111 MBq of 99mTc-nanocolloid (volume: 0.3-0.4 ml). Planar images were performed 30 min. p.i. A hand-held gammprobe was used to identify hot nodes during the surgical procedure. When sentinel lymph node (SN) was affected axillary lymph node dissection was done. **RESULTS:** A total of 70 SN were identified (93%) during surgery. Lymphoscintigraphy identified 73 SN (73/75) that correspond to 72 patients. In 1 of the 2 cases where SN was not found in the scintigraphy it could be located by intraoperative hand-held gammprobe. However in 4 patients SN detected in scintigraphy were not found during the surgery. Among the 24 patients that had previous nodulectomy (32%) in 1 patient SN was not found nor in scintigraphy nor in surgery and in 1 patient SN was not found in scintigraphy. A total of 117 SN were removed (mean per patient 1.58). Metastatic nodal disease was identified in the SN of 14 patients (3 patients had micrometastasis) of which 6 had other lymph nodes affected when axillary lymph node dissection was done. In our group axillary lymph node dissection was avoided in 56 patients (75%). The scintigraphy showed parasternal SN in 5 patients but they were not removed during the SLNB procedure (axial SNs were negative in these patients). During the follow up period (mean: 10.29 months) none of them had developed axillary recurrence. **CONCLUSION:** SLNB detected sentinel lymph node in most of the cases and could avoid unnecessary lymphadenectomy, also in patients with previous nodulectomy that in our group represented a third of the patients.

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Breast cancer (BC) preoperative staging: the role of Molecular Breast Imaging (MBI) with a high resolution dedicated breast camera (DBC)

A. Spanu¹, F. Chessa¹, D. Sanna¹, P. Cottu², A. Manca³, S. Nuvoli¹, G. Madeddu¹; ¹Dept. of Nuclear Medicine - University of Sassari, Sassari, ITALY, ²Dept. of Surgery - University of Sassari, Sassari, ITALY, ³Dept. of Pathology - University of Sassari, Sassari, ITALY.

Aim: Conventional imaging methods proved of limited value in the preoperative staging of BC, often underestimating local tumor extension. In the present study we evaluated whether MBI with a high resolution DBC may play a role as an adjunctive diagnostic imaging tool to Mx in BC preoperative staging. **Methods:** Two-hundred and nine consecutive female patients, aged 41 to 81 yrs, with Mx findings highly suggestive for cancer (BI-RADS category 5) scheduled to breast surgery were retrospectively reviewed. In all cases, MBI was acquired, using 99mTc-tetrofosmin as radiotracer, by means of a high resolution (1.6 mm spatial resolution) semiconductor (CZT) based DBC mounted on a mammography unit. The images were acquired in both cranio-caudal and mediolateral oblique views (600 sec/view) with mild breast compression during acquisition. All patients had been submitted to both clinical examination and Mx. MBI results were correlated with Mx findings. Breast surgery was planned in all cases after MBI, taking into account both MBI and Mx findings. A primary BC was confirmed at surgery in all cases. **Results:** 99mTc-tetrofosmin MBI was true positive in 204/209 patients (97.6%) and false negative in the remaining 5 cases, 3 of whom with a unifocal invasive ductal carcinoma (5-7 mm in size) and 2 with a multifocal BC (invasive ductal in one case and mucinous in the other case) in whom, however, only the index tumor (range size: 5-14 mm) was evidenced at Mx. In the 204 BC patients positive at MBI, the latter was more accurate than Mx in assessing tumor extension in 57/204 (27.9%) cases evidencing the intraductal component sited around invasive cancer in 37/57 and new tumor invasive foci in 20/57 cases, as confirmed at surgery. The new tumor foci (range size: 4-10 mm), all clinically occult, were ipsilateral in 16 cases and contralateral in 4 cases. MBI changed the surgical management in 11/57 cases (19.3%). **Conclusions:** 99mTc-tetrofosmin MBI with a high resolution DBC proved a useful diagnostic tool in the preoperative staging of BC patients. The procedure demonstrated a higher accuracy than Mx in assessing local tumor extension, contributing to correctly change surgical planning in some cases. A wider application of MBI, as an adjunctive diagnostic tool to Mx, is thus suggested in BC patients before operation.

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Sentinel lymph node biopsy in male breast cancer

A. A. Rodriguez-Revuelto¹, J. Martin-Miramón¹, C. Díaz Martín¹, L. Berná¹, J. Font², O. Aparicio², S. Barcons², R. Rovira³, C. Serra³, J. Lain⁴; ¹Udiat Centre Diagnostic, Sabadell, SPAIN, ²Hospital Parc Tauli, Sabadell, SPAIN, ³Hospital General de Vic, Vic, SPAIN, ⁴Hospital General de Terrassa, Terrassa, SPAIN.

Introduction: At early stages, the morbidity risk associated to axillary lymphadenectomy of breast cancer in male patients is similar to female patients. Selective sentinel lymph node biopsy (SLNB) has become a routine technique in female breast cancer and it can be useful in male patients to reduce their morbidity. **Objectives:** The aim of this study was to analyse retrospectively our experience in SLNB in male breast cancer. **Material and methods:** Between January 2005 and December 2009 were performed 1033 SLNB in breast cancer, 8 of them (0.78 %) were male patients (mean age 68 y.o., range 46-87 y.o.). Breast carcinoma was diagnosed by core needle biopsy: 7 ductal infiltrant carcinoma, 1 high-grade intraductal carcinoma; mean tumour size was 21 mm (range: 11-32 mm). Before SLNB, all patients underwent to locoregional study by axillary echography and breast MRI. Lymphoscintigraphy was performed by intratumoral injection of ^{99m}Tc -albumin nanocolloid (Nanocol, 111 MBq / 0.3 ml), under sonographic guidance, and static images were acquired 4 h. post injection (p.i.). Surgery was performed 24 h. p.i., and the localisation of the sentinel node (SN) was made by the aid of a gamma probe. In case of positive SLNB, axillary lymphadenectomy was completed. **Results:** Lymphoscintigraphy showed at least one SLN in all patients. 13 SLN were removed by selective biopsy (1.62 SLN per patient, 100 % surgery detection). In 7 patients SLN was identified in axillary region, and in one patient was identified in axillary and mammary regions. In 5 patients (63%) the intraoperative biopsy of SLN was positive: 3 metastatic disease and 2 micrometastases (in 2 of them it was the only lymph node affected). At present, all patients are remaining relapse-free of disease, with a clinical monitoring mean of 21 months (range 3-54 months). Positive axillary involvement ratio (63 %) in male was higher than in female patients (32 %), during the same period. **Conclusions:** SLNB is an optimal technique for axillary nodal staging in male breast cancer. In this study, 37 % of patients get benefit from SLNB, avoiding axillary lymphadenectomy.

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Role of sentinel lymph node mapping in accessory breast tissue cancer: A case report

H. Ahmed, M. K. Nawaz, I. Munir, A. I. Khan, S. Mansoor, S. Muzahir, M. Saadullah; Shaikat Khanum Memorial Cancer Hospital & Research Center, Lahore, PAKISTAN.

BACKGROUND: Cancer of accessory breast is a rare commodity. The role of sentinel lymph node scintigraphy in the management of early breast cancer is well established but not in the accessory breast cancer. This technique is used for reducing the surgical morbidity. We present a rare case of accessory breast cancer and role of sentinel lymph node mapping in the staging workup. **OBJECTIVE:** Our aim was to assess the practicability and usefulness of sentinel lymph node scintigraphy in axillary accessory breast cancer. **MATERIAL AND METHOD:** The patient is a 50-year-old lady who presented with a hard lump in accessory breast tissue measuring 2 x 3 cm in size. On Tru-Cut biopsy it was invasive ductal carcinoma with ER and PR negative and HER 2-Neu 2+. The patient was scheduled for the surgery at our hospital. A day prior to surgery sentinel lymph node mapping was performed with 40 MBq of ^{99m}Tc HSA nanocolloid of the normal right breast as well as accessory breast at 3 and 6 O'clock and 9 and 12 O'clock positions respectively. Images were acquired at 45 minutes after injection and later on delayed images were taken. Sentinel node for accessory breast was very well visualized. **CONCLUSION:** This case demonstrates that sentinel lymph node scintigraphy is clinically useful and rational procedure for reducing the surgical morbidity and unnecessary axillary surgery even in accessory breast tissue cancers. Still more studies are needed to prove its advantage in rare accessory breast tissue cancer.

P37 — Monday, October 11, 2010, 16:00 — 16:30, Hall Z

Oncology Clinical Science: Lung

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The value of dual-time-point 18F-FDG PET imaging for lymph node characterization in the patients with non-small cell lung cancer

D. Kim, C. Kim, S. Park, S. Jung, W. Kim; Wonkwang University School of Medicine, Iksan, Jeollabuk-do, KOREA, REPUBLIC OF.

BACKGROUND: Several studies have explored the usefulness of delayed or dual-time-point FDG PET in improving detection of tumors, distinguishing malignant from non-malignant (benign and inflammatory) lesions. The purpose of this study was to evaluate the value of dual-time-point FDG PET imaging for lymph node characterization in the patients with non-small cell lung cancer. **METHODS:** Fourteen consecutive patients (10 men and 4 women; mean age, 65.9±6.2 years) with non-small cell lung cancer were included prospectively. All patients had curative operation with intra-operative mediastinal lymph node biopsy. After the selecting 2 consecutive axial images of early PET/CT scan, regions of interest were drawn manually on same slices of early and delayed PET/CT images, and maximum SUVs were acquired (SUV1, mean SUV of early imaging; SUV2, mean SUV of delayed imaging). **RESULTS:** Fourteen primary lesions and 32 lymph nodes were included, and 3 mediastinal lymph nodes were histologically confirmed as a metastasis. All patients showed SUV elevation of primary lesion on the delayed imaging (Mean SUV1=9.97±4.6, mean SUV2=12.69±5.6, retention index [RI, %]=28.7±14.2), excepting 1 patient with BAC (SUV1=1.67, SUV2=1.43, RI=-14.4%). SUV1, SUV2 and RI of metastatic lymph nodes (2.73±1.42, 3.57±2.55 and 23.57±24.13, respectively) were higher than those of non-metastatic lymph nodes (2.46±0.56, 2.65±0.77 and 7.09±14.5, respectively), but none was statistically significant. **CONCLUSION:** Dual-time-point FDG PET imaging may show better performance to characterize mediastinal lymph nodes in patients with non-small cell lung carcinoma. The further study with sufficient number of patients was demanded.

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Does Whole Body CT is Necessary for PET/CT Evaluation of SPN

N. Can¹, M. Ünlü²; ¹Medicana International Hospital, Ankara, TURKEY, ²Gazi University Medical Faculty Nuclear Medicine Department, Ankara, TURKEY.

In the conventional protocol from eye to thigh patient radiation dose in PET/CT examination differs between 19 to 25mSv. Approximately 6.5-12mSv of the total dose comes from CT part of the examination. In this study we investigated if only thorax CT - whole body PET scan is useful as whole body PET/CT scan without any clinical information loss or not? **Material-method:** We analyzed whole body PET/CT scans retrospectively which were sent for assessment of solitary pulmonary nodules (SPN). In our data pool, there was 126 SPN patients out of 3900 (3 %). We evaluated thorax PET/CT and whole body non-AC PET images. **Results:** There was 126 patient with SPN (88 male, 38 female). All nodules range between 7mm - 30mm in diameter and mean diameter was 14mm. In 69 scans, SPN was negative in PET scan. In the rest of the patients (n: 57), mean SUVmax was 6.1 ± 3.74. There was extrathoracic 18F-FDG uptakes in 17 patients (13%). Histopathologically confirmed extrathoracic 18F-FDG foci were as follows: 6 thyroid (1 papillary carcinoma, 2 thyroiditis, 3 adenoma), 4 parotis gland (Warthin tumor), 2 gluteal subcutaneous inflammation, 1 cervical lymph node (reactive), 1 larynx (epidermoid ca), 1 prostat gland (prostat ca), 1 adnexial mass (enflammatad ovarian cyst), 1 urinary bladder (uroepithelial ca). All these sites were evident in non AC PET scan except urinary bladder. **Conclusion:** By using this patient tailored protocol for SPN, patient radiation dose could be lowered by ranging 3.9-7.2mSv without loss of any significant diagnostic information.

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Functional Imaging with Tc-99m-Depreotide (NeoSPECT) in Small Cell Lung Carcinoma.

G. P. Gerasimou¹, E. Eleftheriadou², E. Moralidis¹, E. Dedousi¹, N. Papadimitriou¹, N. Lytras¹, G. Liaros¹, E. Hildis¹, T. Aggelopoulou¹, P. Makrantonakis³, P. Zarogoulidis², E. Papanastasiou¹, K. Zarogoulidis², A. Gotzamani-Psarrakou¹; ¹Institute of Nuclear medicine-Ahepa Hospital, Thessaloniki, GREECE, ²Lung Cancer Clinic-G Papanikolaou Hospital, Thessaloniki, GREECE, ³Oncologic Clinic-Ahepa Hospital, Thessaloniki, GREECE.

Small Cell Lung Carcinoma (SCLC) is a highly aggressive tumor. It has been mentioned that this kind of tumor expresses somatostatin receptors subtypes (mainly subtype 2). Molecular imaging with Tc-99m-Depreotide (NeoSPECT-NES) has been proven to be useful in the diagnosis and extension of disease. The aim of the present study is to clarify the usefulness of NES in the evaluation of disease extension of patients with SCLC, compared to anatomical imaging modalities (CT). We have evaluated the CT and NES data of twenty patients (3 females), aged 52-74 years (61.2±5.6). The diagnosis of SCLC was proven by biopsy All patients underwent all exams dedicated for these cases (chest radiograph, CT of the chest, brain and abdomen), plus NES. Molecular imaging with NES was performed 3-4 hours post iv injection of 740 MBq of the radiopharmaceutical. A total body survey, plus tomographic imaging of chest (in all patients) and finally spot views of the skull and abdomen were acquired to all patients. NES study was positive and matching to CT chest data concerning primary focus to all but one patient. Complementary, in 7 of the patients, 8 additional lesions were detected by NES, matching with CT data, plus 4 lesions (three ipsilateral and one contralateral to the primary site of the tumor) in 4 of the above mentioned seven patients. Secondary lesions revealed by CT in the brain (2 patients), liver (3) and adrenals (2), were not detected by NES, whilst secondary bone involvement was mentioned to one patient. Accordingly to the above mentioned, NES is a valuable tool in patients with SCLC, concerning evaluation of disease extension. Its value seems to be limited in secondary brain lesions, probably due to the small size of them and poor resolution of the technique, in hepatic metastases due to accumulation of the radiopharmaceutical to the liver and finally in adrenal lesions (lack of somatostatin receptors?).

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Brain 18F-FDG PET-CT in lung cancer patients: Approximation towards clinical indication

A. Palomar Munoz, A. M. Garcia Vicente, J. P. Pilkington Woll, A. Soriano Castrejon, V. M. Poblete Garcia, A. Nunez Garcia, M. E. Bellon Guardia, B. Gonzalez Garcia, M. P. Talavera Rubio, J. M. Cordero Garcia, I. Cepedello Boiso; Hospital General Ciudad Real, Ciudad real, SPAIN.

Aim: To assess the diagnostic impact of a brain PET/CT for detecting metastatic lesions in patients with lung cancer in order to establish its possible indication. **Material and methods:** 270 patients, neurologically asymptomatic, with suspicion or confirmed lung cancer were prospectively included. All patients underwent an initial standard whole body PET/CT, using a 3D protocol (3 minutes/bed) followed by a selective brain study PET/CT (10 minutes/bed) without the administration of intravenous contrast. All studies were assessed by two blinded observers to determine the tumour stage and evaluate the brain parenchyma. A brain PET/CT study was considered pathologic if any FDG uptake greater than background brain activity was detected. Neurological involvement was confirmed or ruled out by intravenous contrast brain CT/MRI or a clinical follow-up longer than 6 months. **Results:** 108 patients were excluded due to lack of histological confirmation of lung malignancy or a follow-up time of less than 6 months in the absence of brain radiological studies. 163 patients were included, 152 males and 11 females (mean age of 67 years, range 39-87), 17 microcytic and 146 non-small cell lung cancer, epidermoid being the most common histology (n=69). 28 patients were in stage I, 14 stage II, 69 stage III and 52 in stage IV. Brain metastases were diagnosed in 15 patients, 12 in stage IV, 2 in stage III and 1 in stage II. PET/CT detected hypermetabolic lesions in 6 patients. After revision, 2/9 patients with false negative results showed hypometabolism in brain PET/CT, that was associated to peritumoral edema in CT. The false positive PET/CT corresponded to an area of ischemia diagnosed by MRI. The sensitivity, specificity, positive predictive value (PPV) and negative predictive values for brain PET/CT in detecting metastases, attending to hypermetabolic lesions were: 40%, 99%, 86% and 94% respectively. If hypometabolic malignant lesions were considered these parameters were: 53%, 99%, 89% and 95% respectively. **Conclusion:** In a patient with primary lung neoplasm, a hypo/hypermetabolic brain lesion, in absence of known vascular disorders, should be considered suspicious of malignancy and further assessment is necessary. Therefore even though brain PET/CT had limited sensitivity in the diagnosis of brain metastases this procedure could be useful specially in advanced stages due to its better PPV when compared to clinical assessment.

P442**PET/CT in non-small cell lung cancer: 18-FDG SUV max and tumour grading and histotype**

M. L. De Rimini¹, S. Piccolo¹, F. Setola², L. Brunese³, S. Cappabianca², A. Rotondo², P. Muto¹; ¹Nuclear Medicine AORN Monaldi, Naples, ITALY, ²Institute of Radiology, Second University of Naples, Naples, ITALY, ³Department of Radiology, Molise University, Campobasso, ITALY.

Introduction: Relationships among 18F-fluorodeoxyglucose (18FDG) maximum standardized uptake value (SUVmax) at PET/CT and tumor grading are poorly investigated in the literature vs histological type. **Purpose:** Aim of the study was to evaluate in lung large lesions (between 30 mm and 70 mm), whether the SUVmax of 18FDG uptake by the tumour correlates with tumour size and histological variables (tumour grade and histotype) in NSCLC. **Material and methods:** The study consisted of 70 patients who underwent 18FDG PET/CT scan for lung lesions evaluation, retrospectively selected on the following inclusion criteria: a histologically or cytologically confirmed NSCLC, size tumor required to range from 30 mm to 70 mm. Tumour type and size, cell differentiation and the SUVmax were defined and the degree of relationship was estimated in pathologically proven NSCLC (29 adenocarcinomas, 20 squamous cell carcinomas, 1 pleomorphic carcinoma, 8 large cell carcinomas and 12 unspecified NSCLCs). **Results:** All tumours were large (mean \pm SD, 43 \pm 10.68 mm). The mean SUVmax was lower in adenocarcinomas than in squamous cell carcinomas ($p < 0.05$) and large cell carcinomas ($p < 0.05$). FDG uptake was lower in well/moderate differentiated NSCLCs than in poorly/undifferentiated NSCLCs. **Conclusion:** In our population of 70 patients affected with NSCLC, FDG uptake differed among histologic types. SUVmax was significantly higher in squamous cell carcinomas and large cell carcinomas than in adenocarcinomas. In addition, the degree of FDG uptake seemed to depend on tumour cell differentiation.

P443**Is there a time for changing algorithm in the management of patients with Lung Cancer? The impact of 18F-FDG PET/CT**

M. Zsiray¹, Z. Markoczy¹, Z. Lengyel², A. Fekeshazy³, M. Kasler⁴, K. Borbély⁴; ¹National Koranyi Institute of Pulmonology, Budapest, HUNGARY, ²Positron Diagnostic LTD, Budapest, HUNGARY, ³PET-CT LTD, Budapest, HUNGARY, ⁴National Institute of Oncology, Budapest, HUNGARY.

Objectives: 18F-FDG PET/CT proved to be the most sensitive non-invasive imaging modality for the evaluation of solitary pulmonary nodules (SPN). The anatomic-metabolic PET/CT method is superior to CT in terms of sensitivity and specificity for the diagnosis, staging, and restaging of lung cancer. In our study we tested the clinical impact of PET/CT in patients with lung cancer. **Methods:** Six hundred sixty six studies were performed in 650 patients between May 2006 and April 2009. There were 329 female and 321 male patients with mean age of 61 years (23-82ys). PET/CT studies were performed with indication of metabolic characterization of SPN (n=310), preoperative staging (n=245), or restaging (n=111) of primary lung carcinoma. The results of PET/CT studies were analyzed retrospectively and compared to clinical follow-up and radiologic data. **Results:** The sensitivity, specificity, positive predictive value and negative predictive value of 18F-FDG PET/CT was 93%, 84%, 89%, and 94%, respectively. **Conclusion:** The optimal therapy requires precise diagnosis. Therefore, the most effective diagnostic methods are recommended for selection of patients for the most appropriate therapy. On the basis of our results PET/CT had a high impact on the management of patients with lung cancer by improving dramatically the sensitivity and diagnostic accuracy compared to the conventional imaging techniques. However, positive findings have to be analyzed thorough due to the relative low specificity of the method, especially following therapeutic intervention.

P444**The Value of FDG-PET/CT Imaging In Dermatomyositis As A Paraneoplastic Syndrome In Malignancy Suspicion**

T. Ones, F. Dede, F. Novruzov, M. Aras, S. Güngör, S. Inanir, T. Y. Erdil, H. T. Turoglu; Marmara University School of Medicine, Istanbul, TURKEY.

INTRODUCTION: Dermatomyositis is a clinical syndrome with inflammation involving the skeleton and the heart muscle because of unknown etiology. Five basic diagnostic criteria of dermatomyositis are; symmetrical proximal muscle weakness, abnormal muscle biopsy, increased skeletal muscle enzyme levels, abnormal electromyography and typical skin findings with or without dysphagia and shortness of breath. The incidence is 1/1000000 in the population, and may be seen with primary rheumatologic syndromes and in various types of cancers as "Paraneoplastic Syndrome". It is thought that in patients with malignancy, dermatomyositis develops due to a reaction against cancer cells, but the pathophysiology of dermatomyositis could not be explained yet. First, in 1916 Stertz showed the relationship between gastric cancer and dermatomyositis. In patients with dermatomyositis various types of malignancies can be seen. Cancer risk in patients with dermatomyositis is greater than normal population and the risk is highest in the first year after following the diagnosis. Antinuclear Antibody (ANA) seropositivity, has a supporting role in the diagnosis of dermatomyositis and it is thought that if ANA is (+), the probability of having underlying malignancy is low. However in cancer studies very different levels of ANA have been reported in cancer induced dermatomyositis patients. In this case report the value of FDG-PET/CT in the work-up of dermatomyositis as a "Paraneoplastic Syndrome" was discussed. **CASE REPORT:** A 45-year old male patient with ANA seropositivity and symptoms of dermatomyositis suggestive of "Paraneoplastic Syndrome" was admitted in the dermatology service. His thoracic CT revealed multiple nodular densities especially near the superior/posterior segment of the right lower lobe. Whole body FDG-PET/CT imaging was planned to determine the metabolic characteristics of the lesions. FDG-PET/CT demonstrated intense FDG uptake in the suspected pulmonary nodular lesions with the involvement of multiple mediastinal lymph nodes. Symmetric hypermetabolic activity involving the proximal muscles of the upper/lower extremities also showed moderate degree of FDG uptake at the sites of inflammation due to dermatomyositis which was later confirmed by muscular biopsy too. NSCLC verified with histopathologically. The patient is still alive and after chemotherapy the typical skin findings for Paraneoplastic Syndrome (Dermatomyositis) disappeared. **CONCLUSION:** In patients with dermatomyositis even if they are ANA seropositive, one has to be careful for the probability of

cancer and thus further studies should be performed to elucidate the possible relationship between cancer and dermatomyositis. FDG-PET/CT seems to be one of the first line methods to be utilized to pursue this goal.

P445**The Diagnostic Role of F-18 FDG PET/CT in Patients with Pleural Thickening and Pleural Effusion**

M. S. Eren¹, C. Karaman², M. Aslan¹, O. İtli², A. Akkoçlu², O. Özdoğan¹, B. Degirmenci¹; ¹Dokuz Eylül University Department of Nuclear Medicine, izmir, TURKEY, ²Dokuz Eylül University Department of Chest Medicine, izmir, TURKEY.

AIM: To investigate the diagnostic role of F-18 FDG PET/CT in patients with pleural thickening and pleural effusion. **METHODS:** The mean age of the patients were 61.9 \pm 12.7 (26 patients; 21 male) in this retrospective study. Three patients had only pleural effusion (PE), 4 patients had both PE and pleural thickening (PT), and the rest of the patients had pleural nodules (PN) and PT. A low-dose CT was performed prior to the PET images (1.5 min/bed position). The final diagnosis was reached histopathologically and clinical follow-up. The highest SUVmax values for each patient were used for statistical analyses (Mann-Whitney U test). **RESULTS:** All lesions were benign in PE patients. The final diagnosis revealed a malignant lesion in 2, and a benign lesion in the other 2 referred with both PE and PT. In PN and PT group 12 were diagnosed to have malignant lesions and the rest were benign. The mean SUVmax value of the benign PE was 2.6 \pm 0.9. One of the two patients with both PE and PT was diagnosed to have fibrous pleuritis (SUVmax:6.5) and the second with tuberculosis (no increased uptake). The remaining 2 patients were diagnosed as metastatic pleural involvement; one with a metastatic lesion due to a prostate cancer was F-18 FDG negative, the other with nonsmall cell lung cancer had a SUVmax of 12.9. In 19 patients with PT and PN the diagnoses was benign pleural changes (7 patients), malignant mesothelioma (6 patients) and metastatic pleural involvement (6 patients). The mean SUVmax were 2.43 \pm 2.15, 10.13 \pm 3.0, and 9.05 \pm 6.0 for benign lesions, malignant mesothelioma and metastatic involvement, respectively. The SUVmax values ranged between 1.0-6.80 and 1.0-21.5 in benign and malignant lesions respectively. There was a significant difference of SUVmax values between benign and malignant lesions ($p < 0.0001$), and benign and malignant mesothelioma lesions ($p < 0.001$). There wasn't any difference of SUVmax values between malignant mesothelioma and metastatic lesions ($p > 0.25$). In malignant mesothelioma patients, PET/CT demonstrated two nodular lesions which were located in paracaval (SUVmax:5.0), paracardiac (SUVmax:10.0) regions that were not reported by diagnostic CT study. A high F-18 FDG uptake was also demonstrated on femoral diaphysis. **CONCLUSION:** PET/CT may be valuable diagnostic tool in evaluating patients with pleural lesions. It should be taken into consideration that benign lesions could demonstrate reasonably increased FDG uptake. The crucial diagnostic role of PET/CT may be the demonstration of extrapleural dissemination and the determination of small lesions that were not reported on CT.

P446**Application of Positron Emission Tomography Response Criteria in Solid Tumours (PERCIST) in Non-Small Cell Lung Carcinoma (NSCLC)**

I. Cepedello Boiso, A. Garcia Vicente, P. Talavera Rubio, A. Palomar Munoz, B. Gonzalez Garcia, J. Torres, M. Bellon Guardia, A. Leon Martin, V. Pobleja Garcia, J. Cordero Garcia, J. Pilkington Woll, A. Nunez Munoz, A. Soriano Castrejon; Hospital General de Ciudad Real, Ciudad real, SPAIN.

Aim: To analyse the application of PERCIST criteria while evaluating NSCLC's treatment response. **Materials and Methods:** Retrospective study spanned from 2006 to 2009 over a sample of 16 patients (14 men and 2 women; 61 mean age) with NSCLC stages IIIA/B (8 squamous and 8 non-squamous) treated by chemo and radio therapies. Patients were subjected to a Baseline and Post-Treatment PET-CT (last one for 1-4 months after the end of the treatment), following the standard protocol of our department (60 minutes after administration of a intravenous dose of 370 MBq of 18F-FDG; 3D acquisition mode and 3 minutes per bed; GEDSTE-16). Treatment response was assessed with PERCIST criteria and the patients were classified as Responders (Complete Metabolic Response and Partial Metabolic Response) and Non-Responders (Stable Metabolic Disease and Progressive Metabolic Disease). Clinical and radiological follow-up was extended up to 6 months after the end of the treatment and patient evolution was classified into three categories according to its progression or non-progression. All collected data were analysed using the Statistics suite SPSS (version 16.0) and EPIDAT. **Results:** Overall, following PERCIST criteria, 1 patient developed Complete Metabolic Response (CMR), 9 Partial Metabolic Response (PMR), 2 Stable Metabolic Disease (SMD) and 4 Progressive Metabolic Disease (PMD). The detailed results table is listed below.

Metabolic Response (PERCIST)	FOLLOW-UP		
	NON-PROGRESSION	PROGRESSION	
CMR	1	0	1
PMR	9	0	9
SMD	0	2	2
PMD	1	3	4
	11	5	16

Chi-Square test, $p < 0.05$. Furthermore, the relation between the groups of responders and non-responders with according to their evolution was also studied, obtaining the following outcome: 100% positive predictive value (PPV) and 83.3% negative predictive value (NPV). **Conclusion:** PERCIST criteria could provide a useful tool for the evaluation of treatment response in NSCLC. Nonetheless, further researches with broader samples and long term post treatment monitoring are needed to firmly settle its reliability.

P447**18FDG-PET/CT utility in the assessment of TNM parameters in patients with pleural mesothelioma**

A. Notaristefano, A. Niccoli Asabella, C. Altini, D. Rubini, G. Rubini; Nuclear Medicine Unit, University of Bari, Bari, ITALY.

Aim: To evaluate the role of 18-Fluorine-labelled 2-deoxy-2-fluoro-D-glucose positron emission tomography/computed tomography (18FDG-PET/CT) compared with computed tomography (CT) for assessment of TNM parameters in follow-up and restaging of patients (pts) with pleural mesothelioma treated with surgery, radiotherapy (RT) and/or chemotherapy (CHT). **Materials and methods:** 34 pts with pleural mesothelioma who performed 18FDG-PET/CT and CT (age range 55-76 years) were retrospectively evaluated. 22/34 pts were underwent surgery, the others 12/34 did not satisfy the criteria for resectability. 30 pts performed CHT and 29 pts performed RT. We have also calculated the concordance by Cohen's Kappa (K) for patients. **Results:** About T parameter, CT and 18FDG-PET/CT were concordant in 26/34 pts; in 22/34 pts both techniques showed pleural recurrence, in 4/34 pts both techniques didn't show any disease, in 8/34 pts CT showed pleural thickening without 18FDG-uptake. $K=0.393$ (95% i.c.: 0.117-0.393). About N parameter we considered hilar and mediastinal lymphnodes. 18FDG-PET/CT and CT were concordant for hilar lymphnodes in 29/34 pts, discordant in 5/34 pts (3 pts with negative CT and positive 18FDG-PET/CT, 2 pts with CT evidence and without 18FDG-uptake). 18FDG-PET/CT and CT were concordant for mediastinal lymphnodes in 24/34 pts and discordant in 10/34 pts (3/10 were positive at CT and negative at 18FDG-PET/CT, 7/10 were negative at CT and positive at 18FDG-PET/CT). $K=0.258$ (95% i.c.: -0.052-0.521). About M parameter we considered pulmonary, chest wall and extrathoracic recurrences. About pulmonary recurrences CT and 18FDG-PET/CT were concordant in 28/34 pts, and discordant in 6/34 pts (2/6 pts with positive 18FDG-PET/CT and 4/6 negative 18FDG-PET/CT). $K=0.085$ (95% i.c.: -0.085-0.362). The two techniques were concordant for chest wall locations in 30/34 pts ($K=0$), in the others 4/34 pts CT were negative and at 18FDG-PET/CT were positive. For secondary nature in extrathoracic organs there were concordance between the two techniques in 28/34 pts ($K=0.157$, 95% i.c.: -0.071-0.523) while in the others 6 pts CT were positive for liver and skeletal localization but negative for 18FDG-uptake in the same localizations. **Conclusions:** 18FDG-PET/CT is more useful than CT for restaging and follow up of patients with story of mesothelioma confirming CT results and allowing to detect more sites of recurrences than CT. 18FDG-PET/CT is a better technique for the management of pts with pleural mesothelioma.

P448**Can Maximum Standardized Uptake (SUVmax) of F-18 FDG be an indicator of predicting the adjuvant chemotherapy in early stage Non-Small Cell Lung Cancer?**

E. Sürücü¹, C. Karaman², Y. Demir¹, I. Öztop³, N. Özdemir⁴, A. Akkoçlu², T. Şengöz¹, B. Degirmenci¹; ¹Dokuz Eylül University, School of Medicine, Department of Nuclear Medicine, izmir, TURKEY, ²Dokuz Eylül University, School of Medicine, Department of Pulmoner Medicine, izmir, TURKEY, ³Dokuz Eylül University, School of Medicine, Department of Medical Oncology, izmir, TURKEY, ⁴Dokuz Eylül University, School of Medicine, Department of Chest Surgery, izmir, TURKEY.

BACKGROUND: The exact staging in Non-Small Cell Lung Cancer (NSCLC) is the most important parameter in the management of patients. The adjuvant chemotherapy after surgery in stage IIIA NSCLC patients is evidence-based therapeutic modality. There is still debate about the need of the adjuvant chemotherapy after surgery in early stage NSCLC patients. **PURPOSE:** In this study, we aimed to investigate a prediction value of SUVmax in primary tumor for the decision of the adjuvant chemotherapy. We also investigated the correlation between SUVmax in the tumor and the histopathological parameters such as arteriovenous, lymphatic, perineural and pleural invasions. **PATIENTS AND METHODS:** In a retrospective study, 33 NSCLC patients (31M, 2W) were included in this study who were diagnosed stage I and II (IA:8 patients, IB:15 patients, IIB: 10 patients). Primary tumors were removed and the marginal regions of all tumors were negative for all patients. 20 patients received adjuvant chemotherapy (CT), 13 patients did not receive (Non-CT). The average follow-up duration is 11 months ($\pm 0,7$). All of the patients underwent F-18 FDG PET-BT imaging before surgery for staging. SUVmax's were obtained in the primary tumor. Histopathological evaluation was performed for all patients. Mann-Whitney U test, Pearson correlation test and Kaplan Meier analysis were performed for statistical evaluation of the study. **RESULTS:** The average SUVmax were 9.44, 10.33 and 8.09 in all patients, CT and Non-CT groups, respectively. There was no statistical difference in SUVmax between the CT and Non-CT groups ($p=0,397$). Disease free survival (DFS) was not significantly different between CT and Non-CT groups. DFS was significantly shorter in patients with SUV>11 than in patients with SUV<11 ($p=0,027$) (table). Although DFS was shorter in both CT and Non-CT group patients with SUV>11 than in patients with SUV<11, the statistical significance was not found. This is probably due to limited number of patients. There is no significant difference between SUVmax and artery ($p=0,557$), venous ($p=0,271$), lymphatic ($p=0,259$), perineural ($p=0,302$), visceral pleural ($p=0,285$) and parietal pleural invasions ($p=0,826$). **CONCLUSION:** This preliminary study indicates that SUVmax of 11 or greater may be considered as a threshold value for predicting DFS for early stage NSCLC. SUVmax may be considered as an independent predictor of prognosis about DFS since no correlation was found between SUVmax and histopathological parameters. Adjuvant chemotherapy may be used for early stage NSCLC with SUVmax>11. Further studies with a large number of patient are needed to examine this hypothesis.

P449**A pilot study of PET with [11C]-sodium butyrate for diagnosis of lung cancer**

M. S. Tlostanova¹, A. S. Petrov², D. D. Ryzhkova¹; ¹Russian Research Center of Radiology and Surgical Technology, St.-Petersburg, RUSSIAN FEDERATION, ²St-Petersburg State University, St.-Petersburg, RUSSIAN FEDERATION.

The aim of the study were to evaluate feasibility of PET with [11C]-sodium butyrate ([11C]-SB) for diagnosis of lung cancer and to compare the results of PET with [11C]-SB and [18F]-FDG.

Methods: Seven patients with histologically proven lung cancer were included in the study. Three patients with pneumonia were served as a control. All patients underwent whole body PET with [11C]-SB and [18F]-FDG in different days. **Results:** The foci of glucose hypermetabolism were revealed in all cases of lung cancer and pneumonia by [18F]-FDG PET (SUV over 2,5). We observed high uptake of [11C]-SB in all cases (3 pts) of lung adenocarcinoma and in only one case from four in patients with squamous lung carcinoma. We didn't obtained any focal high uptake of [11C]-SB in lungs in patients with pneumonia. **Conclusion:** In spite of absence of false positive results, PET with [11C]-SB doesn't seem to be valuable tool for diagnosis of lung cancer because of lower sensitivity in comparing with [18F]-FDG.

P450**How efficient is PET/CT in metabolic characterization of lung lesions?**

Z. G. Ozkan¹, C. Turkmen¹, Y. Sanli¹, B. Ozkan², S. A. Toker², M. Ereleli³, I. Adalet¹; ¹Istanbul University, Istanbul Medical Faculty, Nuclear Medicine Department, Istanbul, TURKEY, ²Istanbul University, Istanbul Medical Faculty, Thoracic Surgery Department, Istanbul, TURKEY, ³Istanbul University, Istanbul Medical Faculty, Chest Diseases Department, Istanbul, TURKEY.

Aim: Incidentally detected lung lesions in asymptomatic patients is frequent in clinic practice. Characterization of these lesions is essential for management of patients. Although gold standart modality for diagnosis is histopathologic examination, it is not always possible to achieve. In such situations, PET-CT can be a choice for metabolic characterization. We aimed to determine the efficiency of PET-CT in metabolic characterization of lung lesions. **Method:** We evaluated retrospectively 40 patients who had PET-CT between April 2009 and January 2010 in Istanbul Medical Faculty Nuclear Medicine Department for metabolic characterization of lung lesions. There were 10 female, 30 male patients whose ages were 20-88 (mean age: 60,5). For every patient, SUV_{max} values were calculated and sizes of lesions were measured. Presence of mediastinal lymph nodes and extrathoracic lesions were noted. The evaluation was done separately by two nuclear medicine physicians and then final diagnosis was established by consensus. Finally, PET-CT results were compared with histopathologic data. **Results:** According to histopathologic data, 26 of 40 patients had malignant diseases (Group 1); 14 of 40 patients had benign lesions (Group 2). In Group 1, histopathologic diagnoses of patients were: 10 adenocarcinoma, 12 squamous carcinoma, 2 bronchioloalveolar mixed adenocarcinoma, 1 small cell lung carcinoma, 1 carcinoid. SUV_{max} values of the lesions were 3,66 -37,01 (mean: 17,67±8,92) and sizes were 2,6 - 7,3 cm (mean: 4,5±1,33) in Group 1. In Group 2, histopathologic diagnoses were 3 bacterial infections, 1 tuberculosis, 2 chronic granulomatous inflammation, 1 vasculitis, 1 chondromatous hamartoma, 6 nonspecific inflammation. SUV_{max} values were 0,83 - 11,37 (mean: 4,14±2,79) and sizes of lesions ranged between 1,5 to 4,8 (mean: 3,2±1,2) in Group 2. There was no statistical relationship between SUV_{max} values of Group 1 and 2 ($p>0,05$). For whole group, there was no statistically significant relationship between SUV_{max} values and lesion sizes ($p>0,05$). In Group 1, 16 of 26 patients had mediastinal lymph nodes and in Group 2, 4 of 14 patients. In Group 1, 8 patients had distant metastases. In our study, sensitivity of PET-CT in discriminating malignant lesions than benign lesions was 96%, specificity 64%, positive predictive value 83%, negative predictive value 90%, accuracy 85%. **Conclusion:** PET-CT is an efficient method of imaging for metabolic characterization of lung lesions. Its high sensitivity and high negative predictive value enable the choice of patients for histopathologic verification or follow-up. One of drawbacks of metabolic imaging is that abnormal 18F-FDG uptake is not specific for malignancy.

P451**A Novel FDG-PET/CT Image Analysis Approach for Quantification of Lung Cancer**

B. Saboury¹, N. Foroughi¹, G. Bodapati¹, S. Alapati¹, F. Hofheinz², T. Evans¹, B. Eaby¹, T. Werner¹, A. Alavi¹, D. A. Torigian¹; ¹University of Pennsylvania Medical Center, Philadelphia, PA, UNITED STATES, ²ABX, Radeberg, GERMANY.

Objectives: To assess novel image analysis software to delineate and quantify metabolically active volumes (MAV), partial volume corrected (PVC) mean SUV, and metabolic volumetric products (MVP) of lung cancer on FDG-PET/CT. **Methods:** 28 patients with non-small cell lung cancer with pretreatment FDG-PET/CT were retrospectively identified. Tumor volumes and uncorrected/corrected mean SUVs and MVPs (where MVP=MAVxSUV) of 299 lesions were quantified from PET by two readers using the ROVER software package (ABX GmbH, Germany). Comparisons of repeated PET measures were performed using Bland-Altman analysis. **Results:** Mean differences + standard deviations (SD) and 95% limits of agreement (LOA) of repeated PET measures of tumor MAV, uncorrected and corrected mean SUV, and uncorrected and corrected mean MVP were 0.2±3.0 cc (-5.7-6.0cc), 0.0±0.1 (-0.3-0.2), 0.0±1.2 (-2.3-2.3), 1.1±12.8cc (-24.0-26.1cc), 2.6±33.2cc (-62.5-65.6cc), respectively. The effect of PVC upon mean SUV was an average increase of 101.6%. **Conclusion:** It is feasible to quantify MAV and uncorrected/corrected mean SUV and MVP of non-small cell lung cancer on FDG-PET/CT using novel image analysis software. PET measures of MAV and uncorrected mean SUV are reproducible, whereas measures of uncorrected mean MVP and corrected mean SUV/MVP are somewhat less reproducible. PVC has a significant effect upon mean SUV quantification.

P452**Additional value of dual time point 18F-FDG PET/CT imaging in suspected pulmonary nodules**

E. Özkan¹, P. Tan², S. Yağcı¹, S. Laçın¹, G. Erbay¹; ¹Ankara University Department of Nuclear Medicine, Ankara, TURKEY, ²Meram Research and Educational Hospital Department of Nuclear Medicine, Konya, TURKEY.

INTRODUCTION: Many malignant and benign processes exist in solitary pulmonary nodules' etiology and only %20-25 of them are symptomatic. Nowadays, F18-FDG PET is a widelypreadly used imaging tool in the assessment of non-specific pulmonary nodules. %40-50 of these clinically detected nodules are malign lesions whereas %50-60 are benign. 18F-FDG PET is mostly

used for the exclusion of malignancy but false positive and false negative results must be taken into account. In this recent study, we compared the diagnostic accuracy of standard PET/CT and dual time point PET/CT imaging and correlated the PET/CT findings with histopathology and clinical follow-up. **MATERIAL-METHOD:** 36 patients (30 male, 6 female, age range 37-89) with suspected pulmonary nodules (10-29mm) underwent PET/CT at 2 time-points: First scan was obtained as whole body image at 60-75 min, and the second as spot image of chest at 130-150 min, after the i.v injection of 340-495 MBq 18F-FDG. Regions of interest were overlaid onto each fully corrected image in the areas of radiographically known lung densities. The maximal standardized uptake values (SUV) were calculated for both time points (SUVmax 1 and SUVmax 2). PET/CT findings were confirmed with histopathological examination and/or clinical follow-up. **RESULTS:** Patients were classified as malignancy positive and negative groups according to histopathological and/or clinical examinations. In group I with 18 patients, 17 patients had malignant nodules confirmed by histopathological exam after surgery and 1 had malignant mesothelioma diagnosed in the clinical follow-up. The SUVmax values in this group were higher than the accepted threshold value (>2.5) and ranged between 2.6-17.4 for SUVmax 1 and 5.0-26.6 for SUVmax 2. In the second group, surgical excisions or bronchoscopy biopsies were performed in 7 patients and histopathological examination confirmed benign processes. The other 11 patients were followed after the PET/CT scan and no malignancy was observed in the surveillance. SUVmax 1 and SUVmax 2 ranged between 1.78- 10.4 and 2.16- 18.1 in this group, respectively. **CONCLUSION:** Pulmonary lesions with increased FDG uptake are mostly malignant but false positive results due to inflammatory processes must be considered. In this cases, delayed imaging of suspected nodules was useful to differentiate malign lesions from benign ones. On the other hand, nodules with highly increased FDG uptake do not always necessitate a second scan but delayed imaging may contribute the diagnosis of lesions with mildly increased FDG uptake. Thus, this method is suggested only in selected patients.

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The value of FDG-PET/CT in the evaluation of patients with solitary pulmonary nodule

H. S. Yavuz¹, M. O. Tamam¹, A. Yavuz², M. Mulazimoglu¹, T. Ozpacaci¹; ¹Okmeydani Training and Research Hospital, Istanbul, TURKEY, ²Selimpasa Hospital, Istanbul, TURKEY.

Aim: A solitary pulmonary nodule (SPN) is defined as a discrete, well-margined, rounded opacity less than or equal to 3 cm in diameter that is completely surrounded by lung parenchyma, does not touch the hilum or mediastinum. Although most solitary pulmonary nodules have benign causes, 30-40% of these nodules are malignant. The prevalence of solitary pulmonary nodules ranged from 8-51% 18F-fluoro-2-deoxyglucose positron emission tomography /computed tomography (FDG-PET/CT) has reached widespread application in the assessment of pulmonary nodules. The aim of this study was to evaluate the increased diagnostic benefit of FDG-PET/CT interpretation in evaluating solitary pulmonary nodules for malignancy. **MATERIAL-METHODS:** This retrospective analysis was conducted on 36 patients (27 male, 9 female, mean age, 61±15 years; range: 22-84 years) with suspected malignant lung nodules detected by computed tomography, and referred for routine FDG PET /CT between January 2008 and April 2010 for the evaluation of a SPN. Lung nodules with maximum standardized uptake value SUVmax ≥2.5 were considered malignant. Absence of significant lung nodule enhancement at CT was considered strongly predictive of benignity. The diagnosis of these lesions was confirmed by biopsy or follow-up CT. In addition to the clinical features of nodule size, growth rate, location, contour, presence of calcification and radiological features has an important role in benign-malignant separation. **RESULTS:** The mean diameter of the SPN was 10,5mm (range of 3-20mm). Eight patients with SPN considered as malignant were operated. Histological verification revealed 1 low-differentiated neuroendocrine tumor, 3 adenocarcinoma, 4 squamous-cell cancer. In 15 patients, minimal FDG uptake (SUVmax < 2.5) and in 11 patients no uptake was seen. These 26 patients were monitored with follow-up CT with 3 months intervals. During the follow up no growth was detected. After clinical and radiological follow up these SPN's were accepted as benign. **CONCLUSION:** FDG-PET/CT is proved to be a valuable method for the assessment of undetermined solitary pulmonary nodules.

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Preoperative lymph node staging in patients of non-small-cell lung cancer: accuracy of 18F-FDG PET/CT

C. S. Wu; Chi Mei Medical Center, Liouying, Tainan County, TAIWAN.

Aim: To evaluate and verify the accuracy of integrated positron emission tomography with 18F-fluoro-2-deoxy-D-glucose (FDG) and computed tomography (PET/CT) in preoperative lymph node staging in patients with non-small-cell lung cancer (NSCLC). **Materials and Methods:** We retrospectively reviewed 43 patients of NSCLC with surgical nodal staging and its 18F-FDG PET/CT scan was performed within one month before operation. Nodes showing clearly higher 18F-FDG uptake than mediastinum were regarded as being positive for malignancy but we also judged it with the others including distributed pattern of FDG uptake in the mediastinum and pulmonary hila, lymph node calcification or not, and lymphatic drainage pathway of the tumor. The histological nodal results were used as reference standard. Statistical evaluation of 18F-FDG PET/CT result was performed on a per-patient and per-nodal-station bases. **Result:** A total of 221 nodal stations (148 mediastinal, 26 hilar, and 47 intrapulmonary) were evaluated in 43 patients. The overall sensitivity, specificity, and accuracy of 18F-FDG PET/CT for detecting metastatic lymph nodes were 53.8%, 86.7%, and 76.7% on a per-patient basis, and 33.3%, 96.5%, and 90.5% on per-nodal-station basis. With regard to N2 disease, the 18F-PET/CT accuracy was 74.4% and 94.5% on a per-patient and on a per-nodal-station basis. **Conclusion:** Our data show that 18F-FDG PET/CT provides high specificity but low sensitivity in lymph node staging of NSCLC patients and underscore the continued need for surgical staging.

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Role of (18)FDG-PET/CT and SUV evaluation in the management of Non-Small Cell Lung Cancer in different stages

A. Cistaro¹, N. Quartuccio², A. Rimicci², P. Fania¹, U. Ficola²; ¹Positron Emission Tomography Center IRMET S.p.A, Turin, ITALY, ²Nuclear Medicine Dept. "La Maddalena" Hospital, Palermo, ITALY.

Aim: to evaluate the correlation between SUVmax and clinical outcome in patients with NSCLC in stage I-II undergoing surgery and in patients with NSCLC in stage III-IV undergoing chemotherapy. **Methods and materials:** 135 patients (49 stage I-II, 86 stage III-IV), underwent at least 2 FDG-PET whole body and for each one SUVmax and dimension of the primary neoplastic lesion were recorded. In the group of patients in stage I-II SUVmax and clinical outcome were put in relationship by Student-t test, and the optimal cut-off value of SUVmax to predict prognosis was calculated. The probability of Disease-Free Survival was investigated through the univariate analysis of Kaplan-Meier. In the group of stage III-IV patients we looked for a possible correlation between SUVmax and best response, and for the most significant cut-off value of SUVmax to predict prognosis. **Results:** Stage I-II patients with SUVmax<9 (cut-off value) and diameter of lesion>30mm (cut-off value) reported the worst prognosis. In stages III and IV, no reliable cut-off value of SUVmax was found in correlation with prognosis and response to therapy. **Conclusion:** In stages I and II of NSCLC SUV parameter provides useful information regarding the prognosis and an important correlation exists between responses according to CT and FDG-PET. In stages III and IV SUV loses most of its prognostic significance.

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Comparison of the diagnostic value of F-18 FDG PET(-CT) and bone scintigraphy in lung cancer patients with bone metastases

G. Rendl¹, H. Stark¹, L. Rettenbacher¹, M. Studnicka², C. Pirich¹; ¹Department of Nuclear Medicine and Endocrinology, Paracelsus Private Medical University, Salzburg, AUSTRIA, ²Department of Pneumology, Paracelsus Private Medical University, Salzburg, AUSTRIA.

Aim: To compare the diagnostic value of F-18 fluoro-deoxyglucose (FDG) PET, FDG PET-CT and bone scintigraphy (BS) in the evaluation of bone metastases in patients with lung cancer and their possible impact on patient management. **Materials and methods:** 235 lung cancer patients (mean age 65 years, 169 male and 66 female patients) who underwent F-18 FDG PET (n=71) or PET-CT (n=164) and BS with Tc99m-hydroxy-methylene-diphosphonate (HDP) within 14 days were analyzed in this retrospective study. Bone metastases were confirmed by autopsy, histological verification or clinical follow up. Analysis of bone metastases was patient and lesion based. **Results:** Out of 235 patients, 175 (74.5 %) patients had no evidence of bone metastases while 59 patients (25.5 %) had. FDG PET showed a sensitivity, specificity and accuracy of 100 % for the identification of bone metastases. FDG PET-CT exhibited a specificity of 100 %, a sensitivity of 97.7 % and an accuracy of 99.4 %. Sensitivity, specificity and accuracy of BS were 88.3 %, 98.9 % and 96.2 %, respectively. FDG PET and PET-CT scans of 59 patients positive for bone metastases identified 523 lesions totally (FDG PET: 93 lesions in 17 pat., FDG PET-CT: 430 lesions in 42 pat.). Bone scintigraphy found a total of 364 bone metastases. Thus, FDG PET, FDG PET-CT and BS detected an average number of 5.1, 10.4 and 6.1 lesions per patient, respectively. Based on both scintigraphic modalities, disagreement concerning the stage of disease was found in 3 patients. **Conclusion:** This study demonstrates that FDG PET and integrated PET-CT perform at least equally to BS in the evaluation of bone metastases in lung cancer. FDG PET-CT can be recommended for the initial staging of patients with non-small cell lung cancer (NSCLC) without the use of bone scintigraphy for the detection of bone metastases.

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Catch of the Day: An incidental detection of lung cancer from Tc-99m MDP bone SPECT/CT imaging

S. Han, F. W. Poon, J. B. Neilly; Nuclear Medicine, Glasgow Royal Infirmary, Glasgow, UNITED KINGDOM.

Introduction: Hybrid SPECT/CT imaging can improve the diagnostic accuracy of nuclear medicine by better localisation, attenuation correction and characterisation of scintigraphic lesions. It can also occasionally detect significant unexpected findings from the accompanying CT component. **Aim:** This case report is to highlight the importance of thorough review of both scintigraphic and cross-sectional images in SPECT/CT bone scan. **Summary:** A 70 year old man with newly diagnosed prostate cancer attended our centre in October 2008 for staging bone scan. Whole body Tc-99m MDP scintigraphy showed focal increased tracer uptake in manubrio-sternal junction. SPECT/CT upper chest was proceeded to further characterise this focal lesion which showed periarthral sclerosis in manubrio-sternal junction consistent with degenerative changes. However, a 35mm spiculated lung mass was incidentally found in the posterior segment of right upper lobe in the low dose un-enhanced CT component of the SPECT/CT and reported as highly suspicious of a bronchial carcinoma. Subsequent diagnostic contrast enhanced CT chest confirmed this finding and provisionally staged as T2N0M0 (stage IB). F-18 FDG PET/CT revealed an intensely FDG avid mass (SUVmax 15.2) and intensely FDG avid right hilar node, right lower paratracheal node and left upper paratracheal node, and upstaged to T2N3M0 (stage IIIB). CT guided biopsy of the right lung mass finally confirmed adenocarcinoma (NSCLC). The patient was treated with high dose palliative radiotherapy to the lung cancer and was clinically stable at 14 months after the diagnosis of lung cancer. **Discussion:** Hybrid SPECT/CT imaging has been shown to improve reporters' confidence and diagnostic accuracy. Significant incidental findings have also been reported from myocardial perfusion SPECT/CT. We use Tc-99m MDP bone SPECT/CT mainly to localise the scintigraphic lesions and usually covers a limited region. In this case SPECT/CT was performed to characterise the focal manubrio-sternal uptake and by chance detected a suspicious lung cancer on CT component of SPECT/CT. This highlights the importance of thorough review of the CT component of hybrid images despite using low dose un-enhanced CT. This case also demonstrated the superiority of PET/CT over CT in nodal staging in NSCLC. **Conclusions:** Hybrid SPECT/CT imaging improves diagnostic accuracy as well as can reveal clinically significant incidental findings and requires careful evaluation of both scintigraphic and cross-sectional images.

P458**¹⁸F-FDG PET/CT evaluation of radiofrequency ablation of lung tumours.**

M. Coronado, S. Rodado, C. Escabias, A. C. Hernandez, M. D. Marin, D. Mendez, J. Coya, J. M. Oliver, L. M. Martin; Hospital La Paz, Madrid, SPAIN.

Aim: Radiofrequency ablation (RFA) is a novel imaging-guided percutaneous ablative procedure, used in patients with primary or metastatic lung tumours who are not suitable candidates for surgery. The aim of this study is to evaluate the utility of ¹⁸F-FDG PET/CT in assessing response of lung tumours to RFA. **Material and methods:** We prospectively evaluated nine patients (8 males, 1 female) who underwent RFA of lung tumours. All patients were selected by the hospital's joint thoracic tumour board, and were non-surgical candidates because of comorbidities (especially limited cardio-respiratory function). Mean age at treatment was 75 years old (66-88). One patient was treated twice. Five patients had primary lung tumours (3 squamous cell, 2 adenocarcinoma) two patients had metastatic lung tumours (from squamous cell carcinoma) and two patients had lung metastases of colorectal carcinoma and soft tissue sarcoma, respectively. ¹⁸F-FDG PET/CT scan was performed before and 2,9 months after RFA (1-12). Lesion's metabolic activity and size were recorded before and after treatment. Lesion response was considered based on the metabolic reduction relative to baseline, measured by visual analysis and SUV. Early and late complications as well as clinical evolution were also recorded. **Results:** A total of 8 patients and nine lesions were evaluated (one patient died as a late complication of RFA). Mean lesion size was 3.6 cm of maximum diameter (1.8-5.6). Lesion location was: LSD (1), LSI (3), LID (3), LII (2). Lesion size after RFA was slightly reduced in two lesions and increased in seven lesions. 5/9 lesions (56%) showed metabolic response. All these lesions had decreased metabolic uptake in the visual analysis; SUV value was stable in one lesion and decreased in four lesions in a variable range (3-88% from baseline). 4/9 lesions (44%) did not show metabolic response, all of them corresponding to primary lung tumours: two lesions corresponded to a patient who had incomplete ablation and was unsuccessfully re-treated; other to a large tumour that showed local progression after RFA; the last lesion remained unchanged after RFA. Clinical follow up from RFA was made for a medium of 5 months. All patients are alive: seven have stable lung disease and one shows local progression. Two patients presented pneumothorax after RFA, one of them required chest tube placement. **Conclusions:** ¹⁸F-FDG PET/CT accurately indicates treatment response of unresectable lung tumours treated with RFA. A larger group is needed to evaluate metabolic parameters to predict regrowth and grade of response.

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Oncology Clinical Science: Esophageal**P459****FDG PET/CT for esophageal cancer: Effect of pathological factors on its visibility and potential value of predicting indication for endoscopic submucosal dissection**

M. Nakajo¹, A. Tani¹, Y. Kajiyama¹, A. Ikenoue¹, S. Kanzaki¹, S. Tanaka², H. Shirahama³, M. Higashi⁴, M. Nakajo⁵; ¹Department of Radiology, Nanpoh Hospital, Kagoshima, JAPAN, ²Department of Pathology, Nanpoh Hospital, Kagoshima, JAPAN, ³Department of Pathology, Imakiire General Hospital, Kagoshima, JAPAN, ⁴Department of Human Pathology, Field of Oncology, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, JAPAN, ⁵Department of Radiology, Kagoshima University, Graduate School of Medical and Dental Sciences, Kagoshima, JAPAN.

Abstract Purpose: To clarify which pathological factors affect the FDG PET/CT visibility of both advanced and superficial (early-stage) esophageal cancers and to examine the value of the visibility for predicting indication for endoscopic submucosal dissection (ESD). **Materials and Methods:** We retrospectively examined the pathological factors affecting esophageal cancer visibility by PET in 37 lesions of 32 patients who underwent PET before surgery or ESD. The 37 lesions were also divided into the ESD indicated and unindicated groups according to the following pathological factors; depth of invasion, nodal status and vascular invasion. The criteria of indication for ESD consisted of the depth of invasion \leq sm1, negative nodal and negative vascular invasion. Cancers without the above criteria assumed not to be indicated for ESD. **Results:** Esophageal cancer visibility was significantly associated with tumor length, macroscopic type, depth of tumor invasion, lymph node status, vascular invasion ($P < 0.001$ each) and Glut-1 expression ($P = 0.005$). The cancer visibility was significantly higher in larger tumors, protrude type, the depth of invasion \leq sm2, positive nodal metastasis, positive vascular invasion and higher Glut-1 score. All 19 ESD indicated cancers were invisible and 17 of 18 ESD unindicated cancers were visible. The sensitivity, specificity, positive predictive value and negative predictive value and accuracy for predicting indication for ESD were 100% (19/19), 94% (17/18), 95% (19/20), 100% (17/17) and 97% (36/37), respectively. **CONCLUSIONS:** FDG PET visibility of esophageal cancer was significantly associated with pathological tumor length, macroscopic type, depth of tumor invasion, lymph node status, vascular invasion and Glut-1 expression. The cancer visibility on FDG PET may become one of the indicators to determine indication of ESD in esophageal cancer.

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Oncology Clinical Science: Esophageal**P460****Repeated radioembolisations in patients with advanced primary and secondary liver tumors and progressive disease after first SIRT: safety and effectiveness.**

A. Zarva, K. Mohnike, R. Rühl, R. Damm, G. Ulrich, M. Seidensticker, J. Ruf, M. Pech, J. Ricke, H. Amthauer; Otto-von-Guericke Universität Magdeburg, Klinik für Radiologie und Nuklearmedizin, Magdeburg, GERMANY.

Aim: Evaluation of the safety and effectiveness of repeated Y-90-selective internal radiotherapy (SIRT) with resin microspheres in patients with extensive primary and secondary liver tumors after failure of first SIRT. **Methodology:** Between 2007 and 2009, 11 patients (6 w, 5 m, mean age 61.1 years) with non-resectable advanced liver tumors (CRC n=4, breast cancer n=2, HCC n=4, CCC n=1) were repeatedly treated by SIRT. Extrahepatic metastases were found in 4/11 Pat. To preserve liver function, whole liver treatment was achieved with sequential radioembolisations (RE) by treating the left and right liver lobe selectively within 6 weeks in most of the cases. Toxicity was assessed by CTCAE 4.0 criteria due to laboratory parameters, MRI- and clinical examinations 3 days, 6 weeks and every 3 months after SIRT. Metric variables were evaluated employing Student's t-test. Progression free survival (PFS) and overall survival (OS) were determined by Kaplan-Meier-statistics. **Results:** Patients received 1.5-2.5 sequential interventions corresponding to 1.75 whole liver treatments on average. Mean total activity given was 2.35 ± 0.66 GBq. Mean follow up was 13.9 (6.0-25.1) months. Before the first treatment, the pulmonary shunt accounted for $5.5 \pm 1.9\%$, before the second treatment it increased to $8.8 \pm 4.3\%$ (in 6 patients were reevaluated). Median PFS after first RE was 3.2 (1.5-7) months. At the time of analysis, 8 patients had died. Median OS was 17.7 months after first RE and 8.0 months after the last RE. In one patient, a treatment related duodenal ulcer occurred. 2 patients showed reversible grade III to IV toxicities according to laboratory changes that returned to pretreatment levels after 6 weeks. No radiation induced liver disease was observed in any of the patients. **Conclusion:** In advanced liver tumors and a sequential approach, repeated whole liver treatments with Y90 microspheres can be performed with an acceptable toxicity profile.

P461**Efficacy of Y-90 microspheres in the treatment of unresectable hepatocellular carcinoma**

M. Ozhan¹, S. Nisli¹, L. Kabasakal¹, F. Gulsen², M. Cantasdemir², S. Pekmezci³, K. Saribeyoglu³, F. Numan², I. Uslu¹; ¹Department of Nuclear Medicine, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, TURKEY, ²Department of Radiology, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, TURKEY, ³Department of General Surgery, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, TURKEY.

Introduction: Over the past few years, selective internal radiation treatment (SIRT) has been used clinically for treatment of nonresectable hepatic metastases in the absence of extrahepatic metastases. The aim of the present study was to evaluate the first experience of this type of treatment carried out in our department. **Materials and methods:** From March 2009, patients with unresectable liver cancer either primary or secondary who had failed to respond to conventional treatment including chemotherapy, intraarterial chemoembolization or local ablative treatment were considered for SIRT with SIR-Spheres[®]. All patient had unresectable primary and metastatic liver disease with histologic confirmation of the primary cancer. Patients suitable for SIRT then underwent pre-treatment planning with a visceral angiography. At the completion of the angiography, the patients were injected with 5 mCi (0.18 GBq) of Tc-99m macroaggregated albumin (MAA) via the hepatic artery. 99m Tc-MAA scanning to assess extrahepatic shunting were performed in all patients. An extrahepatic shunt of less than 20% was considered suitable for SIR-Sphere injection. The activity to be administered for each patient was determined by the body surface area method. The administration of the 90Y microspheres is performed in an angiography suite. The patients were then taken to nuclear medicine department to have a whole body scan in order to map the distribution of injected SIR-Spheres. Following the therapeutic injection, the patients underwent a standard follow-up protocol in our unit. **Result:** A total of 17 patients underwent assessment for SIRT but 1 patient were rejected on account of excessive shunts. 16 patients (10 men, 6 women, ages between 51 and 76) received SIR-Spheres. Most patients had hepatocellular carcinoma (n=6); Other pathologies included the following: colorectal metastases (n=5); cholangiocarcinoma (n=2); metastatic tumours from neuroendocrine tumours (n=2); leiomyosarcoma (n=1) and carcinoma of unknown primary (n=1) The mean administered activity was 1.95 GBq (range 1.59 - 2.19 GBq). There was a significant improvement in PET activity measured with SUV before and 6 weeks after SIRT (n=9). There was metabolically complete/partial response in 9 patients and decrease in level of tumor markers in 3 patients. **Conclusion:** Selective internal radiation treatment is a promising new modality in the treatment of patients with unresectable liver cancer. Results suggest that there is significant mean reduction of hepatic metastatic tumor load (metabolism) and number of lesions. It has been shown to have good clinical outcome.

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Oncology Clinical Science: Urogenital**P462****Role of diuretic enhanced FDG-PET/CT in patient with renal cell carcinoma**

C. N. B. Harisankar, K. K. Kamaleshwaran, R. Kashyap, A. Bhattacharya, B. Singh, B. R. Mittal; PGIMER, Chandigarh, INDIA.

Introduction: FDG-PET is being increasingly tried in staging, restaging and surveillance of various cancers. Difficulty in interpretation of FDG-PET in urologic tumors is being overcome with diuretic administration. Inclusion of FDG-PET may aid patient management by avoiding futile surgeries, guiding appropriate biopsy site and identifying early metastases. **Aim:** To study the role of FDG-PET/CT in the evaluation of patients with pathologically diagnosed RCC. **Materials and methods:** Records of patients with renal cell carcinoma who were subjected to FDG-PET were retrospectively analyzed. All patients underwent whole body PET-contrast enhanced CT unless contra-indicated. 20 mg of furosemide was administered along with FDG injection. **Results:** 28 patients (21 males, 7 female) were eligible for the analysis. The indications for PET scan was as follows: Initial staging - 4 patients, Restaging - 9 patients, Surveillance - 6 patients, Characterization of an equivocal radiologic abnormality - 9 patients. All except the four patients

for initial staging had undergone nephrectomy. 3 patients had undergone chemotherapy, 2 had undergone immunotherapy. Radiotherapy for brain metastases was given for 1 patient. Four patients referred for initial staging had borderline renal function and were subjected to non-contrast CT and PET. Widespread metastatic involvement was noticed on PET. Surgery was deferred and the patients were subjected to chemotherapy. Five of the 9 patients having equivocal radiologic abnormality didn't reveal FDG uptake at the sites of radiologic abnormality indicating benign nature of the disease. In remaining 4 patients, PET confirmed metastatic involvement. PET (performed at a median time of 13 months post surgery) revealed metastatic involvement in all the 9 patients studied for restaging. Lung metastases was the most frequent (6/9 patients). Other sites of involvement were regional and mediastinal lymph nodes, pancreas, adrenal, brain, bone and liver. Six patients underwent surveillance PET scans at a median of 4 months after treatment. None of the patients had any abnormality on PET-CT and are on follow up. **Conclusion:** FDG-PET is a valuable modality in evaluation of patients with RCC. The yield is greatest in restaging of patients and in patients with equivocal radiological abnormalities thus avoiding additional invasive investigations. FDG-PET is an extremely good alternative for evaluation of patients with impaired renal function, who are suspected to have malignant renal mass. PET performed for disease surveillance had very low yield and hence further studies are required to study its cost-effectiveness for this purpose. Diuretic intervention helped in better evaluation of pelvic area.

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The value of 18F-FDG-PET/CT in restaging patients with Testicular carcinoma compared to other imaging techniques.

L. Gogou¹, D. Kechagias¹, F. Vlachou¹, R. Efthimiadou¹, K. Dalianis¹, N. Eftychiou², A. Nikaki², A. Tsaroucha¹, J. Andreou¹, V. Prassopoulos¹; ¹D.T.C.A. Hygeia Department of PET/CT, Athens, GREECE, ²Saint Savvas Cancer Hospital Nuclear Medicine Department, Athens, GREECE.

Aim: The incidence of Testicular cancer has increased over the last decades. 18F FDG-PET/CT might be useful to overcome the diagnostic problems in restaging testicular carcinoma. This study was designed to determine the value of 18F FDG-PET/CT compared to MRI and CT, in the evaluation of recurrence disease and post-chemotherapy residual mass in testicular carcinoma. **Materials and methods:** We examined 54 patients who underwent 56 18F-FDG-PET/CT scans. All patients with testicular carcinoma and after first line therapy underwent PET/CT for restaging. 52 of the patients were subjected to 53 CT scans (GROUP A) and 10 patients to 10 MRI (GROUP B) for disease evaluation just before the PET/CT scan. In 34 out of 56 patients tumor markers (αFP, β-HCG) were estimated. Results: 16/56 had positive PET/CT scan, 42/53 positive CT and 6/10 positive MRI. GROUP A: 28/53 (52.8%) had match findings in PET/CT and CT scans (18 cases with negative results and 10 with positive). In 19/53 (35.8%) cases with positive CT, PET/CT was negative with findings concerning lymphadenopathy and lung nodules (16 patients) and 3/19 other masses or lesions. In 2/53 (3.7%) cases we had mismatch findings. In first case PET/CT revealed no hypermetabolic activity in large lymph nodes but both PET/CT and CT were positive in lung nodules and in second case PET/CT revealed hypermetabolic activity in prostate (metastasis) while CT scan revealed only lymph node enlargement. In 4/53 (7.7%) cases CT was negative but PET/CT positive with findings concerning bone lesions and lymph node invasion. GROUP B: In 6/10 (60%) cases we observed match findings between PET and MRI examination (3 cases with negative results and 3 positive). In 3/10 (30%) cases where MRI was positive PET/CT was negative with MRI findings concerning lymph node enlargement. In 1/10 (10%) case MRI was negative and PET/CT positive with findings concerning hypermetabolic activity in lymph nodes. In 34 patients tumor markers were estimated. 7/34 patients had elevated blood levels and 27/34 had normal values. In 3/7 (43%) with high values of tumor markers had positive PET/CT while MRI and CT was negative. In 5/27 (18.5%) had normal levels had positive PET/CT while 15/27 (56%) had positive MRI and CT. **Conclusion:** 18F-FDG-PET/CT is a sensitive and reliable modality in detecting residual disease in patients with testicular carcinoma. Particular in patients with elevated tumor markers PET/CT is a more accurate technique than conventional imaging.

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Feasibility of FDG-PET/CT to Detect and Characterize Solid Malignant Renal Masses- A Preliminary Study

Z. Nakhoda, B. Saboury, A. Alavi, D. A. Torigian; University of Pennsylvania Medical Center, Philadelphia, PA, UNITED STATES.

Purpose: To evaluate the feasibility of FDG-PET/CT for detection of solid malignant renal masses, and to assess for metabolic differences between renal masses based on histopathology. **Methods:** Twenty solid malignant renal masses in 14 subjects who underwent FDG-PET/CT and prior CT or MR imaging were evaluated in this study. Qualitative analysis of the sensitivity of FDG-PET/CT for visual detection of renal masses was initially performed in blinded fashion. Subsequently, SUV measurements of renal masses were obtained and correlated with a) primary or metastatic site of origin, and b) histology of primary renal malignancy. Results: Of 20 solid malignant renal masses, 13 were RCC, 3 were due to lymphoma, and 4 were metastatic to the kidney. Eighteen of 20 (90%) malignant renal masses were visually detectable by FDG-PET/CT (size range 1.2-8.1cm, volume 16.9cc; IQR 26.5cc, 10 of 20 exophytic in location). SUV maximum and mean for RCC were 4.7 (IQR 5.1) and 2.8 (IQR 1.8), respectively. SUV maximum and mean for lymphomatous renal tumors were 7.7 (IQR 5.9) and 4.1 (IQR 3.0), respectively. SUV maximum and mean for metastatic renal tumors were 21.6 (IQR 10.5) and 12.4 (IQR 7.6), respectively. Among RCC, SUV maximum and mean for papillary subtype was 3.7 and 2.9, respectively; SUV maximum and mean for conventional subtype was 5.8 and 2.4, respectively; SUV maximum and mean for clear cell subtype was 4.9 and 2.8, respectively. **Conclusion:** Despite the renal excretion of FDG, FDG-PET/CT had a sensitivity of 90 % for the detection of malignant renal lesions. FDG-PET/CT demonstrated some differences in metabolic activity based on renal tumor histopathology, although no significant differences were observed between RCC subtypes.

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The role of FDG PET/CT in preoperative staging of bladder cancer

A. Aliyev¹, S. Yilmaz¹, M. Ozhan¹, M. Halac¹, B. Kanmaz¹, K. Sonmezoglu¹, C. Demirdag², C. Obek², I. Uslu¹; ¹Department of Nuclear Medicine,

Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, TURKEY, ²Department of Urology, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, TURKEY.

Aim: The standard treatment of non-metastatic bladder cancer is surgical removal of the entire organ by radical cystectomy. However, these patients may already have tumour spread to the locoregional lymph nodes (N) or occult distant metastases (M) at the time of initial diagnosis. Depending on the stage of the bladder tumour, this occurs in about 25% of cases for tumours invading the muscular layer only and in about 50% for tumours extending into the perivesical tissue. CT and MRI encounter difficulties because tumour involvement is not necessarily reflected by changes in the shape or texture of an affected lymph node. PET with F-18 FDG has been considered of limited value for detection of bladder cancer because of the urinary excretion of the tracer. The purpose of this study was to evaluate the use of F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) in this indication. **Methods:** Whole body FDG PET-CT were performed in ten patients with non-metastatic invasive bladder cancer for preoperative N-M staging. Patients underwent PET/CT from head to the upper thighs 60 min after the intravenous injection of F-18 FDG. Additional pelvic images were acquired 1 h after the first scan. PET-CT findings were confirmed by cystoscopy or biopsy. **Results and Conclusion:** PET-CT was able to detect bladder lesions in 12 of 15 patients. PET/CT revealed FDG-positive lymph nodes in three patients. One of these patients, PET/CT detected false positive (SUVmax=6.9) pelvic lymph nodes. In the other two patients PET/CT detected true positive lymph nodes (SUVmax=11.7) in the iliac and paraaortic regions. There was false negative millimetric lymph nodes in one patient. An unexpected bone metastasis was found in two patients and an unexpected lung metastasis was found in another patient. In conclusion, FDG PET/CT has a limited value for staging in bladder cancer especially for preoperative nodal staging. However in detecting unexpected distant metastases, the PET-CT is the mainstay technique.

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Oncology Clinical Science: Prostate

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Comparison between the physiological distribution of ¹⁸F-FMCH and ¹⁸F-FECH

A. Filice, M. Asti, M. Roncali, A. Fraternali, M. Casali, M. Di Paolo, C. Guidotti, A. Versari, D. Salvo; Nuclear Medicine-Santa Maria Nuova Hospital, Reggio Emilia, ITALY.

Objectives: it is known that prostate cancers show low glucose avidity and that ¹⁸F-FDG PET/CT is generally not suitable for assessing prostate cancer recurrences. Moreover, urinary activity is also an important limitation in ¹⁸F-FDG PET/CT scans. Conversely, ¹⁸F-labelled choline derivatives show a potential value in the imaging of prostate cancer since this kind of tumors exhibit increased choline metabolism. The aim of this study was to compare 2-[¹⁸F]-Fluoroethylcholine (¹⁸F-FECH) and [¹⁸F]-Fluoromethylcholine (¹⁸F-FMCH) uptake in some PET/CT negative scans in order to evaluate the physiological distribution of the two tracers. **Materials and methods:** PET/CT images of fifty patients suspected for prostate cancer recurrence were acquired with an ¹⁸F-labelled choline analogue. For ten of these patients the result of the examination was negative and after three months, they were further acquired with the other ¹⁸F-labelled analogue. On a blind basis, the images obtained were independently compared by five physicians with a high expertise in PET/CT interpretation using choline analogues. The physicians were asked to critically evaluate the examinations and express a preference between the two acquisitions of the same patient. **Results:** All the physicians did not find relevant differences in the physiological distribution of the two analogues. ¹⁸F-FECH and ¹⁸F-FMCH images were preferred in the 53 % and 47 % of the cases, respectively. Radiopharmaceutical uptake in the bowel was slightly more diffused for ¹⁸F-FMCH with respect to ¹⁸F-FECH analogue but, generally, the observers were not able to discriminate between the images obtained by using one analogue with respect to the other. **Conclusions:** In our experience, both the ¹⁸F-labelled choline derivatives can be successfully used for detecting prostate cancer recurrence. The two tracers showed comparable physiological distribution and uptake.

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Usefulness of 11C-Choline PET/CT in detection of prostate cancer recurrence. Relationship with serum PSA-level

C. Trampal¹, P. Plaza², R. Herance³, M. Simo⁴, J. Gispert³; ¹Instituto de Alta Tecnología-CRC MAR, Barcelona, SPAIN, ²Nuclear Medicine CRC Quirón, Barcelona, SPAIN, ³Instituto de Alta Tecnología-CRC Corporació, Barcelona, SPAIN, ⁴Nuclear Medicine CRC Quirón, Barcelona, SPAIN.

Aim To assess the usefulness of 11C-Choline PET/CT for detection of recurrent prostate cancer in patients with increased serum PSA-level and to assess a relationship between 11C-Choline detection rate and serum PSA-level. **Material and Methods** 31 patients (mean age 69 years; range 50-82) with suspicion of recurrent prostate cancer based on clinical elevated PSA-level were studied. Mean PSA-levels were 13,19 ng/ml (range 0.10-66 ng/ml). Whole body PET/CT examination was performed five minutes after intravenous injection of a mean of 740 MBq 11C-Choline, using a ST Discovery PET/CT scanner. PET findings were classified as positive or negative based on pathologic tracer uptake by visual and semiquantitative analysis using SUV (standardized uptake value). PET results were validated with histology or clinical/radiological follow-up. A relationship between 11C-Choline detection rate and serum PSA-level was calculated. **Results** 11C-Choline PET/CT showed pathological uptake consistent with recurrence in 19/31 patients: nine of them had local recurrence, seven patients distant disease (bone metastasis in four, nodal metastases in one, bone plus nodal metastases in one, lung metastases in one) and three patients showed local recurrence plus distant metastasis. Visual analysis of PET images was sufficient for diagnosis of disease. Mean SUV was 2.95 (range 1.75-8.50). Based on PET findings, local radiation was performed in the group with local recurrence (n=9) and systemic therapy (hormonal or chemotherapy) in the others (n=10) except radical radiation in one patient with nodal involvement. All patients showed decrease in PSA-levels after treatment. 11C-Choline was negative in 12/31 patients: eight were not treated and in four local radiation was performed

assuming microscopic local disease. No evidence of recurrence was detected by clinical or radiological follow-up in 10 patients (mean follow-up six months) but further increase in PSA-level was diagnosed in two at follow-up, including one treated with local radiation. Regarding relationship between detection rate of 11C-Choline and serum PSA-level, 11C-Choline detected disease in 3/10 patients (30%) with PSA-level ≤ 3 ng/ml and in 16/21 patients (76.19%) with PSA-level > 3 ng/ml. **Conclusion** 11C-Choline PET/CT is an useful procedure in patients with biochemical suspicion of prostate cancer recurrence with implications on therapeutic management, detecting the site of recurrent disease and providing substantial influence in the treatment strategy. The detection rate of 11C-Choline is depending on PSA, showing positive relationship with serum PSA-level, finding most of positive examinations in patients with PSA-level > 3 ng/ml.

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Investigation on serum Neuron-Specific Enolase in prostate cancer patients during endocrine therapy

M. T. Siabanopoulou¹, T. Vasilidi², M. Dikeakou², P. Mitsakis², N. Salem², A. Gotzamani-Psarrakou¹, S. El-Mantani Ordoilidis³, ¹2nd Nuclear Medicine Dept. of the Aristotle University, Thessaloniki, GREECE, ²Theagenio Cancer Institute, Thessaloniki, GREECE, ³Nuclear Medicine Dept., Biomed Diagnostics, Thessaloniki, GREECE.

Introduction: Prostate cancer (PCa) is the most common cancer in men. Initially most tumors present as androgen -sensitive adenocarcinomas but the histology becomes more undifferentiated along with clinical progression and hormone resistance. Neuroendocrine cells (NE) is a part of such dedifferentiation and serum levels of NE proteins such as neuron-specific enolase (NSE) may supply prognostic information. **Aim:** The aim of this study was to evaluate the expression of serum NSE levels in patients with primary or metastatic PCa and assess the prevalence of this marker in monitoring PCa patients under endocrine therapy and to evaluate, if any, its prognostic significance. **Methods:** Serum samples from 59 patients (median age 72 yrs, range 46-88 years) with clinically and histologically documented PCa were analyzed for PSA and NSE. All tumors were graded by Gleason score. All patients had undergone medical or surgical castration at the time of serum sampling. Bone scanning revealed the presence of metastatic lesions in 21 patients. 30 healthy blood donors serving as control group were enrolled in the study. NSE was measured using an immunoradiometric analysis (IRMA) and a cut-off value of 10ng/ml separated normal from elevated values. **Results:** 37, 3 % of the patients in our study had elevated PSA levels. 4 (18,8%) of the 22 patients with PSA >10 ng/ml had elevated levels of NSE. There was no evidence of correlation between PSA and NSE. NSE values were higher in PCa patients with bone metastases and did not differ significantly among the patients with organ confined or locally advanced disease. A reduced performance status, multiple bone metastases and elevated NSE levels indicated poor prognosis. **Conclusions:** Our results support the concept that in combination with known clinical parameters, serum NSE determination could be a potential prognostic factor for monitoring prostate cancer.

P42 — Monday, October 11, 2010, 16:00 — 16:30, Hall Z

Oncology Clinical Science: Gynecological

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Staging of Cervical Cancer Patients with FDG-PET

O. Mukhortova¹, I. Aslanidis¹, I. Shurupova¹, I. Ekaeva¹, L. Ashrafjan², D. Alimardonov², Z. Shavladze³, A. Konov³, ¹Bakoulev Scientific Center for Cardiovascular Surgery, Moscow, RUSSIAN FEDERATION, ²Russian Scientific Center of Roentgenradiology Rosmedtechnology, Moscow, RUSSIAN FEDERATION, ³Research Center of Medical Radiology, Obninsk, RUSSIAN FEDERATION.

Purpose: to evaluate the potential value of FDG-PET in the different groups of cervical carcinoma patients. **Methods:** PET results of 66 patients were analyzed retrospectively with different purposes: in 27 patients with locally advanced cervical carcinoma PET was done for primary staging (I group), in 18 patients with no evidence of disease recurrence PET was performed in follow up period (6-18 months after the end of treatment) (II group), in III group there were 14 patients with verified relapses and 7 patients with suspicion of relapses. Whole-body PET images were obtained in 60-90 minutes after administration of 350-420 MBq FDG and assessed visually or with SUV calculation. PET results were compared with results of conventional diagnostic methods, clinical follow-up in all patients, with postsurgical histopathological data in 19 patients and with biopsy results in 6 patients. **Results:** In group I previously unknown metastases were detected by PET in 7 patients: regional lymph nodes metastases were revealed in 4 patients, supraclavicular lymph nodes metastases - in 2 patients and in 1 patient were identified multifocal bone lesions. All lymph nodes metastases were confirmed by postsurgical histopathological data. In 2 patients PET results didn't confirmed solitary bone metastases and suspected IV stage of disease was excluded. According to PET results treatment plan was changed in 7 (26%) patients. In group II PET identified lymph nodes metastases in 3 patients who had negative CT and ultrasound findings. PET results were confirmed by following MRI and postsurgical histopathological data in 1 patient. Treatment was started in all 3 (17%) patients. In group III PET results confirmed recurrence of disease in 12 from 14 patients with verified relapses. In 2 (10%) patients pelvic lymph nodes metastases were missed by PET. In 7 patients with suspicion of relapses PET results correctly identified 5 patients with disease progression and 2 patients with no signs of disease. **Conclusion:** FDG-PET is very useful in cervical carcinoma patients. PET results provide important information for accurate pre-treatment staging, for confirmation of suspected disease progression and for early detection of recurrence in patients with no evidence of disease.

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Detection rate of FDG-PET/CT in patients with treated ovarian cancer in relation to cancer antigen (CA) 125 levels

A. Palomar¹, C. Nanni², P. Castellucci², G. Montini², V. Allegri², V. Ambrosini², A. Soriano¹, S. Fanti², ¹Hospital General Ciudad Real, Ciudad real, SPAIN, ²Ospedale S.Orsola Malpighi, Bologna, ITALY.

INTRODUCTION: Patients treated for ovarian cancer are usually referred for a FDG-PET/CT in case of increased CA125 and negative conventional imaging tests. However, there is no literature regarding the detection rate of FDG-PET/CT in relation to the level of CA125 at the moment of the scan. **AIM:** To assess the detection-rate of 18-FDG-PET-CT in relation to the levels of CA125 in patients with treated ovarian cancer. **MATERIAL AND METHODS:** We studied retrospectively 175 patients, mean age of 65.2 y (range 24-88 y) treated for ovarian cancer (chemotherapy, surgery or combination), subject to a standard FDG-PET/CT and with a measure serum level of CA125 one month around the scan. PET/CT was considered positive if demonstrated areas of abnormally increased metabolic activity on the basis of a visual analysis without relation to physiological uptake were detected. The diagnostic accuracy results of PET/CT imaging were compared to the level of CA125, and receiver operating characteristic (ROC) curves were plotted and area-under-the curve (AUC) statistics were computed. Furthermore patients were divided into 5 groups depending on CA125 value and PET detection rate was calculated. **RESULTS:** The average level of CA125 107.7 (range 3-867, SD 166.1). PET/CT was positive in 125/175 cases (71.4%), mean value of CA125 132.2 (SD 182.9) and negative in 50/175 (28.6%) mean value of CA125 46.4 (SD 89.3). In descriptive ROC analyses, the discriminatory power of this marker was relatively high (AUC statistics 0.77, range = 0.703-0.8). The optimal cutoff point of CA125 after the treatment to value active disease in the PET/CT scan was 18 U/ml corresponding to a detection rate of 85.6%. The group by group results are reported in the following table:

CA125	NR	PTS	PET+	DETECTION RATE %
<30	78		41	53
31-75	37		30	81
76-150	26		25	96
151-285	16		13	81
>285	18		16	89
TOT	175		125	71

We found no relation between PET/CT negativity and the histological type of the tumour. **CONCLUSION:** PET/CT was able to detect active disease at relatively low titers of CA125, thereby facilitating the early diagnosis of recurrence or residual disease. Also in patients with low CA125 levels (<30) PET/CT had a relatively high detection rate (53%). According to our preliminary results, the use of FDG PET/CT in patients treated for ovarian cancer is justified also in case of low serum marker levels.

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Kinetic Modeling with ¹⁸F-FDG PET in Advanced Ovarian Cancer: Evaluation of Heterogeneity in Metabolism and Early Treatment Response.

M. Narayanan¹, A. T. Shields², H. K. Tamimi³, B. A. Goff³, S. E. Hawes⁴, A. E. Wilson⁴, J. G. Rajendran², ¹Philips Research North America, Briarcliff Manor, NY, UNITED STATES, ²University of Washington, Department of Radiology, Seattle, WA, UNITED STATES, ³University of Washington, Division of Gynecologic Oncology, Seattle, WA, UNITED STATES, ⁴University of Washington, Department of Epidemiology, Seattle, WA, UNITED STATES.

Objectives: In spite of aggressive treatment regimes, advanced ovarian cancer (AOC), recurs in a large majority of patients. Most women with AOC are likely to die with chemotherapy-resistant disease. Therefore, more-sensitive methods are needed to predict and evaluate treatment response during and after therapy. Quantification of change in tumor ¹⁸F-FDG kinetics may provide an early indication of treatment response. In this study, we evaluated two parameters--pre-treatment tumor heterogeneity and change in metabolism on sequential ¹⁸F-FDG PET scans after the first cycle of neoadjuvant chemotherapy in patients with AOC. **Methods:** Two patients with cytology-proven AOC underwent sequential dynamic FDG scans (0-45 min) before ("pre") and 17-19 days after ("mid") the first cycle of chemotherapy. A total of 4 peritoneal deposits were evaluated both for heterogeneity of tumor metabolism and for early treatment response. Using a 2-tissue compartmental model, kinetic analysis was performed and parametric images of FDG rate constants (k_1 , k_2 , k_3) and FDG influx (K_1) were generated. Metabolic response was evaluated using relative changes in the kinetic parameters as well as the standardized uptake value (SUV). Pre-treatment tumor heterogeneity was evaluated for each lesion using Shannon's entropy for all FDG uptake measures where a value of zero indicates homogeneity and larger values denote increased heterogeneity. **Results:** Evaluation of early metabolism changes (Table 1) indicates that both K_1^{\max} and k_3^{\max} show a greater percentage decrease than do SUV^{max} values after the 1st cycle of chemotherapy. Visual evaluation of the parametric (K_1 and k_3) and SUV images indicates the presence of intratumoral heterogeneity in most of the evaluated lesions. Average tumor heterogeneity for pre-treatment SUV, K_1 and k_3 images were 2.86, 2.69, and 2.31, respectively. Pre-treatment tumor heterogeneity estimates were also strongly correlated with pre-therapy SUV^{max} ($r=-0.952$), K_1^{\max} ($r=-0.971$) and k_3^{\max} ($r=-0.989$) values. **Conclusions:** After the first cycle of chemotherapy, both K_1 and k_3 show larger percentage decreases than SUV measures indicating a role for kinetic analysis in evaluating early treatment response. Pre-therapy tumor heterogeneity estimates show a strong negative correlation with all pre-treatment FDG uptake measures. Additional patient studies and longer follow-up will be needed to establish the ability of these measures to predict treatment response.

Table 1: Average pre, mid and percentage changes values for all FDG parameters

	SUV ^{max}	K_1^{\max} (1/min)	k_3^{\max} (1/min)
pre	9.91	0.041	0.227
mid	8.29	0.019	0.152
percentage change	+17.28	+45.31	+39.42

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P472**F-18 FDG PET/CT findings of endometrial cancer**

W. Choi¹, S. Kim¹, J. O¹, I. Yoo¹, Y. Chung², S. Chung¹; ¹Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, KOREA, REPUBLIC OF, ²Incheon St. Mary's Hospital, The Catholic University of Korea, Incheon, KOREA, REPUBLIC OF.

Objective: To analyze F-18 FDG PET/CT findings of endometrial cancer. **Materials and Methods:** Endometrial cancer patients with pre-operative PET/CT from June 2005 to October 2009, as well as pre-operative enhanced CT or MRI, and subsequent surgery were included (n=33, post-menopause 25, pre-menopause 8). Visual analysis was used to divide the FDG uptake pattern of the primary endometrial tumor as focal or diffuse. Semiquantitative analysis was made by measuring the tumor SUVmax. In addition, accuracy of PET/CT for detecting lymph node (LN) metastasis was compared to that of CT or MRI. **Result:** Of the 33 cases, 2 cases showed no perceptible FDG uptake and these tumors measured 0.3 cm and 0.4 cm each in post-operative histology. The SUVmax of primary tumor in the remaining 31 cases ranged from 2.0 to 29.3. Mean SUVmax was 6.7±3.3 for lesions with focal uptake pattern (n=22), and 12.0±7.5 for lesions with diffuse uptake (n=9). The SUVmax was significantly higher in primary tumors with diffuse FDG uptake pattern (p=0.009). No significant difference was noted in the SUVmax according to menopause state, depth of myometrium involvement (less than half vs. over half), or LN metastasis. LN metastasis was present in 5 out of 33 cases. Only PET/CT detected LN metastasis in 1 case. On lesion basis, out of total 13 metastatic LNs, PET/CT detected 10 LNs, while CT or MRI detected 7 LNs. In particular, retroperitoneal LN metastasis was present in 3 cases, and only PET/CT detected the metastatic LNs, while CT or MRI missed the LNs. **Conclusions:** Endometrial cancer appeared on PET/CT more often with focal FDG uptake pattern, but the SUVmax was higher when the primary tumor had diffuse uptake pattern. FDG PET/CT may be very useful for detecting LN metastasis, especially for LNs in retroperitoneum.

P473**Diagnostic value of 18F-FDG PET/CT in the suspicion of ovarian carcinoma recurrence**

J. Jiménez-Bonilla, R. Quirce, I. Martínez-Rodríguez, I. Banzo, M. De Arcocha, H. Portilla-Quattrociocchi, P. Medina-Quiroz, A. Rubio-Vassallo, R. Castillo-Matos, J. M. Carril; HU Marqués de Valdecilla. Universidad de Cantabria, Santander, SPAIN.

Aim: To evaluate the diagnostic yield of ¹⁸F-FDG-PET/CT scan in the suspicion of ovarian carcinoma recurrence (SOCR). **Materials and methods:** Twenty one patients with 23 episodes of SOCR were evaluated by 24 ¹⁸F-FDG-PET/CT scan. ¹⁸F-FDG-PET/CT scan was acquired 90 minutes after the intravenous injection of 370-555 MBq of ¹⁸F-FDG. SOCR was based on either an increased of serum concentration tumour markers or in radiological abnormalities. In 16 episodes of SOCR tumour markers were increased (CA 125 in all of them and CA 15.3 in five). In the other 7 episodes of SOCR with suspicious CT, tumour markers levels were within normal ranges. Final diagnosis was established by histology in 7 cases and by clinical follow up in 16. **Results:** In our study there were 18 ovarian cancer recurrence. ¹⁸F-FDG-PET/CT identified 17/18 recurrences and was equivocal in one. In a patient with an infectious concomitant process, an evolutive ¹⁸F-FDG-PET/CT allowed us to determine the extension of the recurrence. In all 16 episodes with increased tumour markers levels recurrence was confirmed. ¹⁸F-FDG-PET/CT allowed the diagnosis in 15/16 but was equivocal in one. In these patients CT was negative in 6 episodes, and equivocal or suggestive in 9. In 1 episode CT was not performed. In the seven episodes within normal ranges of tumour markers, recurrence was excluded in 5. ¹⁸F-FDG-PET/CT examination was negative in 4 and false positive in 1 due to mediastinal nodal anthracosis. In all of them CT examinations was suggestive of recurrent disease. **Conclusion:** ¹⁸F-FDG-PET/CT showed in our study a sensibility of 94%, an specificity of 80% and a diagnostic accuracy of 91%. ¹⁸F-FDG-PET/CT was positive in a wide range of pathological tumour markers values and also in the normal range. ¹⁸F-FDG-PET/CT is an useful technique to diagnose ovarian cancer recurrence specially when biochemical suspicions and radiological findings are in disagreement.

P474**A Preliminary Study of a Novel Image Analysis Methodology for Quantification of Cervical Cancer on FDG-PET/CT**

N. Foroughi¹, B. Saboury¹, S. Alapati¹, F. Hofheinz², T. Tomson¹, L. Lin¹, G. Bodapati¹, T. Werner¹, A. Alavi¹, D. A. Torigian¹; ¹University of Pennsylvania Medical Center, Philadelphia, PA, UNITED STATES, ²ABX, Radeberg, GERMANY.

Objectives: To assess novel image analysis software to delineate and quantify metabolically active volumes (MAV), partial volume corrected (PVC) mean SUV, and metabolic volumetric products (MVP) of primary cervical cancer on FDG-PET/CT. **Methods:** 8 patients with cervical adenocarcinoma with pretreatment pelvic MRI and FDG-PET/CT were retrospectively identified. Primary tumor volumes were measured manually on T2-weighted MRI. Tumor volumes and uncorrected/corrected mean SUVs and MVPs (where MVP=MAVxSUV) were quantified from PET by two readers using the ROVER software package (ABX GmbH, Germany). Comparisons between PET and MRI measures and between repeated PET measures were performed using Bland-Altman analysis. **Results:** Mean tumor volumes measured from PET and MRI were 57.5±31.15cc and 74.6±33.45cc, respectively, with mean difference (95% limits of agreement (LOA)) of 17.2cc (-39.9-74.2cc). Mean differences and 95%LOA of repeated PET measures of tumor MAV, uncorrected and corrected mean SUV, and uncorrected and corrected mean MVP were 2.6cc (-6.3-11.5cc), 0.2 (-3.1-3.4), 1.7 (-6.8-10.2), 22.5cc (-239.5-284.5cc), 83.6cc (-300.8-468.1cc), respectively. The effect of PVC upon mean SUV was an average increase of 39.9%. **Conclusion:** It is feasible to quantify MAV and uncorrected/corrected mean SUV and MVP of primary cervical cancer on FDG-PET/CT using novel image analysis software. PET measures of MAV tended to overestimate MRI based tumor volumes. PET measures of MAV and uncorrected mean SUV are somewhat reproducible, whereas measures of corrected mean SUV and uncorrected/corrected MVP are less reproducible. PVC has a significant effect upon mean SUV quantification.

P475**Concordance between PET/CT results and serum tumor markers in restaging ovarian cancer patients**

F. Vlachou¹, V. Filippi¹, L. Gogou¹, D. Savidou¹, A. Nikaki², N. Eftychiou², K. Dalianis¹, K. Gogos¹, J. Andreou¹, V. Prassopoulos¹; ¹D.T.C.A. Hygeia Department of PET/CT, Athens, GREECE, ²Saint Savvas Cancer Hospital Nuclear Medicine Department, Athens, GREECE.

AIM: Ovarian cancer accounts for 4% of all cancer diagnosis and 5% of all cancer death. The tumor's poor prognosis is known. This study was scheduled to estimate the concordance of PET/CT with serum tumor markers (STM) in patients suffering from ovarian cancer, to compare it with the according correlation of CT and serum tumor markers. **MATERIAL- METHOD:** The files of 34 patients with ovarian cancer, with known STM who underwent PET/CT examinations, were retrospectively examined. All patients had previously received the appropriate therapy (surgery, chemotherapy, radiotherapy) and were referred for PET/CT examination either because their tumor markers were elevated, or during follow up. PET/CT findings were correlated with STM (CA 125 at 32 cases, a-fetoprotein at 1 case and testosterone/ progesterone at 1) and were compared to CT findings. **RESULTS:** Elevated STM values varied between 30- 2000 with mean STM value 127±/65. PET/CT was positive at 20 cases where STM were elevated and at 6 cases where STM were of normal values. PET/CT was negative at 1 case where serum a-fetoprotein was elevated and at 7 cases where STM were of normal values. Our results in detail are shown on the table. PET + refers to PET revealing active disease, PET - to negative PET. CT + and CT - evidence or absence of disease on CT, eq (equivocal) when CT didn't come to conclusion.

	PET +/CT +	PET +/CT -	PET +/CT eq	PET -/CT +	PET -/CT -
STM elevated	9	9	2	0	1
STM normal values	2	2	2	2	5

Of note, PET/CT did not reveal any hypermetabolic lesions at 2 cases that CT was positive: one of them concerned small pulmonary nodules, while the second one concerned a mass at the area of spleen shown at CT after splenectomy and chemotherapy and was falsely mistaken for tumor implantation, as it actually was fibrinoid tissue. In 5 cases where both PET and CT were positive, PET revealed more extended tumor burden, which involved mainly peritoneal dissemination and lymph node invasion. **CONCLUSIONS:** Although our results are referral biased, and mean STM are highly elevated, concordance between PET/CT findings and STM is better than CT findings and STM. PET/CT is a useful imaging modality for patients suffering from ovarian cancer, necessary when STM are elevated or conventional imaging is equivocal. PET/CT can be positive even if STM are of normal values.

P476**The role of FDG PET/CT in the nodal staging of patients with locally advanced cervical cancer: a histology-controlled pilot study**

I. Apostolova, S. Marnitz-Schulze, C. Köhler, W. Brenner; Charité-Universitätsmedizin Berlin, Berlin, GERMANY.

Aim: Pelvic lymph node involvement in cervical cancer patients changes the therapeutic strategy from surgery to primary chemoradiation, while paraaortic lymph node involvement suggests extended field radiation. Given the limited accuracy of MRI and CT in lymph node staging, the role of PET/CT still remains controversial because sensitivities ranging from 10 to 72% for pelvic lymph nodes and from 58 to 100% for paraaortic involvement have been reported for FDG PET/CT in patients with different tumor stages. The aim of the present study was to evaluate the role of FDG PET/CT in a selected cohort of patients with locally advanced disease in whom the prevalence of nodal involvement is >30%. **Material and Methods:** Ten patients with locally advanced cervical cancer (FIGO IIB-IVA), which obtained FDG PET/CT, were analyzed retrospectively. Eight patients were referred for primary staging, 2 patients with a suspicion of tumor relapse. Six patients underwent laparoscopic lymphadenectomy with lymph node sampling from all lymph nodes from the pelvic and paraaortic regions. In two patients histology was obtained by CT guided biopsy of paraaortic hypermetabolic lymph nodes, the pelvic involvement was assessed by follow up. The results of histology were correlated with PET/CT findings. Lymph node involvement in PET/CT was assessed with regard to the positive nodal stations: right and left pelvic region and paraaortic region. A region was considered positive showing one or more FDG-positive lymph nodes. **Results:** Thirteen lymph node stations were found positive by FDG-PET, which were confirmed as true positive by the gold standard. Fourteen nodal groups were found true negative. In one patient PET/CT was false negative for both the pelvic and paraaortic nodal status. In one patient false positive findings were found for the inguinal lymph node group. There were no false positive pelvic or paraaortic findings. For nodal staging of patients with locally advanced cervix carcinoma PET/CT showed an overall sensitivity, specificity, PPV and NPV of 81%, 100%, 100% and 82%, respectively. Sensitivity for the pelvic region was 80%, and for the paraaortic region 83%. In one patient supraclavicular lymph node involvement, and distant metastases in another 2 patients were found true positive. On a patient basis sensitivity of PET/CT for nodal staging was 87% with an overall accuracy of 90%. **Conclusion:** FDG-PET/CT showed a high accuracy in lymph node staging of patients with locally advanced cervical cancer, and seems to be a promising method for non-invasive therapy stratification.

P477**Findings Of 18F-FDG PET/CT In Patients With Suspected Ovarian Cancer Recurrence**

I. Sahiner, O. Oz, N. Ilgin Karabacak, T. Atasever, M. Unlu; Gazi University School of Medicine, Ankara, TURKEY.

Ovarian cancer is the most lethal type of malignancy among gynecological cancers. Most patients are diagnosed in an advanced stage, therefore prognosis is usually poor. Many patients experience recurrence in the follow up period. PET imaging using 18F-FDG appears to be a useful diagnostic tool especially when cancer antigen 125 (CA-125) levels are rising. **AIM:** To investigate

the results of 18F-FDG PET/CT studies in patients with suspected ovarian cancer recurrence according to rising CA-125 levels. **METHOD:** 18F-FDG PET studies of ovarian cancer patients in follow up with high serum CA-125 levels were retrospectively analysed. In the archives of our department 31 suitable PET/CT records were found in the period from 2006 to present. **RESULTS:** In 28 of 31 studies abnormal PET/CT findings suggesting recurrence of ovarian cancer were observed. One of the 3 patients considered to be negative for recurrence had a biopsy proven breast cancer detected on PET/CT examination, one had no findings of recurrence for a follow period of 16 months and for the other patient no additional data on recurrence is available due to recent PET/CT examination. **CONCLUSION:** FDG PET/CT is a powerful diagnostic tool in the follow-up of patients with rising CA-125 levels and suspected ovarian cancer recurrence.

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Contribution of 18F-FDG-PET in recurrent ovarian carcinoma and role to evaluate peritoneal disease

M. D. Albalá, A. Benítez, F. J. Hidalgo, C. Pacheco, P. I. Contreras, J. M. Latre; University Hospital Reina Sofía, Córdoba, SPAIN.

AIM: To analyze the utility of 18F-FDG-PET in recurrent ovarian carcinoma and determine the diagnosis accuracy detecting peritoneal disease. To compare the FDG-PET findings with CT data. **MATERIAL & METHODS:** We performed a retrospective analysis of 20 18F-FDG-PET in 17 patients (age 42-80 years) referred to us for suspected ovarian cancer recurrence or monitoring treatment response. The PET studies were acquired on a PET scanner, 60 minutes after the administration of 18F-FDG (mean dose 333 MBq), in fasting conditions and with normal glucose levels. Interpretation was based on visual inspection and SUVmax analysis. The FDG-PET findings were compared with CT, acquired in the previous few days. Results were correlated with pathological findings or follow up (mean time 10 months). **RESULTS:** Among the 20 studies performed, only 4/20 18F-FDG-PET and 3/20 CT resulted completely negative. The CT failed in two patients with peritoneal carcinomatosis. The 18F-FDG-PET failed in one patient with peritoneal carcinomatosis (the CT was also negative) and in another patient with local recurrence. We had only one false negative in CT in a patient with peritoneal nodules images who had a negative PET study. We had no false positive in PET studies. In the evaluation of recurrent ovarian carcinomas, the sensitivity (Sn), specificity (Sp) and accuracy (Ac) of the 18F-FDG-PET were found 89%, 100% and 90%, respectively and of the CT were found 89%, 50% and 85%, respectively. 8/17 patients had peritoneal disease, 6 of them diagnosed by surgical biopsy. It was demonstrated certainly with 18F-FDG-PET in 5 patients and with CT in 4 patients. Moreover, one patient with peritoneal disease and false negative CT and true positive PET underwent another 18F-FDG-PET and CT studies for treatment response. At this time, CT demonstrated peritoneal disease. Thus, the Sensitivity, Specificity and accuracy of the 18F-FDG-PET in the diagnosis of peritoneal carcinomatosis were found 63%, 100% and 84%, respectively and of the CT were found 50%, 91% and 74%, respectively. **CONCLUSIONS:** 1. 18F-FDG-PET has been shown to be helpful in the diagnosis of recurrent ovarian carcinoma. 2. 18F-FDG-PET has been shown to be helpful in the diagnosis of peritoneal involvement in patients with recurrent ovarian carcinoma. 3. 18F-FDG-PET shows better accuracy than CT in the diagnosis of recurrent ovarian carcinoma and in peritoneal carcinomatosis.

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The role of 18F-FDG PET/CT in the detection of recurrent cervical cancer

C. Escabias del Pozo, S. Rodado Marina, M. Coronado Poggio, I. Santos Gomez, M. Marin Ferrer, A. C. Hernandez Martinez, D. Mendez Mareque, J. Coya Viña, L. Martin-Curto; La Paz Hospital, Madrid, SPAIN.

Cancer of the uterine cervix is the third most prevalent female malignancy worldwide and approximately 30-35% of patients have recurrent after primary definitive treatment. The aim of this study was to assess the role of 18F-FDG PET/CT in the diagnosis and management of suspected cervical cancer recurrence. **MATERIAL AND METHODS:** This is a retrospective study of 28 patients (p) (median age 56 years, range 35-79) with previously treated cervical cancer, who underwent 35 integrated PET/CT between May 2004 and July 2009 with clinical suspected recurrence. Seven patients had more than one PET/CT. Histologic types includes squamous (20p), adenocarcinoma (7p), neuroendocrine (1p), and the primary clinical FIGO stage at diagnosis was IA (1p), IB (8p), IIA (1p), IIB (8p), IIIA (1p), IIIB (6p), IVA (2p) and IVB (1p). Primary treatment consisted in surgery and radiotherapy (4p), surgery and chemoradiation (12p) and chemoradiation (12p). The gold standard used for analysis of PET/CT results was histology in 9 cases and clinical follow-up in 24 cases, with the median follow-up of 18 months (2-57), being evaluated the clinical impact in all patients. **RESULTS:** The most frequently indications for PET/CT was equivocal lesions on radiologic imaging (85%), detecting more lesions of the suspected in 42% of cases. Among 35 PET/CT, 63% were positives for recurrence, 28% negatives and 9% undetermined. All twenty-two positives PET/CT were true-positive for distant recurrence. There was only one false-negative case in a lung metastases confirmed by clinical follow-up. PET/CT undetermined had recurrent disease, in one case regional lymph node and in two cases distant metastases (lung and retroperitoneal lymph node). PET/CT had an impact on the management in 6p: in 3p suspected disease was ruled out allowing for radical treatment (1p lung metastases surgery and 2p retroperitoneal surgery and radiotherapy), and in 3p previously planned therapeutic approach was changed to find more suspected locations and PET/CT results indicated chemotherapy. **CONCLUSIONS:** In patients with clinical suspected recurrence of cervical cancer, 18F-FDG PET/CT is a sensitive and specific tool, providing more accurate information on the stage of disease, and helping in decision making for appropriate therapeutic management of these patients.

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The role of FDG-PET/CT for staging and/or evaluation of therapy response in patients with cervical cancer

Y. Sanli¹, C. Turkmen¹, B. Bakir², I. Adalet¹, S. Unal¹, A. Mudun¹, C. Iyibozkurt³, S. Topuz⁴; ¹Istanbul University, Istanbul Faculty of Medicine, Department of Nuclear Medicine, Istanbul, TURKEY, ²Istanbul University, Istanbul Faculty of Medicine, Department of Radiology, Istanbul, TURKEY, ³Istanbul University, Istanbul Faculty of Medicine, Department of gynecology

and obstetrics, Istanbul, TURKEY, ⁴Istanbul University, Istanbul Faculty of Medicine, Department of Obstetrics and Gynecology, Istanbul, TURKEY.

Objectives: In the present retrospective analysis, we evaluated the role of F18 FDG-PET/CT imaging in comparison with MRI for staging and/or evaluation of therapy response in cervical cancer. **Methods:** Between May 2009 and March 2010, 42 F18 FDG-PET/CT studies were performed to 41 patients with serical cancer in our institution. All patients had MRI before or after obtaining PET images within one month without receiving any kind of treatment. The indications for F18 FDG-PET/CT imaging were staging (n= 26) purpose or evaluation of recurrence (n= 16) after chemotherapy. **Results:** F18 FDG-PET/CT and MRI findings were similar in 18 (43.9%) patients; whereas F18 FDG-PET/CT demonstrated additional tumoral lesions in 14 patients that couldn't be detected with MRI. Meanwhile lymph node metastasis in 4 patients were found to be with MRI images that was not found with F18 FDG-PET/CT. In 1 patient, false positive result was detected with F1 FDG-PETCT not detected with MRI, whereas again in one patient MRI was thought to be false positive. Meanwhile, MRI was false negative in 1 patient, in whom vaginal cuff recurrence was detected with F18 FDG-PET/CT. **Conclusions:** Despite limited number of patients in the present report, F18 FDG-PET/CT may have an additive value to current imaging modalities such as in patients with serical cancer for staging and evaluation of therapy response.

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The role of [F-18] FDG PET/CT in diagnosis of bone metastasis from colorectal cancer

K. Itoh, T. Kusumi, K. Kamegawa, A. Matsunaga, Y. Nishida, M. Hosokawa; Keiyukai-Sapporo Hospital, Sapporo, JAPAN.

Background: Colorectal cancer is one of the most common neoplasms worldwide, with a high morbidity and mortality. Survival is affected by metastases to lymph nodes, liver and lung. [F-18] FDG PET/CT (PET/CT) is useful in the early detection of local recurrence and metastases described above. Bone metastasis (BM) in colorectal cancer has been described as an uncommon event, Experience with PET/CT in its diagnosis is limited. In the present study, we evaluated clinical characteristics of BM diagnosed by PET/CT. **Materials and Methods:** There were 1038 pts (1618 studies) with histologically proven colorectal cancer in whom PET was performed from January 2006 to December 2009. Of these, 52 pts (31 men and 21 women, 45 to 88 y in age range, median age = 67 y) were suspected of having BM by PET/CT. Patients who had been fasting for at least 4 h received an IV injection of [F-18] FDG which was supplied as a commercial product (Nihon-Medi Physics Co, Ltd, Japan). Sixty minutes after FDG injection, attenuation-corrected image (3D-mode) was performed at 1 bed position per 2.0 min using PET/CT (GEMINI-GXL, Philips, Netherlands). **Results** Forty two pts (4.0%, 95%CI of 2.8%~5.2%) were diagnosed with BM using conventional imaging (CT, MRI) and further follow-up studies. Among these, 5 pts had BM alone, and 37 pts (88%, p<0.001) had BM in combination with extraosseous metastases. The sites commonly involved were pelvic bone, lumbar and thoracic spines. In addition, BM in 35 pts (83%, p<0.001) was detected by the follow-up PET/CT during chemotherapy after the resection of the primary tumor. The rate of solitary BM was equal to the rate of multiple BM. False positive findings were observed in 10 pts (10/52=19%). Most of them were solitary and were observed in the ribs and in the lumbar spines. False positives seems to be related in part to inflammation. Some of them might be due to insufficient expertise of PET/CT in the early days after the introduction of PET/CT. There was no difference in the detection of BM between PET/CT and bone scintigraphy with Tc-99m-HMDP in 12 pts. **Conclusion:** The present analysis indicates that PET/CT appears to be the modality of the first choice for detecting bone metastases in colorectal cancer which commonly complicate extraosseous metastases. In order to minimize false positive results in BM by PET/CT, it should be kept in mind that clinical expertise with PET/CT and bone scintigraphy is required.

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Role of 18F-FDG PET-CT in the diagnosis of recurrent colorectal carcinoma. Initial experience in the Canary Islands.

M. A. Ochoa Figueroa¹, V. Sanchez Rodriguez², M. J. Hernandez Briz¹, C. Isla Gallego¹, F. M. Armas Serrano¹, M. A. Santana Borbones¹, J. Herrera Henriquez¹, J. Miranda Ramos¹, C. Rodriguez Rey³; ¹Hospital Universitario Insular de Gran Canaria, Las Palmas de Gran Canaria, SPAIN, ²Hospital Universitario de Canarias, La Laguna, SPAIN, ³Instituto PET Focuscan, Madrid, SPAIN.

Aim: To evaluate the role of 18F-FDG PET-CT in patients with suspected recurrence of colorectal carcinoma. **Materials and methods:** We underwent a retrospective study which included 56 patients (32 males and 24 females, mean age 63 y.o.) with suspected recurrence of colorectal carcinoma and who were scanned using 18F-FDG PET-CT. Previous to the 18F-FDG PET-CT scan all the patients had surgery of the primary tumor; 7 patients only had surgery; 34 surgery and chemotherapy and 15 radiotherapy and chemotherapy. The physician suspected recurrence because: 21 patients presented increased serum tumor markers (CEA and/or CA 19.9) with negative imaging (US and/or CT) (Group 1); 16 patients presented pathological imaging with increased serum tumor markers (Group 2); 12 did not show increased serum tumor markers, but showed pathological imaging (Group 3); and 7 patients had negative serum tumor markers and negative imaging (Group 4). **Results:** After the physician suspected recurrence of colorectal carcinoma, a PET-CT scan with 18F-FDG was performed and we found an overall sensitivity of 90%, specificity 83%, PPV 88%, NPV 86% and an accuracy of 88% in our study. The subgroup results are: (table 1) 31 cases of recurrence were confirmed with pathology (22 with recurrence and 9 with out recurrence); and 25 (11 with recurrence and 14 with out recurrence) by clinical follow up (over 6 months). **Conclusion:** Once again the great value of 18F-FDG PET-CT is confirmed, showing to be a great diagnostic tool in patients suspected to have colorectal carcinoma recurrence, as many other authors have shown. In our experience 18F-FDG PET-CT

proved to be of great diagnostic utility, even in patients were imaging and tumor serum markers were negative (Group 4), showing to be a good imaging tool for the control of these patients.

Sensitivity / Specificity

Group 1 (imaging -, tumor markers +)	83	77
Group 2 (imaging +, tumor markers +)	91	100
Group 3 (imaging +, tumor markers -)	100	66
Group 4 (imaging -, tumor markers -)	100	85

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Clinical relevance of incidental colonic uptake ^{18}F -FDG PET/CT. Correlation with colonoscopy and histopathology.

H. Fernandes, P. Lapa, G. Costa, J. Correia, J. Pedrosa de Lima; Hospitais Universidade Coimbra, Coimbra, PORTUGAL.

Aim: Colorectal cancer is the second leading cause of cancer related deaths in the western world, and may exist synchronously or metachronously with other malignant tumors. The ability of ^{18}F -FDG PET/CT to detect a wide range of colonic lesions depends on the fact that most of these neoplasias have a strongly increased uptake of ^{18}F -FDG. Several studies have shown that whole-body PET/CT imaging may identify unexpected foci of hypermetabolism within the colon, many of which have clinical significance. The main purpose of this study was to determine the prevalence and clinical importance of unexpected abnormal foci of hypermetabolism at ^{18}F -FDG PET/CT studies performed in our institution during a five year period. **Materials and Methods:** We retrospectively analyzed 5545 consecutive patients who underwent a ^{18}F -FDG PET/CT scan for evaluation of a malignant disease between January 2005 and January 2010. Patients with known or suspected colorectal or occult cancer have been excluded. PET images were obtained 45 to 60 minutes after ^{18}F -FDG injection and low dose CT images were used for attenuation correction and anatomic mapping. Co-registered PET/CT images were obtained for analysis. Incidental ^{18}F -FDG PET/CT findings were correlated with colonoscopic and histopathologic results. ^{18}F -FDG uptake intensity was quantified using SUVmax values. **Results:** Of the 5545 patients evaluated, 56 (31 male; 25 female, mean age 65±7.5 years) displayed incidentally ^{18}F -FDG colonic foci, representing a prevalence of about 1%. Correlative colonoscopic and histopathologic findings were available in 16 (28.6%) of these 56 patients. In the 16 patients we found 18 ^{18}F -FDG colonic foci. Of these 18 abnormalities, 2 were adenocarcinoma (mean SUVmax=24.8), 1 was high grade dysplasia adenoma (mean SUVmax=18.6), 9 were low grade dysplasia adenomas (mean SUVmax=13.5), 5 were benign lesions (mean SUVmax=8.1) and 1 had no colonic abnormality detected (false positive). Two other low grade dysplasia adenomas were detected on colonoscopy but not on the ^{18}F -FDG PET/CT. An apparent positive correlation between ^{18}F -FDG uptake intensity and the severity of the lesion was observed. **Conclusion:** Although incidental colonic lesions were detected in only about 1% of our patients, they were associated with a substantial risk of an underlying cancerous or precancerous lesion. Our results emphasize the need for follow-up of these abnormalities because the majority of the lesions studied represented either a malignant or a premalignant neoplasm, which was not clinically apparent.

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The role of PET/CT in colorectal cancer. Preliminary results.

C. Paniagua Correa, M. A. Balsa Breton, M. P. Garcia Alonso, A. Mariana Monguia, S. I. Vasques Tineo, A. Mendoza Paulini, L. Castillejos Rodriguez, A. Ortega Valle, F. J. Penin Gonzalez, C. Pey Illera; Hospital Universitario de Getafe. Medicina Nuclear., Getafe (Madrid), SPAIN.

Aim: To assess the usefulness of FDG- PET / CT in colorectal carcinoma follow-up. **Materials and Methods:** From May/09 to December/09, PET-CT was performed in 53 patients (39 males and 14 females) with mean age of 65.01 years (43 - 80). Five of them had elevated serum tumor markers (Group A), 14 patients showed unspecific findings with other conventional imaging methods (Group B), 7 both factors (Group C), in 20 patients with known metastatic lesions PET/CT was requested to rule out other possible lesions (Group D) and 7 patients with high suspicious of local recurrence (Group E). All patients were examined in a standard routine examination protocol. Final diagnosis was based on histology or serial follow-up (clinical and/or imaging techniques). **Results:** - Patients in groups A, B and C (26 patients): o PET/CT detected malignant features in 16/26 cases, 15 of them were true positive (TP): 9 cases were histologically confirmed, in 6 the final diagnosis was performed by follow-up, and 1 case was not confirmed. o PET/CT showed absence of disease in 8/26 cases, all of them were true negative (TN): 1 case histologically confirmed and 7 by follow-up. o Two studies (2/26) were indeterminate because of infracentimetric pulmonary lesions. - Patients in group D (20 patients): o The suspicious lesion showed pathological metabolic activity in 14/20 cases, 13 of them were TP and 1 false positive (FP) probably motivated by recent chemotherapeutic treatment. o PET/CT was negative in 6/20 cases: 5 TN and 1 false negative (FN) (this patient was affected by peritoneal carcinomatosis). o PET/CT led a change in therapeutic management in 12/20 patients because surgery was rejected in all cases: In 7 patients we detected new metastasis in addition to previously known lesion, and in the 5 TN cases. - Patients in group E (7). o PET/CT detected malignancy in 4/7 cases and was negative in 3/7. All cases with positive test were TP (3 histologically confirmed, 1 with follow-up) and all the negative ones were TN (confirmed during follow-up). - The values of Sensitivity: 96,9 %, Specificity: 94,1 %, PPV:96,9 %, NPV: 94,1 %. **Conclusions:** Our initial experience confirms the role of PET/CT in colorectal carcinoma follow-up showing high sensitivity, specificity, PPV and NPV values. The studies often detect incidental lesions unknown with conventional imaging modalities. The impact on therapeutic management makes us consider PET/CT as standard surveillance procedure.

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Calculation of SUL from SUV - comparison of maximum and mean values

K. Skougaard, H. W. Hendel; Copenhagen University Hospital, Herlev, Herlev, DENMARK.

The newly developed *Positron Emission Tomography Response Criteria In Solid Tumours - PERCIST* suggest correcting standard uptake mass (SUV) for lean body mass (LBM), SUL - instead of body weight (BW), SUV and measuring the maximum and mean values in a volume of interest (VOI) with a fixed diameter of 1.2 cm centred on the hottest part of the tumour. Scanner specific software capable of measuring both SUV and SUL in the same VOI exists, however if SUL cannot be measured it has been suggested that SUL can be calculated from SUV. **Aim:** To evaluate the possibility of calculating maximum and mean SUL from maximum and mean SUV in a fixed VOI. **Materials & Methods:** 50 patients (mean BW 71.4 kg, mean BMI 24.4) with advanced colorectal cancer were scanned using Philips Gemini PET/CT scanner. In each patient a manually drawn, fixed VOI was placed in the hottest part of the tumour with the highest SUV by a single observer. In a subgroup, 34 patients, a background VOI of 1 cm in diameter was drawn in the descending aorta. Philips PET/CT Application Suite® v. 2.0 software on an Extended Brilliance™ Workspace v. 4.0 was used. Maximum and mean SUVs, SULs, and SD in the VOIs were recorded. The mean and maximum SUV were used to "re-calculate" the maximum and mean SUL (SUVmax or mean/BW (kg) * LBM (by gender)). For comparison Bland-Altman plots and paired samples t-test were used. **Results:** Bland-Altman plots for the tumour VOIs demonstrated good agreement (mean difference; 95% limits of agreement (LOA); p-value) between recorded and calculated maximum SUL (-0.05; -0.40-0.34; p=0.22). Regarding the mean SUL values there was a systematic underestimation of the calculated values and LOA were asymmetrically distributed around zero (-0.54; -1.69-0.59; p<0.0001). For the background areas the corresponding values for maximum SUL were (0.06; -0.14-0.25; p=0.001), and for the mean SUL the values were (-0.01; -0.14-0.12; p=0.003). **Conclusions:** If a single voxel (maximum value) approach is used there are minor differences between the measured and calculated SULs. If a multiple voxel approach (mean value) is used re-calculation of SULs from SUVs is however not valid.

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Evaluation of FDG PET/CT and CT in The Preoperative Staging Of Colorectal Carcinoma

Ö. Vural Topuz¹, L. Kabasakal¹, M. Halac¹, E. Balik², E. Kunduz², M. Gulluoglu³, K. Sonmezoglu¹, I. Uslu¹; ¹Istanbul University, Cerrahpasa Medical Faculty Nuclear Medicine Department, Istanbul, TURKEY, ²Istanbul University, Istanbul Faculty of Medicine, Department of General Surgery, Istanbul, TURKEY, ³Istanbul University, Istanbul Faculty of Medicine, Department of Pathology, Istanbul, TURKEY.

Aim: The aim of our study was to evaluate the value of preoperative and pretreatment FDG PET/CT and CT findings and to compare the results with postoperative pathological findings in patients with colorectal carcinoma. **Materials and Methods:** The files of eight hundred eighty eight patients with colorectal carcinoma who were referred to our PET/CT unit between 2006 and 2009 were retrospectively analyzed. Seventy patients who were recently diagnosed by colonoscopic biopsies and who came for initial staging before surgery were selected. Of this group 24 colorectal carcinoma patients (12F, 12M, mean age 66,8 years) who have not taken any chemo or radiotherapy before operation were included to the study. Preoperative PET/CT and CT data and postoperative pathological staging of these patients were compared and evaluated. **Results:** Among 24 patients PET/CT revealed local lymph node metastases in 13 patients (54%). There were 8 true positive and 8 true negative results. However, there were 5 false positive and 3 false negative results. Among 24 patients CT results were available in 21 patients. Among these patients CT results revealed local lymph node metastases in 13 patients. However, there were 6 false positive and 2 false negative results. The distant metastases found in 13 patients on PET/CT and in 9 patients on CT examinations. The specificity and the sensitivity of PET/CT were 61% and 72% respectively, the specificity and the sensitivity of CT were 50% and 77% respectively. The positive predictive value and the negative predictive value for PET/CT were 61% and 72% respectively, the positive predictive value and the negative predictive value for CT were 53% and 75% respectively. The numbers of patients with distant metastases diagnosed with PET/CT were greater than that of CT examination. In 3 patients with liver metastases and in 1 patient with lung metastases CT was negative and their metastases were primarily detected on PET/CT. **Conclusion:** Our data suggest that there were no significant difference between preoperative PET/CT and CT findings and postoperative pathological findings in initial staging of colorectal carcinomas. However PET/CT may be valuable for diagnosis of distant metastases.

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Anatomic Dependence of Tumor Metabolism in Colorectal Cancer as Quantified with a Novel FDG-PET/CT Image Analysis Methodology

J. A. Poff¹, A. Rives², B. Saboury¹, N. Foroughi¹, H. Zafar¹, F. Hofheinz³, A. Alavi¹, D. A. Torigian¹; ¹University of Pennsylvania, Philadelphia, PA, UNITED STATES, ²Boston University Medical Center, Boston, MA, UNITED STATES, ³ABX advanced biochemical compounds, Radeberg, GERMANY.

Purpose: Semi-automated 3D image analysis approaches that account for partial volume effects encountered on FDG-PET/CT have the potential to reveal variations in tumor metabolism based on anatomic site that may not otherwise be appreciated via traditional measurement approaches. In this study, we assessed for differences in tumor metabolism of colorectal cancer lesions on FDG-PET/CT based on anatomic site without and with the use of partial volume correction. **Methods:** Lesional mean SUV (mSUV) and partial volume corrected mSUV (cSUV) were measured in 91 retrospectively identified subjects (50 male, 41 female) with colorectal cancer via the Region of Interest Visualization, Evaluation, and Image Registration (ROVER) software (ABX GmbH, Germany). Lesions were grouped by location as primary colorectal tumor, lymph node metastases, or solid organ metastases (liver, lung, and spleen), and mSUV and cSUV were individually compared among anatomic sites using a Tukey-Kramer significant difference test. **Results:** SUV measurements were quantified in 274 malignant lesions. Partial volume correction increased mSUV by an average of 171% among all lesions. Primary tumor mSUV (6.2±2.7) was significantly greater than mSUV of both lymph node metastases (4.1±1.4) and solid organ metastases (4.0±1.5). However, with addition of partial volume correction, cSUV of solid organ metastases (11.3±12.8) was greater than cSUV of primary tumor (8.9±3.5) and lymph node metastases (8.7±5.5). **Conclusion:** Tumor metabolism of colorectal cancer lesions as measured from FDG-PET/CT varies with anatomic site, and is only accurately quantified when the partial

volume effect is taken into account. These observations will potentially have important implications related to the prognosis and treatment of patients with colorectal cancer.

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Reliability of negative finding on ¹⁸F FDG PET/CT in colorectal cancer patients with persistent abnormal postoperative CEA level

S. Lee, J. Park, A. Lee, S. Bae; Inje university college of medicine, Pusan Paik Hospital, Busan, KOREA, REPUBLIC OF.

Purpose: ¹⁸F FDG PET/CT is useful tool for the follow-up of malignancy. The aim of this study is to evaluate the reliability of negative finding on ¹⁸F FDG PET/CT in colorectal cancer patients with persistent abnormal postoperative CEA level (>5ng/mL). **Method:** Among 156 patients of colorectal cancer with elevated CEA level (>5ng/mL) on follow-up ¹⁸F PET/CT study, the outcome of 22 patients with persistent abnormal postoperative CEA level and negative finding on ¹⁸F PET/CT was reviewed retrospectively. The clinical outcome was based on follow-up imaging study (CT, ¹⁸F PET/CT), endoscopic finding, physical examination, and histopathological result. **Result:** The mean follow-up period after ¹⁸F PET/CT was 560±276 days, and mean CEA level was 10.6±5.1 ng/mL. 2 of 22 patients showed recurrence during follow-up period (445 and 56days, respectively). One was taking oral chemotherapeutic agent at the time of PET/CT examination, but follow-up ¹⁸F FDG PET/CT revealed recurrent malignant lesion. The recurrent site of the other case was urinary bladder, which is difficult to be detected due to physiological urine activity. But the recurrent lesion can be detected on the non-enhanced CT of ¹⁸F FDG PET/CT retrospectively, and CEA level showed gradual increment (from 30.85 to 102 ng/mL during 56days). On the other hand, 20 of 22 patients did not show recurrence during follow-up period. **Conclusion:** ¹⁸F FDG PET/CT was a reliable follow-up tool in colorectal cancer patients with persistent abnormal postoperative CEA level. But, attention should be paid in the patients taking chemotherapeutic agents, and careful observation for CT of ¹⁸F FDG PET/CT is necessary to avoid false negative result caused by physiological activity in patients showing gradual increment of CEA level.

P44 — Monday, October 11, 2010, 16:00 — 16:30, Hall Z

Oncology Clinical Science: Gastrointestine & Pancreas

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Diagnostic Value Of FDG PET/CT In Advanced Gastric Carcinoma

B. Vidergar-Kralj¹, A. A. Schwarzbarti-Pevac¹, I. Zagar¹, M. Pustovrh²; ¹Institute of oncology, Ljubljana, SLOVENIA, ²General Hospital Celje, Celje, SLOVENIA.

Aim. The purpose of our study was to assess the diagnostic value of 18-F fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) for detecting primary metastatic or recurrent disease in patients with gastric carcinoma. **Materials and Methods.** In a two-year period, FDG PET/CT was performed in 40 patients with gastric carcinoma, who were suspected to have primary metastatic or recurrent disease. Twelve of 40 patients had signet ring cell carcinoma. FDG PET/CT findings were retrospectively correlated with final diagnosis. **Results.** In 20/40 patients, metastatic or recurrent disease was correctly detected by FDG PET/CT. In 3/40 patients, the findings were false positive due to inflammation on anastomosis. In 11/40 patients, the findings were false negative, 2 among these patients had peritoneal carcinomatosis and 9 patients had metastatic signet ring cell type of gastric cancer. The sensitivity and specificity of FDG PET/CT in our patient group were 65% and 67%, respectively. Metastatic or recurrent disease was correctly detected in only 3/12 patients with signet ring cell carcinoma. **Conclusion.** FDG PET/CT is useful for detecting primary or recurrent metastatic disease in patients with gastric carcinoma, except in signet ring cell type of gastric cancer. As inflammation is common at the site of anastomosis, special care should be taken in evaluation of FDG uptake in this area.

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MRI versus 18F-FDG PET /CT in the differential diagnosis of benign and malignant lesions of the pancreas

A. Giorgetti¹, S. Salemi², P. Boraschi², F. Donati², R. Gigoni², M. Del Chiaro³, D. Campani⁴, U. Boggi³, F. Falaschi², P. Marzullo¹; ¹Fondazione "G. Monasterio" CNR/Regione Toscana, Pisa, ITALY, ²2nd Department of Radiology, Pisa University Hospital, Pisa, ITALY, ³General and Transplantation Surgery, University of Pisa, Pisa, ITALY, ⁴Division of Surgical Pathology, Molecular and Ultrastructural Pathology, University of Pisa, Pisa, ITALY.

AIM: To evaluate diagnostic accuracy of MRI and PET/CT in the differential diagnosis of benign and malignant lesions of the pancreas. **Material and methods:** We enrolled 30 patients with focal pancreatic lesion who underwent both MRI at 1.5T-device (Signa Exite HDx, GE Healthcare) and 18F-FDG PET/CT (Discovery-VCT, GE Healthcare) within a 1-month interval. MR protocol included axial T1w/T2w, 2D/3D MRCP and pre- and post-contrast 3D LAVA T1w sequences. PET/CT protocol included image fusion of unenhanced total body low dose CT scan and total body PET scan performed 60 minutes after infusion of 18F-FDG. Final diagnoses, based on surgery and/or imaging follow-up, were: 12 IPMTs, 4 mucinous cystadenomas, 3 serous cystadenomas, 3 endocrine tumors (benign = 2, malignant = 1), 4 focal chronic pancreatitis, and 4 adenocarcinomas (ductal = 3, acinar cell carcinoma = 1). Different observers (two in conference for each technique) blindly classified as benign or malignant the pancreatic lesions on MRI and on 18F-FDG PET/CT (SUV > 2.5 was taken as value of malignancy). **Results:** Both imaging techniques characterized all benign lesions. MRI classified as malignant 4/5 lesions (1 false negative, acinar cell carcinoma), whereas PET/CT classified as malignant 4/5 lesions (1 false negative, malignant endocrine tumor). MRI and PET/CT showed sensitivity of 96% and specificity of 100%. **Conclusion:** MRI and 18F-FDG PET/CT revealed equal high sensitivity and specificity in the differential diagnosis between benign and malignant focal pancreatic lesions.

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Different SUVmax cut-off values improve the diagnostic accuracy of 18-FDG PET/TC in patients with pancreatic lesions.

A. Giorgetti, D. Genovesi, A. Bottoni, E. Filidei, C. Porciello, F. Magagnini, A. Giuntini, O. Sorace, C. Marzuolo, D. Di Taranto, A. Quaranta, E. M. Ferdighini, P. A. Salvadori, P. Marzullo; Fondazione "G. Monasterio" CNR/Regione Toscana, Pisa, ITALY.

AIM To evaluate 18-FDG PET/CT as a tool for the differential diagnosis in the preoperative work-up of pancreatic lesions. **MATERIALS & METHODS** From July 2006 to December 2009, 56 patients (59±12 ys, 22 female) with a suspected pancreatic lesion were prospectively investigated with 18-FDG PET/TC (GE Discovery-VCT). The validation of diagnosis was based on pathologic findings after surgery (45 pts) or on follow-up evaluation (11 pts, median 20 months, range 9-42). In all patients lesion SUVmax values were obtained. Reference pancreatic SUVmax values (controls) were obtained in 40 subjects (60±15 ys, 24 female) referred to PET/CT for suspected malignancy in organs other than pancreas and with negative tomographic results. **RESULTS** Patients were divided into 2 groups: G1 with benign lesions (20 pts: 5 IPMTs, 4 serous cystadenomas and in the follow-up group TC/MRI appearance as single cyst (4), pseudocyst (2) or serous cystadenoma (6)) and G2 with malignant findings (36 pts: 25 adenocarcinomas, 4 IPMTs and 7 mucinous cystadenomas). SUVmax values resulted 1.68±0.38, 2.8±0.7 and 6.0±2.9 in controls, G1 and G2 patients, respectively. ROC curves analysis identified a SUVmax cut-off >2.2 as the best for distinguishing controls from all pathological results providing a global diagnostic accuracy of 0.93 (sensitivity: 0.95; specificity: 0.95). Moreover, ROC analysis showed that a SUVmax cut-off >4 was the optimal to identify patients with malignant findings from benign ones (sensitivity: 0.75; specificity: 0.95; accuracy: 0.92). Using this cut-off we observed only 2 false negatives (1 IPMT and 1 mucinous cystadenoma both with a SUVmax = 3) and 1 false positive (serous cystadenoma with important pancreatitis). **CONCLUSIONS** Reference pancreatic SUVmax values can be used to obtain cut-off values for the recognition of malignant pancreatic lesions, improving the diagnostic accuracy of PET/CT in the preoperative work-up of the patient.

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Usefulness of 18F-FDG PET/CT in differential diagnosis of pancreatic masses.

R. Sánchez-Sánchez, E. Cabrera-Cazorla, A. Rodríguez-Fernández, A. Medina-Benítez, T. Villegas-Herrera, D. Garrote-Lara, M. Gómez-Río, J. M. Llamas-Elvira; Virgen de las Nieves University Hospital, Granada, SPAIN.

Introduction: Pancreatic cancer has very poor prognosis, for this reason, substantially increased research efforts are clearly warranted to understand, detect and control of disease. Preliminary data suggest a significant influence of FDG-PET/CT on treatment planning, although its role is still evolving. **Purpose:** To evaluate the accuracy of integrated positron emission tomography with ¹⁸F-fluoro-2-deoxy-D-glucose (FDG) and computed tomography (PET/CT) in differential diagnosis of pancreatic lesions. **Materials and Methods:** Thirty patients (21 men, 9women) with an average age of 60 years underwent PET/CT examination for differential diagnosis of pancreatic lesion. PET/CT was performed 60min after the injection of 350-450Mq FDG. Presence or absence of FDG uptake in the region of pancreas was evaluated visually. Results were compared with histopathological findings and/or follow up. The sensitivity, specificity, negative predictive value and positive predictive value of PET/CT were determined. **Results:** In 16 patients malignant neoplasms were confirmed (histologically in 15 patients; the other one presented hepatic metastases). In 12 patients benign diseases were confirmed (histologically in six patients; other 6 patients were followed up for 12-20 weeks) without any sign of disease progression. Two cancers showed no FDG uptake and were considered as false negative, both were histologically classified as ductal adenocarcinoma. In patients with benign disease (11/30) no false positive findings were found. The sensitivity, specificity, negative predictive value and positive predictive value of PET/CT were 88.9%, 100%, 85.7% and 100% respectively. Metastatic disease in PET/CT was found in 20% (6/30) of patients, unsuspected in two of them, placed at hepatic parenchyma. **Comments:** Our preliminary results indicate that PET/CT could be an excellent tool in differential diagnosis of pancreatic masses. Additional value of PET/CT in detection of metastatic disease could induce changes on management of patients with malignant lesions.

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F-18 FDG PET/CT in Advanced Signet Ring Cell Carcinoma: Relating to Pathologic Findings including Stage and Immunohistochemical Staining

K. Won¹, Y. Kang¹, S. Kim¹, B. Choi¹, S. Zeon¹, K. Chun²; ¹Keimyung University Donsan Medical Center, Daegu, KOREA, REPUBLIC OF, ²Yeungnam University Hospital, Daegu, KOREA, REPUBLIC OF.

Background: It is well known that the role of F-18 FDG PET in gastric cancer is limited because of its low sensitivity, especially for signet ring cell carcinoma (SRC). The purpose of this study was to find out the meaning of FDG uptake of SRC in F-18 FDG PET/CT and its association with pathologic characteristics including stage and immunohistochemical staining. **Material and methods:** Forty two patients with advanced SRC (55.0±13.8 years, range: 25-75 years, M:F=22:20) were included for this study who underwent F-18 FDG PET/CT within 1 month before operation. SUV of tumor were measured by various methods including maximum SUV, average SUV, etc. Medical records were reviewed including pathologic results and patient's status were followed up (14.2±5.4 months). **Results:** Detection rate of advanced SRC was 83.3%. FDG uptake intensity was significantly different according to venous invasion, T- and N- stage, and tumor size. There was no significant difference of tumor SUV in the immunohistochemical staining of p-53, Rb, Ki-67, C-erbB-2, EGFR and glut-1. Cancer recurrence was seen in 6 patients and tumor SUV didn't show any significant difference between disease free and recurrence of cancer groups. **Conclusion:** FDG uptake intensity of advanced SRC was associated with venous invasion, T- and N- stage, and tumor size. It might be helpful to predict the prognosis, although in this study it has not been proven, maybe due to short-term follow-up period. However, There was no significant difference of tumor SUV in the immunohistochemical staining of p-53, Rb, Ki-67, C-erbB-2, EGFR and glut-1.

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The role of PET/CT in the evaluation of pancreatic cancer and suspected pancreas masses

E. Ozkan, C. Soydal, M. Araz, M. Filik, S. G. Yagci, O. N. Kucuk; Ankara University, Medicine Faculty, Ankara, TURKEY.

Aim: The aim of this study was to compare the PET/CT findings with other conventional imaging modality in patients (pts) with pancreatic cancer or suspicious pancreatic masses. **Method:** 20 pts with pancreatic cancer or masses who underwent both PET/CT and conventional examinations were evaluated retrospectively. The findings of PET/CT and CT and/or MRI were compared. **Results:** 8/20 pts with pancreas ca had pathological FDG uptakes in pancreatic lesions. Focal increased uptakes in the right lung in 1/8, intraabdominal lymph nodes in 4/8 and on ribs and spine in 1/8 patient. In another 1/8 patient, the disease upstaged to 4 from 1 with multiple bone metastasis detected by PET/CT. 4/20 pts with suspicious pancreatic masses underwent PET/CT imaging. 3/4 pts had normal PET/CT scans. In 1/4 patient, PET/CT showed pathological uptake in the pancreatic mass. In 8/20 pts, PET/CT referred to the restaging of pancreatic cancer after surgery. 2/8 pts had normal PET/CT scans. In 1/8 patient with normal CT, PET/CT showed multiple increased uptakes in both of lungs and spine. In another 2/8 pts with suspected pancreatic lesion in postoperative MRI, PET/CT detected multiple metastatic foci. Conversely, 1/8 patient with enlarged peripancreatic and mesenteric lymph nodes in CT and with normal PET/CT scans. 2/8 pts with recurrent disease detected by postoperative CT, MRI and PET/CT. **Conclusion:** PET/CT was found to be more sensitive than the conventional imagings in the evaluation of suspicious pancreatic masses and more accurate staging and restaging of pancreatic cancer.

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The role of FDG-PET/CT in detection of gastric cancer recurrence

M. O. Tamam, H. S. Yavuz, M. Mulazimoglu, O. Eker, T. Ozpacaci; Okmeydani Training and Research Hospital, Istanbul, TURKEY.

AIM: The purpose of this study was to retrospectively determine the efficacy and usefulness of 18F-fluoro-2-deoxyglucose positron emission tomography /computed tomography (FDG-PET/CT) in detecting and re-staging recurrent gastric cancer patients with clinical or radiological suspicion of recurrence. **METHODS:** This retrospective study has been conducted on 41 patients who were treated gastrectomy and postoperatively radiotherapy or/and chemotherapy. Histopathologic diagnosis revealed 2 signet ring cell carcinoma, and 39 adenocancer. All of the patients referred to our department for restaging due to clinical findings, tumor markers and/or radiologic suspicion of recurrence during follow-up. 27 out of 41 were male and 14 female. The mean age was 58±10 years (range 30-75 years). FDG-PET/CT was applied twice to all patients. The first FDG-PET/CT was for staging and restaging. The second was for restaging due to clinical findings, tumor markers and/or radiologic suspicion of recurrence during follow-up. The standard of reference for tumor recurrence consisted of histopathologic confirmation or clinical follow-up information for at least 6 month after FDG-PET/CT examinations. **RESULTS:** Cause of the first FDG-PET/CT application was due to staging in 24 patients and restaging in 17. FDG-PET/CT was negative in 14 patients and positive in 27. Out of 27, 7 patients had recurrence in gastric area, 7 patients had both recurrence and metastases and, 13 patients had metastases. Histological verification was done in 11 patients who were re-operated after the first FDG-PET/CT. The second FDG-PET/CT application to 27 patients was for the assessment of the response to the treatment applied. 4 patients had full metabolic recovery, 11 had progression and 12 had regression. For 17 patients whose first FDG-PET/CT results were negative, the second FDG-PET/CT application was due to restaging for the suspicion of metastases in other radiologic modalities in 6 and high tumor marker levels in 8 patients. The results for the 17 patients were metastases in 5 and negative in 9 patients. **CONCLUSION:** FDG-PET/CT is helpful in confirming the presence of recurrence particularly in patients who were highly suspicious of recurrence, because of its high positive predictability.

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Role of 18F-FDG-PET/CT in patients with pancreatic adenocarcinoma and correlation with serum tumor markers.

N. Eftychiou¹, L. Gogou², R. Efthimiadou², F. Vlachou², D. Savidou², A. Nikaki¹, K. Dalianis², V. Andreou², V. Prassopoulos²; ¹Saint Savvas Cancer Hospital Nuclear Medicine Department, Athens, GREECE, ²D.T.C.A. Hygeia Department of PET/CT, Athens, GREECE.

Aim: Pancreatic adenocarcinoma is the most common pancreatic cancer characterized by high aggressiveness and poor prognosis. Aim of this retrospective study is to evaluate the usefulness of PET/CT in patients with pancreatic adenocarcinoma who had undergone initial staging or restaging with Conventional Imaging (CT, MRI) and PET/CT, and investigate the probable correlation with serum tumor marker levels. **Method and Material:** A total of 30 patients (M=15, F=15) suffering from pancreatic adenocarcinoma were subjected in 31 18F-FDG-PET/CT scans. All patients had undergone staging of their disease by Conventional Imaging techniques (CI) 1-4 weeks prior to PET/CT examination. All patients had measured tumor marker value (Ca19-9, CEA). We compared the results of PET/CT and those of CI techniques. **Results:** In 25 out of 31 cases, serum tumor markers were increased (Group A) and in 6/31 they were of normal value (Group B).

Group A	PET/CT positive results	PET/CT negative results	Total
Conventional imaging positive results	16	1	17
Conventional imaging negative results	6	2	8
Total	22	3	25

In Group A 16/25 cases that had positive results in PET/CT examination, PET/CT and CI agreed in findings in 11 cases, concerning findings in pancreas and local recurrence (10/11), as well as metastatic lesions in liver (2/11) and lymph node invasion (1/11). In 5 cases out of the 16, PET/CT revealed more metastatic lesions, concerning peritoneal dissemination, bone and hepatic

metastasis. In 6/25 PET/CT had positive results concerning lymph node invasion (2/6), hepatic metastasis (3/6) and bone lesions (2/6), while CI was negative. In 1/25 case CI was positive however PET/CT was negative. The findings concerned pancreatic mass with no hypermetabolic activity (true negative). In Group B we had 2/6 cases with PET/CT and CI positive and 1/6 case where CI was negative but PET/CT was positive. In 3/6 cases, where CI detected residual pancreatic mass after chemotherapy, PET/CT revealed no hypermetabolic activity. We noticed that there was no linear correlation between the value of tumor marker and the mean SUVmax of the findings. **Conclusion:** PET/CT results show stronger correlation with serum tumor marker levels, than CI results do. However we did not find any correlation between SUVmax value and blood levels of tumor markers. PET/CT is a whole body imaging modality that seems to be necessary in patients with increased serum tumor markers and negative findings in conventional imaging.

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Is 18F-FDG-PET/CT a useful technique for staging and restaging patients with pancreatic adenocarcinoma? Comparison with Conventional Imaging

L. Gogou¹, V. Filippi¹, F. Vlachou¹, R. Efthimiadou¹, K. Dalianis¹, N. Eftychiou², A. Nikaki², A. Tsaroucha¹, J. Andreou¹, V. Prassopoulos¹; ¹D.T.C.A. Hygeia Department of PET/CT, Athens, GREECE, ²Saint Savvas Cancer Hospital Nuclear Medicine Department, Athens, GREECE.

Aim: Pancreatic carcinoma is a very aggressive tumor with poor prognosis. Early diagnosis and accurate localization of disease are of critical importance for choosing the appropriate treatment and improving the survival. The aim of this retrospective study is to evaluate the role of PET/CT in initial staging and in restaging patients diagnosed with pancreatic adenocarcinoma. **Methods and Materials:** A total of 45 patients (M=22, F=23) underwent 48 18F-FDG-PET/CT scans. All patients were staged by Conventional Imaging techniques (CT, MRI) 1-4 weeks prior to PET/CT examination. A total of 10/45 patients were subjected to PET/CT imaging with purpose of initial staging (Group A). A total of 36/45 patients underwent 38 PET/CT scans for restaging after surgical excision and treatment response (Group B). We compared the results of PET/CT and those of Conventional Imaging (CI) techniques. **Results:** Group A: 8/10 patients showed positive results in PET/CT scan and 2/10 negative, while CI was positive in all patients. In 6 out of 8 patients with positive PET/CT, CI agreed in findings. In 2/8 patients PET/CT revealed more metastatic lesions, concerning lymph node invasion and peritoneal dissemination. Finally in 2/10 patients, findings in CI showed pancreatic mass, however with no uptake in PET/CT examination (true negative-histologically proved). Group B: 20/38 (52.6%) cases showed positive results both in PET/CT scan and CI. Out of the 20 cases, PET/CT and CI agreed in findings in 10 cases. In other 10/20 cases we had mismatched findings and PET/CT revealed excessive lesions concerning lymph node invasion, peritoneal dissemination, bone and hepatic metastasis. In 8/38 (21%) cases CI was negative while PET/CT scan was positive. Findings in PET/CT concerned local recurrence (4 cases), lymph node invasion (2), hepatic (3) and bone metastasis (2). In 6 out of 38 (15.8%) cases where PET/CT was negative, CI was positive. CI revealed residual pancreatic mass in 4/6 cases, residual hepatic metastasis (1/6 case) and a lung nodule (1/6 case). PET/CT revealed no hypermetabolic activity in these findings. In 3/38 (7.9%) cases both CI and PET/CT were negative. Finally in 1 case (2.7%) findings CI were equivocal (lymph nodes slightly increased) and PET/CT was negative. **Conclusion:** PET/CT is a whole body imaging modality, useful in initial staging and evaluating residual disease after surgical excision and treatment response in patients suffering from pancreatic adenocarcinoma. PET/CT seems to be necessary in cases after chemotherapy treatment to evaluate the activity of residual mass.

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A preliminary investigation of Cu-62-ATSM tumor hypoxia PET/CT imaging comparing with FDG PET/CT for pancreas cancer

K. Yoshikawa, S. Ohashi, S. Toubaru, M. Hasebe, H. Ishikawa, K. Tamura, M. Shinotou, S. Yamada, S. Kandatsu, T. Shiraiishi, K. Tanimoto, T. Fukumura, T. Saga, T. Kamada; National Institute of Radiological Sciences, Chiba-shi, JAPAN.

Purpose Cu-62 labeled diacetyl-bis (N(4)-methylthiosemicarbazone) (Cu-62-ATSM) is a well-known hypoxic imaging PET tracer. The purpose of this study was to delineate the differences in intratumoral uptake and tracer distribution of Cu-62-ATSM and F-18 FDG in patients with pancreas cancer. The comparison of two tracers was done before and after carbon ion radiotherapy, and the relationship of tracer uptake and patients prognosis was also investigated. **Mehod** Two male and two female (mean age, 62.5 y, range 52-69 y) with pancreas cancer underwent both Cu-62-ATSM and FDG PET/CT before the initiation of carbon ion radiotherapy (CIRT), and the set of PET/CT studies was done one month after termination of CIRT. Two whole-body PET/CT scanners, Biograph-16 (Siemens) and Aquiduo (Toshiba) were used for data acquisition. Cu-62-ATSM and FDG were administered approximately 740 MBq and 370 MBq, respectively. Tumor uptake of each tracer was analyzed semi-quantitatively by tumor to normal tissue ratio (TNR) for Cu-62-ATSM and by standardized absorption value (SUV) for FDG. **Result** Cu-62-ATSM uptake didn't correlate with FDG uptake before CIRT, but it inversely correlated with FDG after CIRT because FDG uptake tended to decrease in all cases. Correlation coefficient of tumor uptake between Cu-62-ATSM and FDG before and after CIRT was 0.022 and -0.965, respectively. Average Cu-62-ATSM and FDG uptake before CIRT were 2.9 TNR (range 1.4-3.6 TNR) and 6.7 SUV (range 2.9-10.6 SUV), and decreased to 2.7 TNR (range 1.2-4.7 TNR) and 3.8 SUV (range 2.6-4.6) after CIRT, respectively. In three out of four patients before CIRT showed high Cu-62-ATSM uptake that might reflect the trend of them being hypoxic. A patient showed increase of Cu-62-ATSM uptake after CIRT, but FDG uptake of the same patient didn't increase and almost stable after CIRT. It might indicate that change of Cu-62-ATSM uptake didn't necessarily correspond to change of FDG uptake after radiotherapy. Only one patient died after CIRT, and his Cu-62-ATSM and FDG uptake before therapy were not the highest uptake within all patients, but both of them were relatively high. **Conclusion** Cu-62-ATSM and FDG didn't correlate each other before CIRT in pancreas cancer. The change of Cu-62-ATSM uptake didn't necessarily correspond to change of FDG uptake after CIRT. Cu-62-ATSM and FDG uptake of a patient who died after CIRT were not the highest uptake, but were relatively high.

P499**¹⁸F-FDG PET/CT in the evaluation of Gastrointestinal Stromal Tumors**

R. Jover-Diaz¹, T. Vicente-Bártulos², L. Gorospe-Sarasúa², D. Lourido-García², J. García-Poza², M. Pozo³, R. Nuñez-Miller², J. Alfonso²; ¹Instituto Tecnológico de Servicios Sanitarios-Centro Oncológico MD Anderson, MADRID, SPAIN, ²Instituto Tecnológico de Servicios Sanitarios, MADRID, SPAIN, ³Instituto Pluridisciplinar-Univ.Complutense, MADRID, SPAIN.

Purpose: Gastrointestinal stromal tumors (GISTs) are the most common non-epithelial tumors of the GI tract. Because almost 30% of these tumors have distant metastases and/or relapse, imaging based on a combination of morphologic and functional findings, such as with ¹⁸F-FDG PET/CT is rapidly becoming increasingly important for both their diagnosis and for the assessment of their response to imatinib therapy. Our aim in this retrospective study was to evaluate the role of ¹⁸F-FDG PET/CT in assessing the response of GIST patients to therapy with imatinib. **Methods and Materials:** Eighteen patients with surgically confirmed GISTs tumors underwent hybrid imaging on a GE ST 4 PET/CT scanner, before and after imatinib therapy. The CT component of the study was performed "low dose" for attenuation correction of the PET images (4 slices, 120 Kv, 80 mA), including the administration of 1000 ml of positive oral contrast. PET scans were acquired 45-60 minutes after the intravenous injection of ¹⁸F-FDG (0.15 mCi/kg, in 2D mode). In 9 patients, 100 ml of non-ionic intravenous contrast was also given. Visual and semiquantitative (SUV_{max}) analyses of PET/CT images were performed. All studies have been read and reported jointly by a radiologist and a nuclear medicine physician. **Results:** The most common localization for metastases were: liver (n=5), peritoneum/mesentery (n=4) and pelvic organs (n=3). Complete response to imatinib treatment was observed in 10 patients. Partial response (reduction in visual and semiquantitative analyses) was observed in 2 patients, and tumor progression in 6 patients. **Conclusion:** ¹⁸F-FDG PET/CT can characterize the response to imatinib therapy in patients with GIST tumors. Patients who had a complete response to therapy demonstrated complete normalization of ¹⁸F-FDG uptake in their lesions.

P500**Which FDG PET parameter is the most accurate in characterizing borderline adrenal activity in real clinical practice? : Validation of previous literatures**

S. Kim; UPMC, Pittsburgh, PA, UNITED STATES.

Objectives : Several previous studies demonstrated the role of F-18 FDG PET in characterizing adrenal lesions. However, each study used different FDG PET criteria to define positive adrenal lesions such as background activity, SUVmean of the liver, SUVmax of the liver and adrenal/liver SUVmax >1.5. Objective consensus of these parameters to characterize adrenal lesions accurately and consistently is critical especially defining borderline adrenal activity. Our study is to compare each parameter with radiologic and clinical correlation and to find the most accurate PET parameter in characterizing borderline adrenal activity in real clinical practice using. **Methods :** Total of 46 adrenal lesions (12 malignant and 34 benign) and 18 patients (mean age 69, M:F=8:10) with F18 FDG PET/CT with IV contrast were collected retrospectively. Except for clearly obvious PET finding (no adrenal activity or definite adrenal activity to suggest malignancy), all studies with adrenal activity were included. Each study was read 5 different ways using 5 different parameters and compared with clinical (44/46) and histopathologic (2/46) correlation. **Results :** The sensitivity (SN), specificity (SP), PPV, NPV and accuracy (ACC) are as follows. Visual assessment using background activity : 100%, 3%, 27%, 100% and 28% Visual assessment using liver activity : 83%, 44%, 34%, 88% and 54% Quantitative assessment using liver SUV mean : 100%, 21%, 31%, 100% and 41% Quantitative assessment using liver SUV max : 67%, 68%, 42%, 85% and 67% Quantitative assessment using adrenal SUV max/liver SUVmax >1.5: 25%, 97%, 75%, 79% and 78% Among 5 parameters, the overall accuracy and specificity were the highest using parameter of SUVmax/liver SUVmax >1.5 in characterizing borderline adrenal FDG activity although the sensitivity is low. The highest sensitivity was seen using visual background parameter or quantitative liver SUV mean. liver SUV max has overall consistent sensitivity, specificity and accuracy compared to other parameter. **Conclusions :** For high sensitivity, visual background parameter or quantitative liver SUV mean can be used. However, for high specificity, liver SUV max is recommended.

P501**Better parameter for characterizing borderline adrenal activity**

S. Kim; UPMC, Pittsburgh, PA, UNITED STATES.

Objectives : Several previous studies used different criteria in characterizing positive adrenal lesions such as background activity, SUVmean of the liver, SUVmax of the liver and adrenal/liver SUVmax ratio. These criteria seem to be subjective and inconsistent in applying to real clinical practice, especially borderline adrenal activity. Our study is to explore a new parameter in characterizing borderline adrenal activity in comparison with previously suggested FDG PET parameter. **Methods :** Total of 46 adrenal lesions (12 malignant and 34 benign) and 18 patients (mean age 69, M:F=8:10) with F18 FDG PET/CT with IV contrast were collected retrospectively. Except for clearly obvious PET finding (no adrenal activity or definite adrenal activity to suggest malignancy), all studies with adrenal activity were included. Benign and malignant groups were analyzed and compared on multiple parameters such as adrenal SUVmax, adrenal SUV max/liver SUVmax ratio, % change in adrenal SUVmax in follow up PET and % change in adrenal SUV max/liver SUVmax ratio with statistical p value. **Results :** In malignant group, the mean adrenal SUV max, % change in mean adrenal SUV max/liver SUV max ratio over time (average 5 month interval), and % change in adrenal SUVmax/liver SUV max ratio are 4.3±0.8, 1.2±0.3, +40.2% and +38.7%, respectively. In benign group, the mean adrenal SUV max, % change in mean adrenal SUV max/liver SUV max ratio over time (average 5 month interval), and % change in adrenal SUVmax/liver SUV max ratio are 3.7±1.0, 1.0±0.3, -36.7% and -31.5%, respectively. **Conclusions :** Overall, there is less significant difference in adrenal SUV max and adrenal SUV max/liver SUV max ratio between benign and malignant groups. However, there is much more significant difference in % change in adrenal SUVmax in follow up PET and % change in adrenal SUV max/liver SUV max ratio between benign and malignant groups. Our results suggest % change in adrenal SUVmax and % change in adrenal SUV max/liver SUV max ratio in follow up PET (average

5 month interval) would provide additional value in characterizing borderline adrenal activity in FDG PET in clinical practice.

P45 — Monday, October 11, 2010, 16:00 — 16:30, Hall X

Oncology Clinical Science: Lymphoma**P502****FDG uptake in bone marrow after G-CSF administration in patients with non-Hodgkin lymphoma**

K. Hanaoka, M. Hosono, Y. Komeya, N. Tsuchiya, K. Usami, Y. Yamazoe, K. Ishii, Y. Tatsumi, T. Murakami; Kinki University School of Medicine, Osaka-Sayama, JAPAN.

Purpose: To clarify the change in FDG uptake by the bone marrow over time after granulocyte colony-stimulating factor (G-CSF), we evaluated the correlation between the interval from the last day of administration of G-CSF to PET/CT study and bone marrow accumulation in patients with non-Hodgkin lymphoma. **Methods:** One hundred and six cases in 81 patients with confirmed non-Hodgkin lymphoma who underwent FDG PET within 60 days from the last administration of G-CSF were retrospectively reviewed. Thirty healthy control subjects were also included to evaluate physiological FDG uptake. PET/CT examinations were retrospectively reviewed and maximum SUV (SUVmax) was measured by placing volumetric regions of interest over each thoracic and lumbar vertebra on PET images referring to CT images. Bone marrow SUV was defined as the mean SUVmaxs of the vertebrae. The correlation between the interval after G-CSF and the bone marrow SUV was plotted and analyzed with polynomial approximation. **Results:** In control subjects, physiological bone marrow SUV of the spine was determined. In patients with lymphoma, bone marrow SUV decreased over time and reached a plateau at about 14 days after G-CSF administration, and was higher by 5% than the plateau at 10 days. SUV declined to the "physiological range", i.e., mean + 1SD of control patients, at 6-7 days. **Conclusion:** For a PET/CT study, an interval of 10 days after G-CSF is recommended in order to minimize the influence of G-CSF on the bone marrow when evaluating treatment response in patients with non-Hodgkin lymphoma.

P503**Positron Emission Tomography for Assessment of Bone Marrow Involvement in Patients with Malignant Lymphomas**

O. Mukhortova¹, I. Aslanidis¹, I. Shurupova¹, T. Katunina¹, A. Pivnik², D. Stroikovskii³, Z. Shavladze⁴; ¹Bakoulev Scientific Center for Cardiovascular Surgery, Moscow, RUSSIAN FEDERATION, ²Pirogov National Medical Surgery Center, Moscow, RUSSIAN FEDERATION, ³Moscow City Oncologic Hospital №62, Moscow, RUSSIAN FEDERATION, ⁴Research Center of Medical Radiology, Obninsk, RUSSIAN FEDERATION.

Purpose: To compare the potentialities of bone marrow biopsy (BMB) and positron emission tomography (PET) for assessment of bone marrow involvement in patients with malignant lymphomas. **Material and methods:** BMB and PET studies of 212 patients with histological verified Hodgkin and Non-Hodgkin lymphomas performed to evaluate dissemination of disease for primary diagnostics or relapse were analyzed retrospectively. In all patients iliac crest BMB was performed according to standard procedure (in 8 out of 212 - bilaterally). Whole-body PET was performed according to standard protocol in 90 minutes after injection of 350-400 MBq ¹⁸F-FDG. **Results:** Based on BMB and PET studies bone marrow involvement was found in 65 out of 212 patients (31%). Both methods gave concordant data in 29 (14%) patients. In 11 (5%) patients bone marrow involvement was detected only by BMB, in 25 (12%) patients - only by PET. PET results allowed to exclude bone lesions previously detected by structural diagnostics methods in 5 patients. BMB and PET identified patients had different types of bone marrow involvement: BMB mainly identified patients with diffuse type of involvement while PET detected focal lesion in 45 out of 54 patients. PET results changed the treatment in 23 (11%) out of 212 patients. **Conclusion:** PET and BMB are of complementary importance in detection of bone marrow involvement in patients with malignant lymphomas. To improve accuracy of bone marrow involvement diagnostics one should use both methods in correct sequence.

P504**FDG-PET for Differentiation of Aggressive and Indolent Malignant Lymphomas**

O. Mukhortova¹, I. Aslanidis¹, I. Shurupova¹, T. Katunina¹, A. Pivnik², D. Stroikovskii³, Z. Shavladze⁴; ¹Bakoulev Scientific Center for Cardiovascular Surgery, Moscow, RUSSIAN FEDERATION, ²Pirogov National Medical Surgery Center, Moscow, RUSSIAN FEDERATION, ³Moscow City Oncologic Hospital №62, Moscow, RUSSIAN FEDERATION, ⁴Research Center of Medical Radiology, Obninsk, RUSSIAN FEDERATION.

Purpose: To study the value of positron emission tomography with ¹⁸F-FDG (FDG-PET) for differential diagnostic of indolent and aggressive Non-Hodgkin lymphomas. **Material and methods:** FDG-PET results of 150 patients with malignant lymphomas of different histological types were analyzed retrospectively. Whole-body PET with ¹⁸F-FDG was performed according to standard protocol in 90 minutes after injection of 350-400 MBq ¹⁸F-FDG, in 2D mode, followed by semi-quantitative assessment of tracer uptake in pathological foci (SUVmax). **Results:** PET results revealed much more high average value of SUVmax in patients with aggressive types of Non-Hodgkin and Hodgkin lymphomas (17,85±8,43 and 17,33±3,08) than in patients with indolent Non-Hodgkin lymphomas (5,03±2,12), (p<0,001). Crossed range of SUVmax corresponding to either aggressive or indolent Non-Hodgkin lymphomas was found. Significant differences between average value of SUVmax for patients with primary detected and recurrent disease were not found. Given the threshold value of SUVmax =10,0 the sensitivity of FDG-PET in differential diagnostics of aggressive and indolent lymphomas is 94%, specificity - 90%. **Conclusion:** ¹⁸F-FDG uptake correlates with the aggressivity of malignant lymphomas. High level

of tracer uptake is representative only for aggressive types of Non-Hodgkin and Hodgkin lymphomas. High level of ^{18}F -FDG uptake in patient with the indolent lymphoma indicates most probably the transformation of indolent lymphoma into the aggressive one.

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The Role of Pet/Ct in the Evaluation of Bone Marrow Involvement in the Primary Staging of Lymphoma

T. Cakir¹, N. Gokcora¹, U. O. Akdemir¹, N. I. Karabacak¹, N. Akyurek², A. Cakir²; ¹Gazi University Medical Hospital Nuclear Medicine Dept., Ankara, TURKEY, ²Gazi University Medical Hospital Pathology Medicine Dept., Ankara, TURKEY.

Aim Bone marrow involvement is an important parameter that affects the stage, prognosis and the management of lymphoma patients. The aims of our study are; to determine the role of PET/CT in the assessment of bone marrow involvement in the primary staging of lymphoma patients using different quantitative measurement methods, to determine the most accurate quantitative measurement method, to reinterpret bone marrow biopsies using Fluorescent in situ hybridization (FISH) method to ascertain the accuracy of PET/CT in detection of bone marrow involvement and to investigate the effects of laboratory and clinical findings on the accuracy of PET/CT. Materials & methods Primary lymphoma patients who have their PET/CT imaging and bone marrow biopsies done in Gazi University Medical Hospital were included in this study. Using PET/CT data, bone marrow SUVmean, bone marrow to liver SUVmean ratio, bone marrow to blood pool SUVmean ratio and bone marrow to cerebellum SUVmean ratio values were obtained. Pathology reports, laboratory and clinical findings of the patients were recorded retrospectively. FISH was used to evaluate involvement of atypical lymphoid cells in the bone marrow of patients with mature B cell lymphoma using BCL2, BCL6, MYC and PAX5 probs. Results Fifteen bone marrow biopsies were positive with routine histopathological examinations. FISH method didn't increase the total number of the patients with bone marrow involvement. Two patients have positive bone marrow biopsies with FISH examination. There is no significant difference between the quantitative measurement methods of PET/CT in respect to detection of bone marrow involvement. However we decided that bone marrow to liver SUVmean ratio (BM/L SUV) is a suitable criterion to assess bone marrow involvement of primary lymphoma patients. Optimum cut off value for BM/L SUV ratio was found to be 1.8. Using this cut off value sensitivity, specificity, PPV and NPV of PET/CT is %53, %90, %53 and %90, respectively. In a selected subgroup of patients with aggressive lymphoma these values improved to %83, %97, %83 and %97, respectively. Using this cut off value, among patients with false negative results indolent lymphoma patients and patients with low lymph node SUVmax were more frequent. There is no significant laboratory difference (Sed, CRP, WBC, % Neutrophil) between patients with false positive and true positive results. Conclusion PET/CT had a high negative predictive value. Therefore in the primary evaluation of aggressive lymphoma patients with normal bone marrow PET/BT findings, PET/BT is a noninvasive alternative over bone marrow biopsy.

P506

The role of FDG-PET in pediatric Non-Hodgkin lymphoma

K. Nakatani¹, Y. Nakamoto¹, T. Suga¹, K. K. Miyake¹, K. Kurihara¹, T. Saga², T. Higashi³, K. Togashi¹; ¹Kyoto University Graduate School of Medicine, Kyoto, JAPAN, ²Molecular Imaging Center, National Institute of Radiological Sciences, Inage, JAPAN, ³Research Institute, Shiga Medical Center for Adults, Moriyama, JAPAN.

Objectives: Several reports have been indicating the usefulness of FDG-PET in pediatric Hodgkin lymphoma (HL); however, that in pediatric non-Hodgkin lymphoma (NHL) is not fully investigated. The characteristic of pediatric Non-Hodgkin lymphoma (NHL) is different from pediatric HL as well as from NHL in adults. We retrospectively evaluated the clinical value of FDG-PET for staging, monitoring therapy response, and post-therapeutic surveillance in pediatric NHL. Methods: FDG-PET was performed in 18 patients under 20 years old between Feb. 2000 and Jul. 2009 with histologically-proven NHL (Burkitt lymphoma 6; lymphoblastic lymphoma 5; diffuse large B-cell lymphoma 4; anaplastic large cell lymphoma 2; NK/T-cell lymphoma 1). Overall, 67 studies were performed: 3 for pre-chemotherapy staging (Group A), 35 for response assessment (Group B), and 29 for post-therapeutic surveillance (Group C). In Group A and C, we assessed the diagnostic performance and influence on treatment decisions in comparison with conventional imaging modalities (CIM). In group B, we investigated the influence on treatment. We also assessed whether PET for response assessment in time of the completion of chemotherapy (n=11, subgroup B') can help predicting outcome. Results: In Group A, PET results were comparable as yielded by CIM in all studies, without any alteration of therapeutic plans. In Group B, PET diagnoses were concordant with CIM in 21 studies and discordant in 9 studies (CIM was not available in 5 studies). In the discordant cases, PET suggested remnant lesions in 5 cases and CIM suggested in 4 cases; however, it was difficult to judge which modality was more reliable. PET modified the therapeutic strategies in 4 cases, in which PET detected new extra-nodal lesions: bone involvement in 2 cases, peripheral nerve involvement in 1 case, and thymic involvement in 1 case. In subgroup B', relapse was observed in 3 patients (27%); the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for prediction of relapse were 67%, 75%, 50%, 86%, and 73%, respectively. Consequently, the likelihood ratio was 2.67. In Group C, no relapse was observed, with the specificity of 86%. Conclusion: These preliminary data suggest that the contribution of FDG-PET to therapeutic strategy and its prognostic value at the completion of chemotherapy may be limited, compared to pediatric HL or adult NHL. Nevertheless, FDG-PET would have a complementary role as it can identify unexpected extra-nodal involvement even during chemotherapy.

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Automated quadruple fusion of primary and interim PET/CT study pairs in lymphoma patients

L. Papp¹, N. Zsoter¹, A. Panyik¹, A. Illes², S. Barna³, U. Luetzen⁴, I. Garai³; ¹Mediso Medical Imaging Systems Ltd., Budapest, HUNGARY, ²3rd Department of Internal Medicine, Medical University of Debrecen, Debrecen, HUNGARY, ³PET-CT Medical Diagnostic Ltd, Medical University of

Debrecen, Debrecen, HUNGARY, ⁴University Clinic Kiel, Nuclear Medicine Department, Kiel, GERMANY.

Aim: Hybrid PET/CT cameras brought great benefits into the field of nuclear medicine providing an implicit solution of image misalignments. Nevertheless, the spatial alignment of primary staging and interim PET/CT study pairs still needs to be solved by post-registration methods for an accurate comparison. In this case four images are present and one transformation is unknown, hence the nature of the fusion dramatically changes comparing to the classic dual fusion. Our goal was to design and evaluate a native automated quadruple fusion framework of hybrid study pairs and to investigate its accuracy comparing to classic dual fusion methods. Methods: 74 whole body PET/CT primary and interim study pairs were collected that were previously evaluated visually as partial metabolic response and stable disease. The reconstructed attenuation corrected PET and its corresponding CT were chosen to represent a study. The average time between the studies was 90 days (after 2 cycle of chemotherapy). A quadruple fusion framework was implemented to get four images from a medical physician. A four-dimensional normalized mutual information (4NMI) similarity measurement was implemented to calculate the similarity of all four images at the same time. Downhill-Simplex optimization method was adopted to determine a transformation for the interim PET/CT pair. To compare the result of the quadruple registration, classic dual registration between the CTs was performed, and the gained transformation was applied to the interim PET as well. The registration process and the result were observed by a physician in a quadruple fusion viewer of InterView Fusion software manufactured by Mediso. Results: The average error of the quadruple registration was 1.2mm (std.dev. 0.87mm), while classic dual registration between CTs had 1.9mm (std.dev. 0.79). The quadruple registration needed 23% less iterations to converge to the optimal transformation. Conclusions: We have presented a quadruple fusion framework which successfully fused the input PET/CT study pairs with a high accuracy. Additionally the method needed less iteration to reach a higher accuracy comparing to the classic dual registration method which is a gold standard in present day medical registration techniques. As the next step of our research we will focus on the automated segmentation and quantification of every corresponding lymphoma on both primary and interim PET images in order to measure their statistical change in time.

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18F-FDG-PET imaging in the evaluation of cutaneous lymphoma

N. Watanabe¹, M. Taniguchi¹, T. Takahashi¹, M. Doai¹, I. Toyoda¹, H. Tonami¹, K. Nakajima², S. Kinuya³; ¹Kanazawa Medical University, Kahokugun, JAPAN, ²Kanazawa University, Kanazawa, JAPAN, ³Kanazawa University, Kanazawa, JAPAN.

The purpose of this study was to investigate the clinical usefulness of 18F-FDG-PET imaging in the diagnostic evaluation of 20 cutaneous lymphoma patients with B cell lymphoma (6/20) and T cell lymphoma (14/20). Methods: Patients were assessed by PET or PET/CT for cutaneous, nodal and solid organ FDG uptake, and comparisons were made to CT data alone and to the physical examination. Results: 18F-FDG-PET/ imaging showed increased uptake in 16/20 patients (80%) and was negative in 4/20 patients (20%). In T cell lymphoma, 18F-FDG-PET imaging showed increased uptake in 11/14 patients (78%). It was negative in 3 patients of early-stage mycosis fungoides. In B cell lymphoma 18F-FDG-PET imaging showed increased uptake in 5/6 patients (83%). It was negative in 1/6 patients (17%). Conclusion: These results suggest that 18F-FDG-PET imaging may be useful for detecting of the primary lesion and for evaluating recurrence after chemotherapy with cutaneous lymphoma. However it may be limited to detect the lesions of early-stage cutaneous lymphoma.

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The clinical impact of 18F-FDG PET/CT in Hodgkin lymphoma

Z. Molnar¹, B. Deak¹, Z. Lengyel², P. Molnar², A. Rosta¹, T. Schneider¹, E. Szaleczky¹, F. Varga¹, E. Varady¹, K. Borbely¹; ¹National Institute of Oncology, Budapest, HUNGARY, ²Positron Diagnostic LTD, Budapest, HUNGARY.

Purpose: Hodgkin lymphoma (HL) is one of the mostly curable malignant diseases. In the optimal management of patients the exact stage of the disease is highly important. CT is the standard method for staging of HL. Approximately two-third of patients present with residual masses after completion of therapy, however, only about 30 % will relapse. The sensitivity of CT is about 40% in this indication. The metabolic information by Positron Emission Tomography - Computer Tomography (PET/CT) is reported to be more accurate. The purpose of this study was to test the clinical impact of 18F-FDG PET/CT in the management of patients with HL. Patients and methods: Two hundred fourteen PET/CT examinations were performed between April 2005 and August 2009 in 138 patients. According to PET/CT indications there were patients for staging (n=32); therapy control (n=47), including interim tests (n=17) and investigation before radiotherapy (RT, n=31); restaging (n=123); suspicion of relapse or progression (n=12). PET/CT results were compared to clinical and/or pathological follow-up data. Results: In 22 patients complete metabolic remission was reported before RT, and no relapse was observed. In 9 patients active residual mass was detected by PET/CT before RT. In 6 patients complete remission was achieved by RT, however, in 3 cases progression was found. The group of patients with suspicion of progression or relapse (n=12) included 7 patients with true negative and 5 cases of true positive results. From the 123 restaging examinations there were 22 true positive and 16 false positive cases. Eighty-three true negative and 2 false negative cases were observed. The sensitivity of the PET/CT was 92 %, specificity 84%, the positive predictive value 58 % and the negative predictive value 98 %. Conclusion: FDG-PET is a highly useful method for staging, and posttreatment evaluation of patients with HL. It has high sensitivity, high specificity, and high negative predictive value as a restaging method. However, positive results must be carefully analyzed.

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Feasibility of ^{90}Y bremsstrahlung emission computed tomography after ^{111}In administration

S. Ito¹, S. Inoue¹, S. Tomiguchi¹, S. Shiraiishi¹, S. Nosaka¹, K. Kawanaka¹, M. Yoshida¹, F. Sakaguchi¹, N. Katsuda², T. Nozaki², Y. Yamashita¹;

¹Kumamoto University, Kumamoto, JAPAN, ²Kumamoto University Hospital, Kumamoto, JAPAN.

Objectives: Yttrium-90 (⁹⁰Y)-ibritumomab tiuxetan has been used for treating patients with relapsed, refractory, low-grade, follicular, and/or CD20+ transformed non-Hodgkin's lymphoma (NHL). ⁹⁰Y biodistribution images are indispensable for confirming its uptake and estimating the absorbed doses. We recently reported how ⁹⁰Y bremsstrahlung emission computed tomography (⁹⁰Y BECT) images can be demonstrated by using a gamma camera equipped with a medium energy collimator. The ⁹⁰Y BECT images in a 57-232 keV window displayed 1 cm diameter ⁹⁰Y globular sources simulating lymph nodes. The patient is administered ¹¹¹In before ⁹⁰Y treatment. When ⁹⁰Y images are acquired by using gamma cameras after ¹¹¹In administration, ¹¹¹In images overlap with ⁹⁰Y images. This study demonstrates images obtained by simultaneous dual isotope ⁹⁰Y/¹¹¹In emission computed tomography (⁹⁰Y/¹¹¹In SPECT), and separates individual images of ⁹⁰Y bremsstrahlung emission computed tomography (⁹⁰Y BECT) and ¹¹¹In single photon emission computed tomography (¹¹¹In SPECT) from ⁹⁰Y/¹¹¹In SPECT images. **Methods:** ⁹⁰Y/¹¹¹In SPECT images of a phantom were acquired by using a gamma camera (SKYLight, Phillips) equipped with medium energy general purpose parallel-hole collimators. The images obtained with nine energy windows (65, 80, 97, 114, 140, 171, 209, 245, and 299 keV; width 20%) were reconstructed by using the ordered subsets expectation maximization (OSEM) methods. ⁹⁰Y and ¹¹¹In images were separated from the SPECT images by using count rates and correction factors in each window. The ⁹⁰Y BECT images were obtained by combining the images of the nine windows. ⁹⁰Y BECT images of three patients were obtained by using this method. **Results:** Individual ⁹⁰Y BECT and ¹¹¹In SPECT images as well as ⁹⁰Y/¹¹¹In SPECT images were displayed in all of the windows. In the ⁹⁰Y BECT images, the 80 keV, 171 keV, and nine windows showed approximately the same resolution and image quality. Loaded activity of ⁹⁰Y was estimated less than an uncertainty of ±6%. ⁹⁰Y BECT displayed biodistribution and quantified ⁹⁰Y activity. One whole body image can be taken for 60-90 min. In some areas, ⁹⁰Y biodistribution was different from ¹¹¹In. **Conclusions:** Individual ⁹⁰Y BECT and ¹¹¹In SPECT images were clearly separated from the ⁹⁰Y/¹¹¹In SPECT images by using correction factors.

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Detection of bone marrow disease in patients with HD and aggressive NHL. (18F)FDG-PET/CT scan versus bone marrow biopsy accuracy: results from a large multicenter study

D. Penna¹, A. Douroukas², A. Amati¹, V. Arena¹, E. Pelosi¹; ¹IRMET S.p.a., Turin, ITALY, ²Nuclear Medicine Unit, Major Hospital San Giovanni Battista, University of Turin, Turin, ITALY.

Objectives: to compare the accuracy of bone marrow biopsy (BMB) and positron emission tomography (PET) in bone marrow disease (BMD) detection, in a large multicentre population of patients with new diagnosis of malignant lymphoma. **Methods:** 330 consecutive patients with new diagnosis of malignant lymphoma, were retrospectively included (127 HD, 203 aggressive NHL); to complete the staging all patients underwent whole-body CECT, BMB and PET/CT scan with (18F)FDG. At the end of the treatment all of them were studied with a second PET scan. Sensitivity, specificity, and accuracy of both techniques in BMD detection were evaluated and compared. **Results:** 85 patients with BMD (24 positives at both exams, 27 only at the BMB and 34 only at the PET study). No significant differences were observed between PET and BMB respect to the sensitivity (68 vs. 60%, respectively), the specificity (99 vs. 100%), the positive predictive value (97 vs. 100%), the negative predictive value (90 vs. 100%) and the accuracy (91 vs. 90%). **Conclusions:** - the sensitivity of PET and BMB is similar (68 and 60%, respectively), - PET and BMB are complementary: in fact out of 85 patients with confirmed BMD only 24 are positive at both exams, while 27 only at the BMB and 34 only at the PET exam, - the integration of PET findings with BMB ones increases the diagnostic accuracy. Consequentially PET is essential during the staging of malignant lymphomas.

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Clinical impact of 18F-FDG-PET/CT in detecting asymptomatic recurrence in the surveillance of patients with lymphoma

B. Gonzalez García, M. E. Bellón Guardia, A. Palomar Muñoz, A. M. García Vicente, P. Talavera Rubio, V. M. Poblete García, P. Pilkington Woll, A. Nuñez García, J. M. Cordero García, I. Cepedello Boiso, A. Soriano Castrejon, Nuclear Medicine Department. Hospital General, Ciudad Real, SPAIN.

AIM: To assess the utility of ¹⁸F-FDG-PET-CT in detecting recurrence in patients with lymphoma free of disease during follow up. **MATERIAL AND METHODS:** We retrospectively assessed 220 PET-CT studies belonging to 100 patients who had achieved complete response confirmed by PET. The mean follow up period from this negative PET was 26 months (ranged 12-48 months). The mean age was 56 (ranged 12-76 y). PET-CT studies were performed following a standardized protocol with a hybrid equipment (GE DSTE-16). PET-CT was considered positive if an abnormal uptake, in a non physiological location, above background activity was detected. Final diagnosis was obtained by pathologic assessment when it was possible or clinical follow up of at least 6 months. **RESULTS:** From the selected patients, 54 had a Hodgkin's Lymphoma and 46 a Non Hodgkin's Lymphoma. According to staging, 6% were Stage I, 39% stage II, 22% stage III and 33% stage IV. 24 PET-CT scan were suspicious of relapse. The most frequent locations were lymph node sites, although 3 cases presented lung lesions and other 2 cases showed bone disease. Only 10 were confirmed as recurrence, while the others were considered false positive after biopsy (2 cases) or follow up. We obtained a sensitivity, specificity, NPV and PPV of PET-CT in detecting recurrence of 100%, 93.1%, 100% and 41.6% respectively. The incidence of relapse in our sample was 10%. **CONCLUSION:** PET-CT has an important role in the follow-up of asymptomatic patients with lymphoma due to his high sensitivity to detect relapse and a high negative predictive value. Nevertheless, because of the high number of false positive results, histological confirmation should be obtain.

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Interim-PET in paediatric Hodgkin's lymphoma

E. Lopci¹, R. Burnelli², L. Guerra³, A. Piccardo⁴, A. Cistaro⁵, C. Nanni¹, E. Derenzini¹, G. C. Montini¹, V. Ambrosini¹, I. Santi¹, M. Celli¹, S. Fanti¹; ¹hospital s. orsola-malpighi, Bologna, ITALY, ²hospital s. anna, Ferrara, ITALY, ³hospital s. gerardo, Monza, ITALY, ⁴hospital Galliera, Genova, ITALY, ⁵IRMET, Torino, ITALY.

Aim: FDG-PET in adult Hodgkin's Disease (HD) has revealed as a significant predictor to progression-free survival (PFS), by resulting also the only independent predictive factor to longer disease-free periods. Not much is known in this same context in paediatric population, therefore we aimed assessing PET role, when performed in children after few cycles of chemotherapy. **Materials and Methods:** For the study we analysed data from 77 paediatric patients (mean age 13years, range 2-18) affected by HD and enrolled for the AIEOP-LH2004 therapeutic protocol in 9 different Italian Centres. Patient characteristics: stage I-II 35pts, III-IV 42pts; 45 bulky, 35 B-symptoms. All patients had a PET scan performed at mid-treatment, after 2/4 cycles of chemotherapy. The scan was done according to standard procedure and thus reported as positive (residual, stable or progressive disease) or negative (disappearance of previous lesions, no new lesions, or no pathological uptake) on a visual and/or semiquantitative basis. All patients were followed up for a mean period of 2years (1-5), and for each child we calculated PFS. True outcome of the patients was defined as remission (no evidence of lymphoma) and disease, on the basis of clinical monitoring, instrumental and histological data at follow-up. A statistical analysis was performed with respect to interim-PET results and PFS, by using Kaplan-Meier survival curves and Cox proportional-hazards regression, in order to define possible predictive factors. A p value less than 0.05 was considered significant. **Results:** Interim-PET results with respect to patients' outcome are shown in the attached table. In 7 patients we documented presence of disease during follow-up (9,1%). Altogether patients had a mean PFS of 29months (range 4-64). No statistical significance was documented in between response rates, as assessed by interim-PET, and patient outcome ($p = 0,48$).

		Interim-PET	
OUTCOME		neg	pos
remission	62	8	70 (90,9%)
disease	5	2	7 (9,1%)
		67 (87%)	10 (13%) 77

Chi-square analysis $p = 0,48$

Also when performing the Kaplan-Meier analysis, interim-PET showed no significant relation with PFS ($p = 0,20$). Other potential predictive factors were considered for the analysis, such as stage, presence of bulky masses, B-symptoms and cycles of therapy performed, but none of them resulted significantly predictive to PFS. **Conclusions:** Unlike adult HD, interim-PET in paediatric population, when performed after 2-4cycles of chemotherapy, shows no value in predicting longer progression-free survival.

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Role of FDG-PET/CT in assessment of gastric lymphoma

M. O. Tamam, H. S. Yavuz, O. Eker, M. Malazimoglu, T. Ozpacaci; Okmeydani Training and Research Hospital, Istanbul, TURKEY.

AIM:18F-fluoro-2-deoxyglucose positron emission tomography / computed tomography (FDG-PET/CT) is widely used for initial staging and follow-up in patients with malignant lymphoma. In this study, we evaluated the efficiency of FDG-PET/CT in staging gastric lymphoma. **MATERIAL-METHODS:** A total of 33 patients with histological diagnosis of gastric lymphoma were referred to our clinic and scanned with FDG-PET following standard procedures. 15 out of 33 were male and 18 female. The mean age was 52,8 ±15,7 years (range 26-80 years). Histopathologic diagnosis of gastric lymphoma was detected generally by endoscopy and revealed diffuse large B-cell lymphomas (DLBCL) (n:16), marginal zone B-cell lymphomas of mucosa-associated lymphoid tissue (MALT lymphomas) (n:5), and B cell high grade lymphomas(BCHGL) (n:12). **RESULTS:** In 8 out of 33 patients the result of FDG-PET/CT was normal (5 patients had total/subtotal gastrectomy, 3 patients was MALT lymphoma). In 6 patients diffuse increased uptake in gastric wall, in 7 patients both gastric and supra-infradiaphragmatic nodal increased uptake, in 7 patients both gastric and infradiaphragmatic nodal increased uptake, in 2 patients both gastric and supra-infradiaphragmatic nodal increased uptake. Out of 3 patients who were operated, 1 patient had infradiaphragmatic lymphadenopathy, and 2 had supra-infradiaphragmatic lymphadenopathy. FDG-PET/CT detected extranodal involvement in 15 patients. In our study, 3 patients with primary gastric MALT lymphoma had a negative FDG-PET/CT scan and 2 had low SUV. Thus, although the diagnostic value of FDG-PET/CT scans for primary gastric MALT lymphoma is less than that for DLBCL or, BCHGL, it might be a better imaging option than CT scans. Post treatment FDG-PET/CT was applied to 16 patients. 5 patients had progression and 11 had regression of gastric lymphoma after treatment. Among 8 patients who had normal result in previous FDG-PET/CT, progression was observed in 2. **CONCLUSION:** Whole-body FDG-PET/CT is highly sensitive in detecting gastric lesions and supra/infradiaphragmatic nodal and extranodal involvement, with the exception of primary gastric MALT lymphoma in which the FDG-PET/CT scan SUV value is low

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Evaluating Interim 18F-FDG-PET/CT in Patients Undergoing First Line Therapy for Lymphoma Using a Comparative Scoring System

J. P. Teixeira, I. Lucena, H. Duarte, L. Costa, F. Lopes, O. Soares, A. L. Bastos; Instituto Português de Oncologia, Porto, PORTUGAL.

Introduction. The role of interim 18F-FDG-PET/CT (iPET) in the early monitoring of Lymphoma treatment has been well established, including the possibility of early change into a more aggressive strategy in non-responders. However, determining what constitutes a functionally positive iPET that justifies immediate escalation of therapy (ieOT) is often a challenge. The aim of this study is to evaluate our early experience using an objective Scoring system to classify iPET,

based on comparison with baseline PET (bPET), as proposed by other authors. Material and Methods Retrospective study of 43 patients (23 male; age 18-82/median 42) with recently diagnosed Lymphoma (12 HL, 31 NHL), who underwent iPET for early assessment of first line therapy between 01/03/2009 and 26/11/2009. iPETs were classified as: S0 (no foci of FDG uptake), S1 (1 residual focus, reduced uptake compared to bPET), S2 (>1 focus but less than bPET, reduced uptake); S3 (same number of foci as bPET, reduced uptake) and S4 (same/increased number of foci as bPET, unchanged/increased uptake). Clinical and imaging data available until 09/04/2010 was reviewed. Results S0: 25 iPETs (9 HL, 16 NHL). None were submitted to iEoT and all achieved complete remission (CR). S1: 8 iPETs (1 HL, 7 NHL). The patient with HL was submitted to iEoT, due to persistent FDG uptake in the lung, achieving CR afterwards. The remaining 7 patients were not submitted to iEoT, and all achieved CR except one, which awaits PET evaluation after Radiotherapy. S2: 9 iPETs (1 HL, 8 NHL). The patient with HL was submitted to iEoT, with CR after completion of therapy. Of the 8 NHL patients 3 were submitted to iEoT, with 1 achieving CR and 2 showing progressive disease (PD), and 5 were not submitted to iEoT, with 2 achieving CR, 2 achieving partial response and 1 showing PD. S3: 1 iPET in a patient with HL, who was submitted to iEoT, with CR after completing therapy. No iPETs were classified as S4. Conclusions This Scoring System can be a useful tool in the evaluation of iPET, particularly in S0 or S1 (good response to therapy predicted) and S3 or S4 (poor response to therapy, iEoT should be strongly considered). iPETs with Score 2 should be correlated with all available clinical data, and patients should be individually considered for eventual iEoT. A study with a larger population and longer follow-up time is required to fully understand the value of this System.

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Prognostic value of interim 18F-FDG PET/CT in mediastinal bulky Hodgkin lymphoma.

N. Beranger¹, L. Vercellino¹, C. Algrin², D. Groheux¹, E. Hindie¹, D. Lussato¹, J. Briere³, P. Brice², A. Martineau¹, C. Thiebemont⁴, J. Moretti¹,
¹Nuclear Medicine Department, Hôpital Saint Louis, PARIS, FRANCE, ²Hematology, Hôpital Saint Louis, PARIS, FRANCE, ³Pathology, Hôpital Saint Louis, PARIS, FRANCE, ⁴Hematology, Hôpital Saint Louis, PARIS, FRANCE.

Aim: Interim 18FDG PET (iPET) is strongly correlated with progression free survival (PFS) in Hodgkin Lymphoma (HL). We wanted to determine if Negative Predictive Value (NPV) remains high in patients who present with mediastinal bulky disease. **Materials and Methods:** We retrospectively investigated 38 previously untreated HL patients (pts) with localized mediastinal bulky disease; 27 were considered unfavourable stage II and 11 stage IV (because of local extension to: pleura, lung, or pericardium). All patients were treated with chemotherapy. Fourteen stage II patients received additional radiotherapy. Three patients (1 stage II, 2 stage IV) received high dose therapy followed by autologous stem cells transplantation. Images were retrospectively visually interpreted by 2 experienced nuclear medicine specialists blinded to clinical history. iPET were interpreted as positive (Pos) (focally increased uptake clearly higher than surrounding mediastinal background), correlated with morphologic CT information and a known previously involved area when baseline PET was available. iPET were interpreted as negative (Neg) in other cases. In case of disagreement, a consensus reading was performed. Results were compared with the clinical status at the last follow up. **Results:** Initial PET examination (T0) was available in 24 patients. A PET/CT imaging was performed after two courses (T2) of chemotherapy in 31 patients, three courses (T3) in one patient, and four courses (T4) in 8 patients. Two patients had two iPET, so that a total of 40 iPET was realized. Thirty one patients (33 iPET) didn't relapse (median PFS of 13.5 months, range 4.8-45.5), among them 27 had a negative iPET. Four had a positive iPET with a median PFS of 17.5 months (range 8-29). Seven patients relapsed: 6 stages II, and one stage IV with a median PFS of 19.4 months (range: 6.9-30). Five had a negative iPET and 2 a positive iPET. Overall, the accuracy of iPET was 76% (29/38), the NPV 85% and the PPV 30% (but follow-up is still short and the number of patients limited).

	Neg iPET	Relapse (pts)	Pos iPET	Relapse (pts)
Stage II	24	5	4	1
Stage IV	9	0	3	2

R=relapse. **Conclusion:** Our results show that NPV of FDG PET remains high (85%) even for mediastinal bulky HL. The ability to predict relapse particularly for unfavorable stage II has to be further assessed.

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Our experiences with ¹⁸F-FDG PET-CT in mantle cell lymphoma

Z. Tóth¹, V. Tóth¹, Z. Varga¹, H. Galgóczy¹, P. Szabó¹, A. Németh¹, T. Györke¹, A. Fekesházy¹, T. Masszi², M. Udvardy³, Á. Illés³, I. Garai¹,
¹PET-CT Medical, Diagnostic Ltd., Budapest, HUNGARY, ²Department of Hematology and Stem Cell Transplantation, St. István and St. László Hospital, Budapest, HUNGARY, ³Department of Internal Medicine, Medical and Health Science Center, University of Debrecen, Debrecen, HUNGARY.

We assessed the accuracy and short term prognostic value of ¹⁸F-FDG PET-CT in pre-treatment staging, interim- and post chemotherapy restaging examinations, pre- and post-Hematopoietic Stem Cell Transplantation (HSCT) evaluation, and in clinically suspected relapse of mantle cell lymphoma. 80 PET-CT examinations of 41 patients were retrospectively analysed (9 pre-treatment, 6 interim, 12 restaging, 13 pre-, 17 post-HSCT examinations, and 23 PET-CT examinations due to clinically suspected relapse). All the staging examinations before initial therapy had revealed pathologic FDG accumulating foci. The bone marrow involvement (6/9) was only detectable in half of the cases (3/6). In 11/80 examinations pathologic FDG accumulation was observed in the gastrointestinal tract. In 2 cases further investigation was not performed, the endoscopic and histological verification proved 4 lymphoma manifestations, 3 adenomas, 1 colon carcinoma, and we had 1 negative endoscopy as well. Among the interim examinations in 4 cases complete metabolic remission (CMR), in 2 cases partial response was found. Among the 7/12 restaging PET-CT examinations indicating CMR, 3 patients relapsed within 1 year. Among the examinations showing CMR on the pre-transplantation PET-CT (8/13), relapse evolved in 1 case in the first year after transplantation. In 1 of 17 examinations CMR was not achieved after HSCT, from the 15 of 17 cases showing CMR on post-HSCT PET-CT, 2 patients

relapsed within 1 year. In 1 of 17 post-transplantation examinations clinical signs of relapse did not develop after positive PET-CT. Clinical relapse suspicion was confirmed by PET-CT in 6 cases, in 3 of 23 cases it was found to be false positive, in the remaining patients relapse did not evolve after negative PET-CT (14/23). FDG PET-CT seems to be an accurate method in the diagnostic workup of mantle cell lymphoma, although it may be false negative in the evaluation of bone marrow involvement, and seems to be specific regarding the gastrointestinal tract. Its short term negative predictive value appears to be acceptable, but remains below the results achieved in Hodgkin- and high grade B cell lymphomas.

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PET-CT appearance of relevant radiological pulmonary findings in patients with lymphoma

N. Fedinecz¹, S. Barna¹, B. Mándi¹, B. Szűcs¹, F. Magyar², Z. Miltényi², Á. Illés², I. Garai¹,
¹PET-CT Medical, Diagnostic LTD., Debrecen, HUNGARY, ²3rd Department of Internal Medicine, University of Debrecen, Debrecen, HUNGARY.

Pulmonary abnormalities are not uncommon on 18FDG PET-CT in patients diagnosed with lymphoma and may often cause differential diagnostic problems. These abnormalities may represent manifestation of lymphoma, inflammation, other pathology or might be clinically irrelevant. The aim of our retrospective study was the evaluation of relevant pulmonary findings with a follow-up period of 1-24 months. The analysis involved 1085 PET-CT examinations of 721 lymphoma patients. Pulmonary nodules smaller than 5 mm and fibrotic changes were regarded as radiologically irrelevant. A distinction was made between infiltrative and solid lesions based on their radiological appearance, and lesions were further characterised by their FDG-PET positivity. Differential diagnosis was made according to histology, clinical course of the disease, laboratory and microbiology results. Relevant radiological abnormalities were found in 116 patients (10.7%), of which 36 were diagnosed with Hodgkin (HL) and 80 with non-Hodgkin lymphoma (NHL). There were 45 infiltrative (8 FDG negative and 37 FDG positive) and 59 solid lesions (19 FDG negative and 40 FDG positive). Twelve patients were lost to follow-up. With regard to PET negative pathologies other than inflammation or lymphoma, there were 2 benign pulmonary nodules and interstitial lung disease was found in one case. Apart from the non-neoplastic cases, there were 2 primary lung tumours amongst the PET positive cases. The pulmonary manifestation of NHL was found to be solid PET-positive in all cases in our study, whereas infiltrative PET-positive finding was twice as common as the solid appearance in HL patients. Our results draw attention to the different appearances of pulmonary manifestations of lymphoma, which can be very useful for the correct staging of the disease.

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Could we avoid contrast-enhanced full-dose CT in lymphoma patients?

I. Navales Mateu, S. Rubí Sureda, X. Setoain, S. Rodríguez, C. Ayuso, B. Domenech, D. Fuster, F. Pons; Hospital Clínic i Provincial de Barcelona, Barcelona, SPAIN.

AIM: This study prospectively compares the agreement between contrast-enhanced full-dose PET/CT (PET/CECT) and unenhanced low-dose PET/CT (PET/NCECT) in initial staging and the evaluation of treatment response in lymphoma patients. **MATERIAL AND METHODS:** 62 biopsy-proven lymphoma patients (21 Hodgkin disease, 41 non-Hodgkin lymphoma), underwent a staging 18F-FDG PET/CT study that included unenhanced low-dose CT and enhanced full-dose CT. The same studies were repeated after the end of treatment. Each modality of PET/CT images was evaluated by a pair of readers: 1 radiologist and 1 nuclear physician, both unaware of the results of the other modality. PET/CT lesions were assessed in cervical, thoracic, abdominal and extra nodal regions. Treatment response was assessed in the same regions as well as to determine the complete or partial remission (CR and PR) or progressive disease (PD). Agreement between techniques was determined by the kappa-statistic. **RESULTS:** STAGING: PET/NCECT detected lesions in the following regions: cervical in 41 patients, thoracic in 31 and abdominal in 29. PET/CECT detected cervical lesions in 42 patients, thoracic in 31 and abdominal in 30. PET/NCECT and PET/CECT detected 22 cases of extra nodal disease. The total number of indeterminate findings for region-based analysis was 4 for PET/NCECT and 11 for PET/CECT. At staging, agreement between the 2 types of PET/CT in lesion detection was almost perfect for each region considered (kappa > 0.8; p < 0.05) as well as for disease stage (kappa = 0.908; p < 0.05) as well as for assessing CR, PR or PD (kappa = 1.00; p < 0.05) without discordant findings. **TREATMENT RESPONSE:** PET/NCECT detected lesions in the following regions: cervical in 3 patients, thoracic in 6 and abdominal in 7. PET/CECT detected cervical lesions in 3 patients, thoracic in 5 and abdominal in 8. PET/NCECT detected 2 cases of extra nodal disease and PET/CECT detected 3 cases. The total number of indeterminate findings for region-based analysis was 6 for both PET/NCECT and PET/CECT. Agreement at treatment response between the 2 types of PET/CT was almost perfect for each region considered (kappa > 0.7; p < 0.05) as well as for assessing CR, PR or PD (kappa = 1.00; p < 0.05) without discordant findings. **CONCLUSION:** Unenhanced low-dose PET/CT should be enough in most lymphoma patients as the only imaging technique for the initial staging and subsequent treatment response evaluation.

P520

The Impact of PET/CT on Clinical Decision Making Process in Lymphoma Patients with Residual Masses after Therapy

S. Lucic, D. Jovanovic, A. Peter, M. A. Lucic, K. Nikoletic, D. Srbovan; Institute of Oncology of Vojvodina, Sremska Kamenica, SERBIA.

Aim: Although PET/CT is well established imaging technique in staging and follow-up of lymphoma patients, until recently it has been a rather rare imaging tool in the routine work in Serbia. Hence, we tried to evaluate would the implementation of FDG PET/CT in the traditional follow-up diagnostic algorithm have impact on the actual clinical decision making process in the lymphoma patients with positive CT finding of after-therapy persistent residual masses. **Materials and Methods:** In 65 lymphoma patients (23 women and 40 man, aged 13-75 years (mean age 36.11±15.06 years); 40/65 with Hodgkin's lymphoma (HL), out of them 1 in IE stage, 3 in stage I, 24 in stage II, 20 in stage III, and 17 in stage IV; and 25/65 patients with non-Hodgkin lymphoma

(nHL), out of them 1 in stage I, 4 in stage II, 9 in stage III, and 11 in stage IV) with chest-abdominal-pelvic CT findings of residual masses, whole body FDG PET/CT has been performed 4-6 weeks after completion of chemotherapy or 3-4 months after the completion of radiotherapy. Results: FDG PET/CT was interpreted as positive or negative on the basis of the response assessment by Revised International Workshop Criteria. FDG PET/CT indicated negative residual masses in 36 (55.4%), positive in 26 (40%) and equivocal in 3 (4.6%) patients. In a HL group of patients we found 27 (67.5%) negative, 10 (25%) positive and 3 (7.5%) equivocal findings, while in non-Hodgkin group there were 9 (36%) negative and 16 (64%) positive findings. Considering the stage of disease, the results of FDG PET/CT evaluation demonstrated negative findings in all patients in IE stage and stage I, while in the stage II group of patients 15 findings (62.5%) were negative, 7 (29.17%) positive and 2 (8.3%) equivocal; in stage III group 9 (45%) were negative and 11 (55%) positive; and in stage IV group 8 findings (47%) were negative, 8 (47%) positive and 1 (6%) equivocal. Conclusion: FDG PET/CT is an efficient method for assessment of therapy in lymphoma patients and, as expected, may significantly improve the clinical decision making process in lymphoma patients with positive CT findings of residual masses.

P46 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Oncology Clinical Science: Leukemia & Myeloma

P521

Value of FDG-PET and somatostatin receptor scintigraphy for detecting multiple myeloma activity in patients with relapsing disease

R. H. J. A. Slart, E. G. M. de Waal, R. A. J. O. Dierckx, E. Vellenga; University Medical Center Groningen, University of Groningen, Groningen, NETHERLANDS.

Introduction: Osseous involvement is one the predominant features of patients with multiple myeloma (MM). Radiography is the standard method for defining skeleton abnormalities but might have limited value in relapsing disease due to preexisting defects. [¹⁸F]-18F-fluorodeoxyglucose positron emission tomography (FDG-PET) imaging can also be useful for detecting osseous involvement in patients with MM and is not hampered by preexisting defects since it reflects enhanced metabolic activity of the malignant plasma cells. Somatostatin receptor scintigraphy (SRS) is an alternative manner for defining MM activity. Recently it was shown that SRS can detect skeleton abnormalities in a high number of relapsing MM patients (Eur.J.Nucl.Med.Mol.Imaging 2010;37:124) even when no X-ray skeleton changes were observed. **Aim:** Comparison of MM activity with FDG-PET, SRS and whole body radiography in relapsing MM patients for osseous and extra-osseous involvement. **Materials and Methods:** A total of 13 patients with relapsing MM disease underwent FDG-PET, SRS and whole body X-ray. Comparison was made between total lesions detected with the separate imaging methods. **Result:** A positive FDG-PET was demonstrated in 62% of the patients, with an average of 4 lesions (range 3 - 12) per patient. The mean SUVmax was 3.5 (range 1.4 - 15.8). SRS was positive in 77% of patients, with an average of 2 lesions per patient (range 1 - 5). In 62% of the patients new X-ray lesion with an average of 2 lesions (range 2 - 4) were found. In 50% of patients both FDG-PET scan and the SRS were positive. In 15% of the patients the FDG-PET scan was negative although the SRS showed enhanced activity of intrapulmonary lesion in these patients. One patient (7%) had new X-ray findings without FDG-PET or SRS lesions. Overall the FDG-PET and SRS showed much more new lesions in the studied patients than the X-ray studies. **Conclusion:** Preliminary results showed that SRS detected more patients with relapsing MM activity than FDG-PET and X-ray, but the number of lesions per patient were higher with FDG-PET scan. FDG-PET and SRS may be used to monitor MM disease activity during follow-up.

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Oncology Clinical Science: NET (Neuroendocrine Tumors)

P522

Comparison of labeled MIBG and somatostatin analogs in imaging neuroendocrine tumors

M. Ozhan, L. Kabasakal, S. Senyuz Mut, S. Nisli, B. Gunes, I. Uslu; Department of Nuclear Medicine, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, TURKEY.

Aim: Neuroendocrine tumors originate from cells programmed to adopt a specific neuroendocrine phenotype. Neuroendocrine tumors express active amine precursor uptake-1 mechanisms and/or specific receptors at the cell membrane. This has been used for both the detection and treatment of such tumors, with the development and application of radiopharmaceuticals reliant upon such specific mechanisms. This study in patients with neuroendocrine tumors was designed to assess octreotide in comparison with standard miodobenzylguanidine (MIBG) scintigraphy and to study functional activity of somatostatin receptors. **Methods:** 111In-DTPA-D-Phe-octreotide (at a dose up to 111-222 MBq) and ¹²³I]MIBG (at a dose of 130-185 MBq) was given as a bolus iv injection to 13 patients. Whole body planar images were obtained after 4 and 24 h and then spect images were obtained (in one of these patients, 99m-Tc-EDDA/HYNIC-octreotate was used in the octreotide scintigraphy). **Results and Conclusion:** In 13 patients with histologically proven neuroendocrine tumors (2 carcinoids, 3 pheochromocytomas, 5 medullary thyroid cancer and 3 paraganglioma) the results of radiolabeled metaiodobenzylguanidine (MIBG) and somatostatin analogs were compared. A total of 50 tumor lesions was detected on standard imaging studies. MIBG scintigraphy correctly localized 11 of these lesions which were observed in 3 patients (2 with medullary thyroid cancer and 1 with paraganglioma). Scintigraphy using labeled somatostatin analogs correctly localized 39 lesions which occurred in 8 patients (1 with carcinoid, 4 with medullary thyroid cancer and 3 with paraganglioma). Concordant scintigraphic results were obtained in 1 patient with medullary

thyroid cancer. Octreotide and MIBG scintigraphy results were negative in 5 patients (3 pheochromocytomas, 1 carcinoids and 1 medullary thyroid cancer). In conclusion, although this series was limited, our results suggest that MIBG is more accurate than somatostatin analogs in imaging paraganglioma. Conversely, somatostatin analogs are more accurate than MIBG in detecting other neuroendocrine tumors such as medullary thyroid cancer.

P523

Clinical application of FDG PET in neuroblastoma for staging and detecting recurrence

Y. Choi, J. Lee, W. Kang, M. Yun, A. Cho, J. Lee, H. Cho, H. Seo; Yonsei university, college of medicine, Seoul, KOREA, REPUBLIC OF.

Neuroblastoma is the most common solid extracranial malignancy of childhood. Although 18F-FDG PET scan has been widely used in oncology field, studies on 18F-FDG PET scan in neuroblastoma are scarce. We evaluated the diagnostic accuracy of 18F-FDG PET scan in neuroblastoma for staging and detecting recurrence. 38 patients were histopathologically confirmed neuroblastoma between January 2003 and October 2009. 23 patients (M:F=14:9; median age, 2.8 yrs) were performed 18F-FDG-PET scan for staging. And 15 patients (M:F=8:7; median age, 4.8 yrs) were performed 18F-FDG-PET scan for follow-up. All patient were performed conventional CT and 29 patient were performed skeletal scintigraphy. 18F-FDG-PET scan detected 22 primary lesions from 23 cases at staging work-up. (Sensitivity : 95.7%) Mean maximum SUV of primary sites is 5.97. One false negative case shows cystic degeneration and maximum SUV is 0.94. At staging work-up, metastatic lesions are noted in 17 cases. They are 12 cases of skeletal metastasis, 12 cases of lymph node metastasis, 2 cases of chest wall metastasis and 1 case of lung metastasis. In cases of skeletal metastasis, 18F-FDG PET scan and skeletal scintigraphy show concordant finding at 13 cases and discordant finding at 8 cases. In discordant cases, 18F-FDG PET scan is superior than skeletal scintigraphy at 6 cases. But skeletal scintigraphy is better than 18 F-FDG PET at only 2 cases. In cases of metastasis except skeletal metastasis, 18F-FDG PET scan and CT are concordant finding at 10 cases and discordant finding at 7 cases. In discordant cases, 18F-FDG PET scan is superior than CT at only 1 case. And CT is better than 18 F-FDG PET at 6 cases. CT find 4 cases of LN metastasis and 1 case of lung metastasis. There were 15 cases that were performed 18 F-FDG PET for follow-up. 6 cases were confirmed recurrence. They are 3 cases of skeletal metastasis, 2 cases of lymph node metastasis, 1 case of pleural seeding and 1 case of abdomen soft tissue. Mean maximum SUV is 3.1 (Range: 0.46-8.91). 18F-FDG PET scan detected 5 cases, and 1 false negative case was occurred at abdomen soft tissue. Its maximum SUV is 0.46. 18F-FDG PET scan showed good diagnostic performance in staging and detecting recurrence of neuroblastoma. 18F-FDG PET scan was useful in depicting primary neuroblastoma and detecting bone metastasis at staging work-up. 18F-FDG PET scan is expected to be useful in recurrence detection due to whole body screening.

P524

Follow up of patients after radioguided surgery of neuroendocrine tumours using 99mTc-octreotide

M. Hodolic, J. Fettich, S. Hojker, I. Slodnjak; University Medical Centre Ljubljana; Department for nuclear medicine, Ljubljana, SLOVENIA.

Aim: To evaluate success of radioguided surgery in patients with neuroendocrine tumours (NETs) using 99mTc-octreotide scintigraphy. **METHOD:** 99mTc-octreotide whole body scintigraphy and abdominal SPECT were performed preoperatively in patients with 27 NETs. For localisation of NETs gamma probe was used intraoperatively and whole body and SPECT study were repeated in 22 patients after 6-12 months. Two patients died before follow up scintigraphy and in 3 cases no scintigraphy was performed. 550-650 MBq of 99mTc-labelled octreotide has been used in every patient. **RESULTS:** Out of 27 NETs detected before surgery 20 NETs were localised successfully using gamma probe, while 7 lesions were not localised. On follow up scintigraphy 6 out of 7 NETs not found during surgery were revealed, while in all intraoperatively successfully localised NETs no abnormal tracer uptake was seen. **CONCLUSION:** Radioguided surgery with 99mTc labelled octreotide seems to be reliable method for treatment of patients with neuroendocrine tumours.

P525

Octreoscan therapy in patients with Neuroendocrine Tumors and metastatic disease: The experience of the Nuclear Medicine Department-ALEXANDRA Hospital

J. Koutsikos, A. Fothiadaki, T. Karianos, V. Valotassiou, S. Tsiouris, D. Tamanidi, O. Karamini, V. Skalistis, T. Liotsou, C. Palestidis, E. Kounadi, C. Zerva, A. Leondi; Alexandra University Hospital, Athens, GREECE.

INTRODUCTION: A large number of patients with neuroendocrine tumors (NET) are found to already have metastatic disease at the time of their first clinic visit. These patients are usually treated with a variety of therapeutic agents without obvious result. At this stage to relieve clinical symptoms, but also in the hope of inhibiting disease progression palliative treatment with somatostatin analogue labeled with therapeutic dose of In-111 (Octreoscan™) is performed. The aim of the study was to evaluate the effectiveness of Octreoscan™ therapy in patients with NET and metastatic disease. **METHODS:** Eleven patients (7 men, 4 women, mean age 60 years) with initially positive diagnostic Octreoscan™ studies were treated with a total of 28 therapeutic doses of Octreoscan™. Complete laboratory, imaging (MRI or CT) and clinic exams were performed before and 6 months after treatment. Eight patients had clinical symptoms at the beginning of therapies (diabetes mellitus, flashing, rush). **RESULTS:** All 8 patients with clinical symptomatology reported relief of symptoms. Progressive disease was observed in 4/11 patients (increase in number or size of metastatic foci), stable tumor status in 5/11 and partial response was observed in 2/11 patients (reduction in number or size of metastases). No patients showed complete response. No toxicity effects were observed during the therapies, neither from the hepatic, nor from renal system. **CONCLUSIONS:** Octreoscan™ therapy has shown to be effective in relieving clinical symptoms but appears to have little effect on disease progression.

P526**Somatostatin receptor scintigraphy using 99m Tc EDDA/HYNIC-TOC in patients with metastatic neuroendocrine cancer of unknown origin.**

R. Golebiewska, A. Nocur, B. Chrapko; Skubiszewski Medical University of Lublin, Lublin, POLAND.

The aim of this study was to assess the diagnostic value of somatostatin receptor scintigraphy (SRS) with 99mTc-EDDA/HYNIC-TOC in staging of patients with neuroendocrine tumor (NET) of unknown primary origin. **Material & methods:** Fourteen patients (6 men, 8 women; age range 32-75 years) were referred for the detection of NET of unknown primary origin. Pathological examination confirmed the diagnosis in each patient. SRS with 99mTc-EDDA/HYNIC-TOC (99mTc-TEKTROYD, POLATOM, POLAND) was obtained 2-4 hours after injection of 740 MBq of the tracer. Anterior and posterior whole body scan and single photon emission computed tomography (SPECT) of the thorax and abdomen were carried out, using a dual-head gamma-camera Varicam (Elsint) with high-resolution and low energy collimator. Computed tomography (CT) was performed in all cases. SRS was evaluated in comparison with CT. **Results:** SRS detected extensive radiotracer accumulation in numerous lesions in all patients. The majority of them correlated with CT scans. Overexpression of somatostatin receptors was seen in metastatic lesions in the liver - 8 cases, in lungs - 5 cases, in bones - 4 cases, in lymph nodes - 7 cases and 1 lesion in the pancreas. CT scans showed lesions, without radiotracer uptake in 3 patients. These changes were located in the adrenal gland in 1 patient and in the lungs in 2 cases. The primary lesion was identified in one patient. **Conclusion:** 99mTc-EDDA/HYNIC-TOC SRS is useful for imaging of SSRT-overexpressing tumors and in staging of NET of unknown primary origin. SRS is less effective in the diagnosis of the primary lesion.

P527**PRRT as a neoadjuvant therapy in patients with neuroendocrine tumours**

A. Sowa-Staszczak¹, D. Pach¹, A. Stefańska¹, M. Tomaszuk¹, R. Mikołajczak², D. Pawlak², M. Trofimiuk¹, R. Chrzan³, A. Hubalewska-Dydejczyk¹; ¹Nuclear Medicine Unit Endocrinology Department, Jagiellonian University, Medical College, Krakow, POLAND, ²Research and Development, IAE Radioisotope Centre POLATOM, Otwock-Swierk, POLAND, ³Department of Radiology, Jagiellonian University, Medical College, Krakow, POLAND.

Introduction: Well differentiated neuroendocrine tumours (NET) usually express somatostatin receptor, they can be targeted with peptide receptor radionuclide therapy (PRRT) with palliative intention. In patients with advanced NET a partial response or stabilization disease after PRRT was observed. But surgery still remains the gold standard in the management of NETs. Surgical resection may improve symptomatic disease and overall survival. **The aim of the study** was to assess using PRRT in primary inoperable NET and show neoadjuvant treatment results in downstaging of the tumor and possibility of the surgery intervention. **Material and methods:** 6 patients - 3 men, 3 women, mean age - 62.5 years, 5 forgut - 4 PNT, 1 midgut were included to the therapy Y90-DOTA TATE every 6-9 weeks. Mean dose was 376 mCi. Mean size of the tumour was 96.2 mm. Only one patient had metastases to the liver. Cytoreduction chemotherapy was not used. **Results:** After the treatment mean size of the tumour decreased to 74mm. Stabilisation of the diseases was observed in 4, partial responses in 2 patients. One patient was qualified to the surgery, but total resection was not possible due to infiltration of the vessels and patient was qualified to additional PRRT courses. The second patient with PR is qualified to surgery. In this group of patients progression of the disease was not observed. Mean time of observation was 24, 8 months (min 10, max 47 months). Mean CgA level decreased from 255,1 to 123,6U/l. PRRT did not cause meliotoxicity and nephrotoxicity. **Conclusions:** 1. After PRRT stabilization of the disease was observed in the majority of patients. 2. In group of patients with partial response after therapy there is a possibility of surgical treatment.

P528**Somatostatin receptors in pulmonary neuroendocrine carcinomas and their metastases visualized with 99mTc-EDDA/HYNIC-TOC scintigraphy**

A. Nocur, R. Golebiewska, B. Stefaniak, B. Chrapko; Medical University of Lublin, Lublin, POLAND.

The aim of our study was to assess the clinical value of somatostatin receptor scintigraphy (SRS) with 99mTc-EDDA/HYNIC-TOC in detection of pulmonary neuroendocrine carcinomas and their metastases. **Material & methods:** We examined 23 patients (mean age 59.5±7.7years) referred to our department for SRS of histologically proven neuroendocrine carcinomas of the lungs (21 primary and 2 recurrent): 18 large cell neuroendocrine carcinomas (LCNEC), including 16 primary and 2 recurrent lesions, 5 primary small cell carcinoma (SCLC). SRS was performed 2-4 hours after injection of 99mTc-EDDA/HYNIC-TOC (POLATOM, Poland) by whole body technique (anterior and posterior projections) and single photon emission computed tomography (SPECT). Double-head gamma camera Varicam was used with high resolution, low energy collimator. SPECT of the chest and abdomen was carried out in all cases. SRS was interpreted in correlation with computed tomography (CT). Radiotracer uptake higher than background was considered abnormal. In the organs with physiological tracer accumulation, like the liver, photopenic foci correlating with metastases in CT were classified as metastases. **Results:** Primary tumor volume calculated based on CT was from 0.6 cm³ to 533.3 cm³ (mean 73.9±125.6). Overexpression of somatostatin receptors was seen in all primary tumors. One SCLC appeared as the rim of activity surrounding the right lung (imitating mesothelioma on CT scans), 22 remaining tumors as focal lesions (in 5 cases with central photopenia due to necrosis). In SRS metastases were present in 15 cases, on CT scans in 16 cases. Numbers of patients with localization of metastases to the individual organs in SRS and CT (respectively) were as following: the mediastinum 8/9, lungs 4/5, liver 2/3, bones 3/2, supraclavicular lymph nodes 1/1, abdominal lymph node 1/1. In 1 out of 2 cases metastasis to the liver was seen in SRS as the large photopenic lesion. Eight metastases to the adrenal glands in 6 patients (in two cases bilateral) detected on CT scans (all from primary LCNEC) did not show

radiotracer accumulation in any case. The volume of these adrenal lesions (based on CT) was 1.8 cm³ to 247.5 cm³ (mean 38±85.2). **Conclusions:** SRS with 99mTc-EDDA/HYNIC-TOC allowed for detection of all primary and recurrent neuroendocrine carcinomas of the lungs. There was visualization of the majority of metastases to the mediastinum, lungs, liver and lymph nodes. SRS revealed bone metastases in one patient more than CT but failed to detect all metastases to the adrenal glands.

P529**Correlation between 68Ga-DOTA-NOC PET/CT SUVmax and NET lesions dimension**

V. Ambrosini¹, D. Campana², C. Pettinato¹, V. Allegri¹, C. Nanni¹, P. Castellucci¹, D. Rubello³, E. Lopci³, G. Montini¹, P. Tomassetti², S. Fanti¹; ¹Nuclear Medicine, Azienda Ospedaliero-Universitaria di Bologna, S.Orsola-Malpighi University Hospital, Bologna, ITALY, ²Internal Medicine, Azienda Ospedaliero-Universitaria di Bologna, S.Orsola-Malpighi University Hospital, Bologna, ITALY, ³Nuclear Medicine, S.Maria della Misericordia Hospital, Rovigo, ITALY.

Background: it has been suggested that lesion dimension may influence the SUVmax value when using a receptor-binding tracer. **Aim:** to investigate the relation between 68Ga-DOTA-NOC PET/CT SUVmax and lesions dimension in NET patients (pts). **Methods:** Among the pts who underwent 68Ga-DOTA-NOC PET/CT between 2007-2009, we included those with NET pathological confirmation not receiving medical treatment (chemotherapy, somatostatin analogues, PRRT) before PET. Overall 13 pts were included. CT images were retrospectively reviewed and the maximum diameter (D) of each NET lesion was measured on transaxial images. Corresponding SUVmax values were measured lesion by lesion drawing a region of interest on the PET transaxial slice presenting the highest uptake. Only lesions detectable on CT were included. Necrosis was not evident on CT and D was higher than partial volume effect limits. 68Ga-DOTA-NOC PET/CT was performed following standard procedure. For each lesion, SUVmax was plotted against D. **Results:** 13 pts were studied (mean age 60ys [39-79]). Primary site included the pancreas (3/13), ileum (7/13) and lung (3/13). Overall 43 NET lesions were evaluated (1 ileum, 2 pancreas, 3 lung, 9 node, 26 liver, 3 bone). Mean lesion diameter was 25.4±10.7mm [8.5-54.2]. Grouping all lesion by the primary site, the mean SUVmax of all lesions of pts with a pancreatic (24.7±14.8) or ileal primary (19.4±14.5) was significantly higher (p=0.002 and p=0.0017 respectively) than mean SUVmax of pts with a lung primary (4.6±2.9). No significant SUVmax difference was evident between pancreatic or ileal primary. A linear correlation was identified between the SUVmax and D (p=0.0001, R²=0.3). **Conclusions:** Our preliminary data show that in NET pts the SUVmax directly correlates with the lesion maximum diameter.

P530**Usefulness of 18-FDG-PET and scintigraphy with 111-In-Pentetreotide in the diagnosis of neuroendocrine tumors (NETS).**

A. Santiago Chinchilla¹, M. A. Muros¹, M. Moreno-Caballero¹, C. Ramos-Font¹, A. Sebastián-Ochoa², M. Navarro-Pelayo-Láinez¹, H. Palacios-Gerona¹, A. Rodríguez¹, M. López³, J. M. Llamas-Elvira¹; ¹Servicio de Medicina Nuclear, Hospital Universitario Virgen de las Nieves, Granada, SPAIN, ²Servicio de Endocrinología, Hospital Universitario San Cecilio, Granada, SPAIN, ³Servicio de Endocrinología, Hospital Universitario Virgen de las Nieves, Granada, SPAIN.

BACKGROUND: The diagnosis of location and extent of neuroendocrine tumors is difficult due to variability of locations. The 111 In-pentetreotide is highly sensitive and specific, especially in abdominal NETS. The 18-FDG-PET has shown a limited role in the diagnosis of these tumours. **AIM:** To compare the usefulness of scintigraphy with 111 In-pentetreotide and FDG-PET in the diagnosis and monitoring of the NETS. **MATERIAL AND METHODS:** We studied 24 patients, 16 men and 8 women, mean age 55 years (36-74) with diagnosis or suspicion of NET. The NETS were: 9 carcinoids, 1 paraganglioma, 1 pheochromocytoma, 1 glucagonoma, 1 medullary thyroid carcinoma, 5 NETS and 6 of unknown origin. The study indication was primary tumour location and staging in 9 patients, and follow-up in 15 patients. 111 In-pentetreotide was performed followed by PET in 14 patients and PET followed 111 In-pentetreotide in the remaining 10 patients. Time between both imaging procedures was less than 6 months. We analyzed findings in three locations: lesions in organs (lung, liver, gastrointestinal, bladder, thymus, etc.), lymph node involvement and muscle-skeletal system lesions. **RESULTS:** FDG-PET detected 42 lesions and 111 In-pentetreotide identified 44. 28 locations were coincident in both techniques. The 111 In-pentetreotide detected 21 lesions in organs compared with 14 detected by the FDG-PET. FDG-PET detected 15 metastatic lymph node compared with 8 detected by 111 In-pentetreotide. Regarding to musculoskeletal lesions, FDG-PET detected 13 and 15 were detected with 111 In-pentetreotide respectively. Between 10 patients with NETS poorly differentiated (grade II-III), PET and 111 In-pentetreotide results were overlapped in 3, PET detected more lesions than 111 In-pentetreotide in 5 patients and 111 In-pentetreotide more than PET in 2 patients. **CONCLUSIONS:** - The number of lesions detected in patients with NETS by FDG-PET and scintigraphy with 111 In-pentetreotide is similar. - Both techniques differ in the location of the lesions: 111 In-pentetreotide identify more lesions in organs and FDG-PET detected more lymph metastasis.

P531**Comparison of 99mTc-EDDA/HYNIC-TATE and 111 In Octreotide in the same patient group with somatostatin receptor expressing tumors**

O. Ekmekcioglu¹, M. Ocak², L. Kabasakal¹, A. Araman², C. Decristoforo³, S. Nisli¹, I. Uslu¹; ¹Department Of Nuclear Medicine, Cerrahpasa Medical Faculty, Istanbul University, Istanbul, TURKEY, ²Department Of Pharmaceutical Technology, Pharmacy Faculty, Istanbul University, Istanbul, TURKEY, ³Clinical Department Of Nuclear Medicine, Medical University Innsbruck, Innsbruck, AUSTRIA.

Introduction: In-111 labelled octreotide as an analogue for somatostatin has been considered as a diagnostic tool for the diagnosis of somatostatin expressing tumours. But one of the major drawbacks of ^{111}In -pentetreotide is its high cost, and the isotope has physical characteristics resulting in suboptimal image resolution and the need for medium-energy collimators that reduce the counting rate. These drawbacks have led to a search for more suitable radioligands based on $^{99\text{m}}\text{Tc}$ for detecting these tumours. $^{99\text{m}}\text{Tc}$ is a product that steadily available cheap. The aim of the study was to compare the diagnostic value of $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE and In-111 ^{111}In -DTPA-octreotide in the same patient group. **Material and Methods:** The study population comprised 22 patients; 13 females and 9 males (age 50.6 ± 12.9 years). There were 11 patients with well differentiated neuroendocrine tumour, 3 patients with thyroid carcinoma, 2 MEN type 1, 1 thymic carcinoma, 3 carcinoid tumours and 2 paraganglioma. Lyophilized kit form of $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-octreotide was produced as described previously. (740 MBq) RS and CT were performed in all patients. All patients were also examined with In-111 Octreoscan. All patients underwent a whole body and a SPECT imaging at 4 hours post injection of 740 MBq of $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-octreotide. All patients were also underwent a In-111 DTPA-D-Phe-octreotide imaging at 24–48 hours after injection. Images were evaluated visually and semiquantitatively. **Results:** The diagnostic results of both studies were similar. However high-quality $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-octreotide images were obtained in all cases, with higher lesion to tumor ratios. The number of lesions detected by $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE were found higher than the number of lesions detected by ^{111}In -DTPA-D-Phe-octreotide. The liver uptake was lower in $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-octreotide images resulting better visualization of liver lesions. Higher quality images have also provided a better localisation of lesion in CT fused SPECT images. **Conclusion:** The present study have suggested that, $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE may be a better alternative to ^{111}In -DTPA-D-Phe-octreotide due to high image quality. Also it may be of advantage in cost-effectiveness and prevent higher radiation dose. **Acknowledgements:** This study was supported by Turkish Scientific and Research Council (TUBITAK) with project no: 109S101

P532

The Effect of Model-based Scatter Correction for Simultaneous Dual-isotope Tc-99m/ In-111 Neuroendocrine SPECT/CT studies

S. Shcherbinin¹, A. Celler¹, S. Chamoiseau²; ¹The University of British Columbia, Vancouver, BC, CANADA, ²Centre Hospitalier de Bigorre, Tarbes, FRANCE.

Aim: A simultaneous dual-isotope Tc-99m DPD /In-111 OctreoScan SPECT/CT study would allow for much more complete analysis of neuroendocrine patients than a series of separate scans. While SPECT/CT study with In-111-labeled OctreoScan provides a 3D localization of neuroendocrine tumors, the Tc-99m DPD scan detects bone metastases. Additional advantages include time-efficiency and an inherit co-registration between two datasets. However, simultaneously acquired images may be degraded by In-111 photons detected in the energy window designated for Tc-99m image (down-scatter effect). Additionally, self-scatter effect (the scattered photons detected in the isotope's own photopeak energy window) impacts both resolution and quantitation. The goal of our study was to investigate to what extent the corrections for these phenomena may improve diagnosis. **Materials and Methods:** In total, we analyzed three patient datasets. Simultaneous Tc-99m DPD /In-111 OctreoScan acquisitions were performed using Infinia Hawkeye 4 (GE Healthcare) hybrid SPECT/CT camera equipped with MEGP collimator. The 925MBq of Tc-99m and 185MBq of In-111 were simultaneously injected 26 hours before acquisition. The data was collected in three energy windows: $140\text{keV} \pm 9\%$ (W1), $171\text{keV} \pm 10\%$ (W2), and $245\text{keV} \pm 10\%$ (W3). Two algorithms were tested for image reconstruction. While the method M1 incorporated the CT-based attenuation map and resolution recovery, the method M2 additionally included an accurate patient-specific modeling of both self-scatter and down-scatter effects. To quantitatively assess performance of these algorithms, two phantom experiments with containers filled with different mixtures of Tc-99m and In-111 activities were performed. **Results:** The patient-specific analysis performed by M2 algorithm showed that in W1 22-23% were Tc-99m scattered photons and 8-9 % were In-111 down-scattered photons. Therefore, the M2 method which corrects for these effects considerably improved the quality of Tc-99m images. Specifically, the resolution and sharpness of images was improved, the bladder limits and kidneys were clearly delineated. Quantitative analysis of phantom experiment confirmed these observations: the absolute Tc-99m activities recovered by the M2 algorithm from (i) dual-isotope and (ii) sequential scans differ by a few percents only. At the same time, method M1 overestimated these activities by 45%-133% depending on Tc-99m/In-111 ratio. In In-111 patient images, practically no diagnostically significant differences between reconstructions M1 and M2 were noticed in spite of quantitative improvements assessed in phantom experiments. **Conclusions:** Incorporation of accurate corrections for self- and down-scatter into reconstruction algorithm improves both quantitative and diagnostic accuracy of simultaneous dual-isotope Tc-99m DPD / In-111 OctreoScan SPECT/CT studies.

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Comparison of ^{18}F -DOPA PET/CT with ^{111}In -DTPA-octreotide SRS (planar and SPECT/CT imaging) in patients with NET

P. B. Malle, S. Kohlfuerst, I. Igerc, M. Lobnig, M. Sorschag, P. Lind, H. J. Gallowitsch; State Hospital Klagenfurt, Klagenfurt, AUSTRIA.

Aim: The aim of the study was to compare the results of ^{18}F -DOPA PET/CT with those acquired from ^{111}In -DTPA-octreotide SRS (planar and SPECT/CT imaging) in patients with NET, respectively. **Methods:** 21 patients (7 female, 14 male, range 32-77 yrs, mean 58 yrs \pm 12,3) with histologically proven (15/21 patients, 71.4%) or clinical and biochemical suspicion of NET (6/21 patients, 28.6%) were studied with planar SRS and SPECT/CT imaging at 4 and 24 hours after injection of 200 MBq ^{111}In -DTPA-octreotide and with PET/CT imaging at 60 min after injection of 5MBq/kg ^{18}F -DOPA. No carbidoa premedication was used before ^{18}F -DOPA PET/CT acquisition. Median time interval between ^{18}F -DOPA PET/CT and ^{111}In -DTPA-octreotide SRS was 29 d, whereas ^{18}F -DOPA PET/CT was performed before ^{111}In -DTPA-octreotide SRS in 11/21 patients (52.4%) and subsequently in 10/21 patients (47.6%). No NET associated therapy was carried out between both nuclear medicine investigations. **Results:** ^{18}F -DOPA PET/CT on the one hand and ^{111}In -DTPA-octreotide planar SRS and SPECT/CT imaging on the other yielded concordant findings (both nuclear medicine methods were negative, inconclusive or visualized a comparable number of lesions) concerning DOPA-decarboxylase activity and SR-status in 16/21 patients (76.2%). Despite absent or less somatostatin receptor expressing activity of lesions for

being visualized on both planar ^{111}In -DTPA-octreotide SRS and SPECT/CT studies ^{18}F -DOPA PET/CT correctly demonstrated intensified tracer uptake in 3/21 patients (14.3%). In 2/21 patients (9.5%) SRS (planar and SPECT/CT imaging) was superior to ^{18}F -DOPA PET/CT, though. **Conclusion:** Increased DOPA-decarboxylase activity is not necessarily associated with augmented SR-expression and vice-versa. Regarding the detection of metastatic disease in patients with NET performing both ^{18}F -DOPA PET/CT and ^{111}In -DTPA-octreotide SRS (planar and SPECT/CT imaging) may contribute valuable additional information to a comprehensive diagnostic work-up.

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Detection of somatostatin receptor-positive tumours using $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-NOC and comparison with $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE in the same patient group

M. Ocak¹, Ö. Ekmekçioğlu², L. Kabasakal², C. Decristoforo³, S. Asa², A. Araman¹, E. von Guggenberg³, I. Uslu²; ¹Istanbul University, Pharmacy Faculty, Department of Pharmaceutical Technology, Istanbul, TURKEY, ²Department of Nuclear Medicine, Cerrahpaşa Medical Faculty, Istanbul, TURKEY, ³Clinical Department of Nuclear Medicine, Medical University, Innsbruck, AUSTRIA.

Introduction: $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE and $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TOC have been introduced as $^{99\text{m}}\text{Tc}$ -somatostatin analogues for imaging somatostatin receptor (sstr) expressing tumours. The majority of tumours studied with radiolabelled somatostatin analogues express mainly sstr 2. To extend the biological activity profile of radiolabelled somatostatin analogues DOTA-1-NaI¹-octreotide (DOTA-NOC) has been synthesized (which had improved affinity to sstr2 and high affinity to sstr3 and sstr5). At present, there are no studies investigating $^{99\text{m}}\text{Tc}$ -EDDA/[HYNIC-1-NaI¹]-octreotide ($^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-NOC) which could be new promising agent in tumours overexpressing sstr. The aim of the present study was to compare the diagnostic value of $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-NOC and $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE in the same patient group. **Materials and methods:** HYNIC-NOC and HYNIC-TATE were obtained from ABX (Germany). $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-NOC and $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE were prepared from a freeze-dried kit formulation. The patients had given written informed consent to participation in the study, which had been approved by the local ethics committee. 17 patients (7 men, 10 women; age range 22 - 86 y; mean age 53.23 ± 14.10 y) were included in the study. There were 5 patients with well differentiated neuroendocrine tumour, 4 patients with thyroid carcinoma, 2 MEN type 1, 2 medullary thyroid cancer, 2 paraganglioma, 1 thymic carcinoma and 1 carcinoid tumour. Each patient received an activity between 370 and 555 MBq corresponding to ~ 12.5 μg peptide. All patients underwent a whole body and a SPECT imaging 1, 2 and 4 hours post injection. Images were evaluated visually and semiquantitatively. **Results:** The number of lesions detected by $^{99\text{m}}\text{Tc}$ -HYNIC-NOC (71 sites) were found lower than the number of lesions detected by $^{99\text{m}}\text{Tc}$ -HYNIC-TATE (112 sites). Both agents demonstrated similar liver uptake, however spleen uptake of $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE was significantly higher than that of $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-NOC. The lesion to background ratios and image quality were found significantly higher in $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE images. In $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-NOC images lesion to background ratios were almost similar at 1, 2 and 4 hours images. With $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE there was not any difference between 1 and 2 hour images and the highest ratios were obtained at 4 hours images. **Discussion and conclusion:** $^{99\text{m}}\text{Tc}$ -HYNIC-EDDA-NOC, may not be a better alternative to the $^{99\text{m}}\text{Tc}$ -EDDA/HYNIC-TATE due to lower lesion uptake and image quality. It may be of advantage in certain patient groups with tumours expressing predominantly other receptor subtypes than SSTR2. **Acknowledgements:** This work was part of COST Action BM0607 and was supported by Turkish Scientific and Research Council (TUBITAK) with project no: 109S101

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Right hepatic artery injection: OctreoScan uptake in metastases localized in the right and left part of the liver

S. E. Pool, B. Kam, G. A. Koning, W. A. P. Breeman, E. P. Krenning, T. L. M. ten Hagen, C. H. J. van Eijck, M. de Jong; ErasmusMC, Rotterdam, NETHERLANDS.

Aim In over 500 patients Peptide Receptor Radionuclide Therapy (PRRT) with [^{177}Lu -DOTA-Tyr³]-octreotate has shown a survival benefit of 40 to 72 months from time of diagnosis, with minor side effects. To further improve PRRT with [^{177}Lu -DOTA-Tyr³]-octeotate in patients with neuroendocrine liver metastases the aim of this study is to explore the effect of locoregional administration of ^{111}In -DTPA-octreotide (OctreoScan) via the hepatic artery on intrahepatic tumor uptake. As we reported before, locoregional administration via the hepatic artery can result in 2.4 x higher uptake of OctreoScan in GEP-NET liver metastasis. Here we describe a case in which the catheter is not located in the hepatic artery but in the right hepatic artery. Thereby only a part of the liver metastasis received the OctreoScan injection locoregionally. The effect on OctreoScan uptake in liver metastasis in right and left part of the liver was assessed. **Materials and methods** A patient with neuroendocrine liver metastases scheduled for PRRT with [^{177}Lu -DOTA-Tyr³]-octeotate was scanned twice after systemic or locoregional administration of OctreoScan with an interval of 2 weeks. Locoregional administration was applied via a catheter placed in the right hepatic artery. Planar and SPECT images of the liver and kidneys were made during the first 12.5 minutes post injection (p.i.) and at 1, 4, 24, 48 and 72 hours p.i. . Blood samples were taken at various time points and the urine was collected for 48 hours after injection. **Results** Preliminary patient data shows up to 2.7 x higher uptake of ^{111}In -DTPA-octreotide in liver metastases in the right part of the liver after loco regional administration compared to systemic administration. Also more tumor sites were detected after locoregional administration. ^{111}In -DTPA-octreotide uptake in a liver metastasis located in the left part of the liver showed similar uptake after locoregional and systemic administration. Dynamic scanning during the first 12.5 minutes after injection shows ^{111}In -DTPA-octreotide tumor uptake to take place in the first 2 minutes after injection. The route of administration did not change kidney uptake, blood and urine excretion. **Conclusion** Locoregional administration of OctreoScan can result in a higher tumor uptake compared to systemic administration. Uptake in tumor lesions outside of the area that receives the administration locoregionally does not seem to be affected and is comparable to the uptake after systemic administration. Tumor uptake of OctreoScan seems to take place in the first two minutes after administration.

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Comparison of Lu-177 obtained from two different commercial vendors for peptide receptor radionuclide therapy of neuroendocrine tumor patients: Preliminary results

C. Lehmann, V. Prasad, C. Schuchardt, D. Mueller, C. Zachert, R. P. Baum; Clinic for Nuclear Medicine / Centre for PET/CT, Zentralklinik Bad Berka, Bad Berka, GERMANY.

Aim: The aim of the study was to find out if there is any difference between the Lu-177 obtained from Perkin Elmer (PE) and Isotope Technologies Garching GmbH (ITG) in terms of labeling efficiency and peptide contents / specific activity of Lu-177 DOTA-TATE/TOC from PE and ITG. **Material and Methods:** Overall 22 patients with progressive neuroendocrine tumor were analyzed. Out of these 9 patients were treated with PE Lu-177 DOTA-TATE (PE group) and 13 with ITG Lu-177 DOTA-TATE (n=11)/ TOC (n=2) (ITG group). Pulse rate and blood pressure changes during therapy were also compared. **Results:** The results are summarized in Table. There were no significant changes in the pulse rate of the patients during therapy among the two groups. 50% of the patients showed more than 20 mm Hg change in systolic / diastolic blood pressure in PE group as compared to 15% in ITG group. The labeling efficiency was the same (>99%) in both the groups. **Conclusion:** There is no difference in the labeling efficiency of Lu-177 obtained from PE or ITG. The amount of peptide (DOTA-TATE/TOC) needed for ITG labeling was lower than PE labeling. Specific activity (radioactivity/mcg) was slightly higher for ITG as compared to PE. Future studies are needed to find out if there is any difference in the response and toxicity profile of the Lu-177 obtained from these two vendors. Table-1

	PE	ITG
Total number of patients	9	13
Injected radioactivity	6.4±1.2	6.9±1.2
Amount of peptide	273.3±86.4	200.6±62.2
GBq/mcg peptide	42.8±11	31±9.9
≥20 mm change in blood pressure (% of patients)	50%	15%

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The role of ^{99m}Tc-Tektrotyd somatostatin receptor scintigraphy in carcinoid tumor patients management

M. Vljakovic¹, M. Rajic¹, M. Stevic¹, M. Matovic², V. Artiko³, N. Nikolic⁴, N. Nikolic⁵; ¹Clinical center Nis, Nis, SERBIA, ²Clinical center Kragujevac, Kragujevac, SERBIA, ³Clinical center of Serbia, Belgrade, SERBIA, ⁴Institute of Nuclear Science Vinca, belgrade, SERBIA, ⁵Institute of Nuclear Science Vinca, Belgrade, SERBIA.

Aim: Since somatostatin receptors are often overexpressed in patients with gastroenteropancreatic neuroendocrine tumors (GEP-NET), the purpose of this study was to evaluate the role of scintigraphy with the somatostatin analogue ^{99m}Tc-EDDA-HYNIC-TOC (^{99m}Tc-Tektrotyd) in diagnosing and staging of patients with GEP-NET. **Material and methods:** Twenty patients (10 female, 10 male; age range: 33-76 years; mean age: 60,6±2,3 years) were studied: 4 patients highly suspected of having GEP-NET and 16 patients who had undergone the surgical removal of GEP-NET. Whole body scintigrams at 4 h postinjection were obtained in all patients using "ROTA" Siemens gamma camera equipped with ICON computer and connected with high resolution collimator. After the reconstruction of radiopharmaceutical according to the manufacturer's instructions, the patients were administered activity of 740 MBq and 20µg octreotide. Other imaging techniques were also applied and analysed in individual cases and compared with ^{99m}Tc-Tektrotyd scan. **Results:** Positive scintigraphy finding (either primary tumor or metastatic spreading) was detected in 5 patients, and negative in 15. Compared with results of other imaging modalities, Tektrotyd scan detected more lesions in 2 out of 5 positive patients. In 15 previously documented negative patients no lesions were found. The values of serum chromogranin A (CrA) were increased in all patients with pathological scan and in one with no evidence of GEP-NET. The high correlation was found between the results of ^{99m}Tc-Tektrotyd scan and CrA (R= 0,882; p<0,001). Two out of five patients with multiple metastases were selected for 90Y/177Lu therapy. **Conclusion:** The ^{99m}Tc-Tektrotyd somatostatin receptor scintigraphy is a suitable one-day acquisition procedure for diagnosing and staging the patients with GEP-NET. It can be used in clinical practice for preoperative evaluation, for localisation of local recurrence or distant metastases, and is particularly beneficial for therapy decision making.

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Oncology Clinical Science: Bone

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Diagnostic accuracy of SPECT-CT in comparison to whole body scintigraphy and SPECT in patients with suspected osseous metastases: first results of a two center study

H. Palmemo¹, C. Marx¹, C. Hoppe¹, A. Ebert¹, B. Kreft², T. Menschik², Y. Ko³, R. Vorreuther⁴, S. Ezziddin⁵, H. Schild⁶, H. Biersack⁵, H. Ahmadzadehfar⁷; ¹Department of Nuclear Medicine, Institute of Nuclear Medicine and Radiology Bonn, Bonn, GERMANY, ²Department of Radiology, Institute of Nuclear Medicine and Radiology Bonn, Bonn, GERMANY, ³Department of Oncology, Hospital Evangelische Kliniken Bonn, Bonn, GERMANY, ⁴Department of Urology, Hospital Evangelische Kliniken Bonn, Bonn, GERMANY, ⁵Department of Nuclear Medicine, University Hospital Bonn, Bonn, GERMANY, ⁶Department of Radiology, University Hospital Bonn, Bonn, GERMANY.

Aim of this ongoing two center study is to evaluate diagnostic and clinical impact of SPECT-CT on patients with suspected osseous metastases. **Material and methods:** In 412 patients (118 prostate, 203 breast cancer, 91 other tumors), a whole body scintigraphy and SPECT was performed for staging and restaging (710 MBq Tc 99-MDP, 2 h p.i. GK + SPECT). Additionally, all patients received a SPECT-CT (low-dose Spiral-CT, Infinia Hawkeye 4 and Siemens Symbia T2). Whole body scintigraphy, SPECT and SPECT-CT were compared with regard to accuracy of localisation, diagnostic accuracy, sensitivity and specificity. All lesions were scored for each technique (score 0 to 4, two nuclear medicine physicians, two radiologists). Follow-up of patients for at least one year serves as gold standard. **Results:** Two hundred five of 412 patients have been evaluated so far. In 58 patients, bone metastases were present. Correct localisation of findings was found in 62% (108/174 lesions) of whole body scintigraphy (WBS), in 76% (132/174) of SPECT exams and in 98% (170/174) of SPECT-CT exams. Sensitivity and specificity for WBS, SPECT, SPECT-CT was 88%, 95%, 99% and 66%, 65%, 98%, respectively. By SPECT-CT, down-staging and up-staging could be achieved in 83 and 3 patients, respectively. Further diagnostic imaging procedures for unclear scintigraphic findings was necessary in only 2% of patients. SPECT-CT improved diagnostic accuracy for extension of multifocal disease in 52% of cases. **Conclusions:** By complementary use of SPECT-CT, specificity of bone scintigraphy can be significantly improved. Sensitivity is only slightly increased. Since the amount of unclear scintigraphic findings is clearly decreased and definition of the extent of metastases is more accurate, SPECT-CT has a significant impact on clinical patient management.

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Comparison of the detectability of bone metastases by FDG PET-CT and bone scintigraphy

L. Jorgov¹, A. Fekeshazy², Z. Varga², H. Galgoczy², Z. Tóth², Z. Kopcsányi³, Z. Galler⁴, T. Györke⁵; ¹Semmelweis University, Budapest, HUNGARY, ²PET-CT Medical, Diagnostic Ltd., Budapest, HUNGARY, ³Péterfy Sándor str. Hospital, Dept. of Nuclear Medicine, Budapest, HUNGARY, ⁴National Korányi Institute for TBC and Pulmonology, Dept. of Nuclear Medicine, Budapest, HUNGARY, ⁵Semmelweis University Department of Diagnostic Radiology and Oncotherapy; PET-CT Medical, Diagnostic Ltd., Budapest, HUNGARY.

Background: Both FDG PET-CT (PET) and bone scintigraphy are sensitive methods for the detection of bone metastases. We compared retrospectively the results of these methods when both investigations were performed within one month. **Materials and methods:** 58 pairs of PET and bone scan investigations (116 investigations) of 55 patients (ages: 34-78 years) were compared. The primary tumours were cancers of breast, lung, rectum, cervix and pancreas and Non-Hodgkin lymphoma. In case of all abnormalities depicted by one of the two methods we evaluated the detectability by the other investigation. Concerning bone metastases we determined the results on a patient by patient and a lesion by lesion base. **Results:** Patient by patient evaluation showed findings of bone metastases with both methods in 18 cases, in 40 cases neither of the investigations raised the suspicion of bone metastases. PET detected however more single lesions in the same patient according to the lesion by lesion analysis in 7 cases. We couldn't perform lesion by lesion evaluation in 1 case because of more diffuse and confluent bone disease. **Conclusions:** For the detection of bone metastatic state bone scintigraphy and PET provided the same effectiveness in each single patient while PET proved more sensitive based on the lesion by lesion comparison.

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Superscan Pattern in In-111 Octreotide Scintigraphies due to Primary Breast Carcinoma Cases

I. Karfis¹, A. Stavrakas², M. Lyra², A. Gouliamos², G. S. Limouris²; ¹Nuclear Medicine Dept, NIMTS Military Hospital, Athens, GREECE, ²Nuclear Medicine Div, Athens Univ Medical Faculty, Athens, GREECE.

Aim: To evaluate bone scans, positive for metastatic dissemination by a subsequent somatostatin receptor scintigraphy in primary breast carcinoma cases. **Patients and Methods:** In the last decade, 75 % of approx 2.500 pts who underwent whole body bone scintigraphy, positive for metastatic dissemination due to breast carcinoma, complained with pain. A small number of them [37 pts (~ 2 %)] resistant to conventional chemotherapy and narcotic opioids were further scanned for somatostatin receptors with In-111 Octreotide. **Results:** Eight cases up to day have been detected to be positive for somatostatin receptor scintigraphy, and only 1 exhibit a superscan pattern, first reported to our knowledge. **Conclusions:** Patients with painful osseous metastases due to breast carcinoma, resistant to conventional treatment might lurk pathological overexpression of somatostatin receptors and thus potentially candidates for Peptide Receptor Radio-nuclide Therapy.

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Clinical Application of SPECT-CT in Cancer Patients With Suspected Bone Metastases

S. B. Sergieva¹, E. Alexandrova², G. Baicheva³, L. Nikolcheva¹, A. Milev², B. Dimitrov¹; ¹Sofia Cancer Center, Sofia, BULGARIA, ²National Oncology Center, Sofia, BULGARIA, ³Military Medical Academy, Sofia, BULGARIA.

Purpose: To assess the role of SPECT-CT images in diagnosis of suspected bone metastases in cancer patients. **Material & Methods:** Eighty nine cancer patients (pts): 54F,35M; age 18-92 yrs underwent whole body bone scintigraphy with following SPECT-CT study. The field of SPECT-CT images correlated with scintigraphically visualized bone foci with abnormal uptake of the tracer and uncertain character in order to differentiate metastatic from degenerative skeletal lesions. Double-headed SPECT camera with 2-slice CT scanner (Symbia T2, Siemens) was used. **Results:** After retrospectively review of whole body bone scan it was specified that indeterminate findings in 36 pts could be correlated with benign degenerative findings on SPECT-CT images; 1-3 solitary metastatic foci were identified in 31 pts. Twenty pts were with locally advanced metastatic bone disease: 8 pts out of them were with osteolytic "cold" spots on the bone scan; 6 pts were with bone lesions contained soft tissue components from directly involved recurrent or metastatic tumoral mass; 6 other pts were with mixed osteosclerotic and osteolytic lesions. Two pts were

with extraosseous lesions: one - with myositis ossificans and the second - with soft tissue calcified metastases. **Conclusion:** Combined SPECT-CT studies have grown in the past years due to the almost simultaneous acquisition of transmission and emission information, thus obtaining optimal fusion in a very short time. Anatomical cross-sectional CT data enables differential diagnosis of the most of uncertain bone lesions, reducing false positive and inconclusive studies and thus increasing specificity of bone scintigraphy which is very important for future management of cancer patients.

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Radioguided Bone Biopsy with Gamma Probe and Portable Gamma Camera in Cases of Lone Osteoblastic Bone Lesion.

U. Vera, M. E. Rioja, V. Castillo, M. P. Orduña, O. Gutierrez, E. Díaz, L. Díez, A. A. Crespo; ramon y cajal, madrid, SPAIN.

INTRODUCTION: The bone scan is a highly sensitive method to detect skeletal metastases, being, in descending order, lung, breast, prostate, kidney and thyroid cancer, the tumors which most commonly produce bone metastasis. The early presence of an osteoblastic lesion often generates diagnostic dilemmas upon finding an unique area of increased uptake in the bone scan. In these cases a biopsy is recommended to achieve a histological diagnosis. **AIM:** To evaluate the efficiency of the gamma-detector probe and the portable gamma camera as a guide for the biopsy of lone bone lesions in oncological patients. **METHODS:** Amongst all the oncological patients who underwent total body scan (post-injection of 740 MBq of 99m Tc-DPD) throughout 2008 and 2009, we selected 4 patients diagnosed with lung Ca, which showed a single uptake in costal region difficult to assess, which could not be interpreted by either the CT nor the PET-CT. Rib biopsy was scheduled radioguided under scintigraphic control and with intraoperative gamma-detector probe after the second administration of bisphosphonates-Tc99m. **RESULTS:** Rib resection was performed, limiting the resection to areas with maximum count, confirming, intraoperatively (during the surgery), the decline in activity after the biopsy with both equipments. **CONCLUSIONS:** The biopsy using gamma probe and portable gamma detector represented in 50% of the patients a change in the staging and the therapeutic approach and in the other 50%, the existence of metastatic bone disease was ruled out. **Results:**

Rib: 11 ^o left-back	Maximun count: 1915 c.p.m.	Background: 318 c.p.m	Pathological anatomy: Poorly differentiated infiltrating adenocarcinoma
Rib: 9 ^o right-back	Maximun count: 1311 c.p.m.	Background: 198 c.p.m.	Pathological anatomy: Infiltration by adenocarcinoma.
Rib: 2 ^o -3 ^o right-anterior	Maximun count: 442 c.p.m.	Background: 254 c.p.m.	Pathological anatomy: Secondary cortical Exostoses / images "pagetoid".
Rib: 6 ^o left-anterior	Maximun count: 785 c.p.m.	Background: 326 c.p.m.	Pathological anatomy: No signs of infiltration.

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Oncology Clinical Science: CUP (Cancer of Unknown Primary)

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18F-FDG PET/CT in Search of Origin in Patients with Unknown Primary Cancer

S. Lucic, A. Peter, M. A. Lucic, D. Jovanovic, K. Nikoletic; Institute of Oncology of Vojvodina, Sremska Kamenica, Novi Sad, SERBIA.

Introduction: Cancer of unknown primary origin is not an uncommon clinical state, usually accounting for 2-7% of all cancer patients. Since it is considered that conventional diagnostic morphoanatomical imaging can be used to successfully diagnose a primary malignancy in only approximately 20% to 27% of patients, and knowing that by defining the primary tumor origin the optimized treatment may be provided to the patient, in this study we tried to establish the possibilities of 18F-FDG PET/CT, as a multimodality diagnostic tool, in diagnostic evaluation of the patients with histopathologically proven metastatic tumours of unknown primary. **Methods and Material:** Twenty-six patients (age range 40-76 years; 15 males and 11 females) with histopathologically proven metastatic tumours of unknown primary (16 patients with adenocarcinoma (61.54%), among them one with mucinous adenocarcinoma, 5 with squamocellular carcinoma (19.23%), 3 patients with melanoma (11.54%) and 2 with poorly differentiated carcinoma (7.69%)) and negative or inconclusive conventional morphoanatomical diagnostic scans were examined on PET/CT Siemens Biograph 64 unit (Erlangen, Germany) using the low-dose CT protocol and the whole body PET protocol in 3D modality with 3 minutes emission scans by bed position (average of 6-8 bed positions), approximately 60±10 minutes after the application of 370 MBq of 18F-FDG. As a positive PET/CT finding we considered clear depiction of at least one anatomical localization highly suspected on primary tumor and as a negative finding 18F-FDG activity within metastatic tumors without the possibility to assume the primary cancer localization. **Results:** 18F-FDG PET/CT indicated the most probable localization of primary cancer origin in 17/26 patients (65.38%). Divided in subgroups by histopathological diagnosis, the primary cancer origin was found in 12/17 patients with adenocarcinoma (70.59%), 2/5 patients with squamocellular carcinoma (40%), and 1/2 patients with poorly differentiated carcinoma (50%). Primary cancer origin remained undetected in 9/26 patients (34.62%), including the patient with mucinous adenocarcinoma and all three patients with melanoma. **Conclusion:** 18F-FDG PET/CT demonstrated the prominent diagnostic capability in diagnostic evaluation of patients with cancer of unknown primary origin, not only by enabling imaging of patient's whole body, but also by integrated multimodal functional/morphological visualization at once. These advantages may already establish 18F-FDG PET/CT as the initial diagnostic method in the patients with cancer of unknown primary origin.

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Use of ^{99m}Tc MIBI for detection of primary cancer site in

patients with brain metastases and unknown primary

P. H. Bochev¹, A. Klisarova¹, A. Kaprelian², B. Chaushev¹, J. Dancheva¹;
¹Nuclear Medicine dept."St.Marina" University Hospital, Varna, BULGARIA,
²Neurology dept."St.Marina" University Hospital, Varna, BULGARIA.

Brain is a relatively common site for metastases in patients with lung cancer, melanoma, renal cell carcinoma, breast cancer or other tumors. In some cases symptomatic brain metastases can be the first presentation of an already spread cancer. The detection of the primary is in these cases essential for the following treatment strategy and consists of different imaging, endoscopic and laboratory tests. In a certain number of patients, however the primary cancer site remains undetected. Aim of our study was to evaluate the use of 99mTc MIBI as a nonspecific tumor seeking agent in patients with brain metastases and unknown primary site. **Materials and methods:** Subject of study were 11 patients with histologically proven brain metastases and no evidence of primary tumor from the routine imaging and other tests. We used 20mCi 99mTc-MIBI single i.v dose as a nonspecific tumor seeking agent. All patients underwent as follows: dynamic perfusion study of the abdomen, scintimammography (females), SPECT of the thorax, whole body scan and Brain SPECT. All tests were performed consecutively, using Dicom Siemens gamma camera. **Results:** Two of the patients presented with a single focus of high MIBI uptake in the lung hilus, both proven to be NSCLC on further imaging and bronchoscopy. Lesions were only evident on SPECT. One patient showed uptake in axillary lymph nodes, but no primary was proven by the further workup. The remaining 8 patients showed no foci of abnormal MIBI uptake, consistent with primary tumor or extracranial metastases. **Conclusion:** 99mTc-MIBI, used as a nonspecific tumor seeking agent can be of value for detecting the primary tumor site in case of brain metastases from unknown primary.

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Detection of unknown primary tumors using ¹⁸F-FDG PET/CT

H. Fernandes, P. Iapa, G. Costa, J. Correia, J. Pedroso de Lima; Hospitais Universidade Coimbra, Coimbra, PORTUGAL.

Aim: Tumors of unknown primary (TUP) accounts for 3-5% of all new cancer diagnosis and is the seventh most common malignancy. TUP is defined as a biopsy proven malignancy whose anatomical origin remains unidentified after passing through extensive diagnostic evaluation. Overall, the PET detection rate of the primary lesion is about 39%. The purpose of our study was to evaluate the clinical value of ¹⁸F-FDG PET in patients with the clinical information of TUP, who performed a scan in our institution during a five year period. **Materials and Methods:** We retrospectively reviewed the charts of 80 patients (33 women; 47 men, mean age 60.3±12.9 years) referred for a ¹⁸F-FDG PET/CT scan because of metastases from unknown primary sites (13 patients with metastatic cervical adenopathy; 67 patients with extracervical metastases), between January 2005 and January 2010. Only patients with histologically or cytologically proven malignancy and who underwent an extensive diagnostic work up previous to the PET/CT scan were included. PET images were obtained 45 to 60 minutes after ¹⁸F-FDG injection and low dose CT images were used for attenuation correction and anatomic mapping. Correlative final histopathologic/cytologically findings and clinical follow-up (for a mean period of 24.9 months) were used to assess the results of ¹⁸F-FDG PET/CT. **Results:** Of the 80 patients evaluated, 48 (60%) showed abnormal tracer accumulations. In 38 (47.5%) of those 80 patients ¹⁸F-FDG PET/CT was true positive, identifying, more frequently, the primary tumor in the lung and oropharynx. In 10 (12.5%) of the 80 patients ¹⁸F-FDG PET/CT was false positive and in 14 (17.5%) did not reveal lesions suspected to be the primary; however, primary tumors were found in these 14 patients during clinical follow up (false negatives). In 18 (22.5%) of the 80 patients ¹⁸F-FDG PET/CT did not reveal lesions suspected to be the primary; however, primary tumors were not found in these patients at clinical follow up. **Conclusion:** In our experience ¹⁸F-FDG PET/CT had a true positive result of 47.5% in the detection of the unknown primary tumor in patients referred with a TUP diagnosis. We believe that our results favor the use of ¹⁸F-FDG PET/CT in an earlier stage in the TUP diagnostic workup but further clinical research and cost-benefit analysis is still necessary.

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The role of fluorine 18 fluorodeoxyglucose positron emission tomography/computed tomography in liver metastases from unknown primary tumour

E. Kaya¹, I. Çiftçi², H. Önem¹, S. Doğan¹, N. Canbolat³, E. Vardareli⁴;
¹Acibadem Kayseri Hospital, Kayseri, TURKEY, ²Kayseri Training and Research Hospital, Kayseri, TURKEY, ³Sonomed Medical Imaging Center, İstanbul, TURKEY, ⁴Acibadem Kozyatağı Hospital, İstanbul, TURKEY.

Background: Fluorine 18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is one of the more frequent imaging modalities in the management of patients with cancer of unknown primary origin. Metastatic liver lesions most commonly originates in the gastrointestinal tracts, lungs, pancreas, breasts, over, malign melanoma, lymphoma and unknown origins. **Aim:** The purpose of this study is to evaluate the role of 18F-FDG PET/CT in detection of primary tumor in patients with liver metastases from unknown primary origin. **Material and Method:** This was a prospective study consisting of 39 patients (28 male, 11 female) to detect primary site and evaluate metastatic areas of patients referred to our clinic in whom metastatic focus were found in liver with conventional methods (ultrasonography, computed tomography, magnetic resonance image) and histopathological examination without primary focus. All pathological 18F-FDG uptake site was delineated at PET/CT scan for further clinical investigation. **Results:** 18F-FDG PET/CT scan located correctly the origine of primary tumour in 13 patients (13/39, 33.3%): lung (n=3), kolorectal (n=3), gastric (n=2), genitourinary tract (n=2), pancreas (n=1), breast (n=1) and skin (n=1). 18F-FDG PET/CT scan did not identify primary tumour focus in 26 patients (26/39, 66.7%). Other diagnostic methods and clinical trials detected primary focus in 3 patients (3/39, 7.6%). The primary tumour origine was not detected in 23 patients (23/39, 58.9%). However, new metastatic lesions were determined by the help of 18F-FDG PET/CT and the stage of the disease was shifted in 5 patients (5/39, 12.8%). So ongoing treatment were re-organized in 10 patients (10/39, 25.6%) according to 18F-FDG PET/CT results. **Conclusion:** 18F-FDG PET/CT provide considerable diagnostic contribution in detection of primary tumour site in patients with liver metastases from unknown primary origine. **Keywords:** 18F-FDG PET/CT, liver metastases, primary unknown tumour.

P547**The value of 18F-FDG PET/CT in the detection of unknown primary tumors sites**

M. L. G. D. Costa, F. Lopes, I. Lucena, J. Teixeira, H. Duarte, O. Soares, L. Bastos; IPOPF, EPE, Porto, PORTUGAL.

Aim: It is known from previous works in literature that PET (Positron Emission Tomography) using ¹⁸F-FDG (¹⁸F-fluoro-2-deoxy-D-glucose) is a useful diagnostic tool to access primary tumor locations. The aim of this study was to substantiate the potential of ¹⁸F-FDG PET/CT in the detection of localization of the primary tumor in patients with metastatic cancer from unknown primary origin. A retrospective (5 years) and broad analysis, of various different cases is presented in this work. **Methods:** From a total of 10307 PET/CT scanned patients in our institution between September 2004 and November 2009, we considered a population of 159 patients previously diagnosed with unknown primary tumor (94 male and 65 female) between 20 and 90 years old. **Results:** The localization of the primary tumor was acknowledged by the ¹⁸F-FDG PET/CT scan in 78 patients of the considered initial population of 159 patients. In 33 of these 78 patients, the localization of the primary tumor was later confirmed by histology (30 patients), analysis of the pleural effusion (1 patient) and biopsy of the metastasis (2 patients). In 45 of these 78 patients, the primary tumor location showed by the PET/CT scan was not confirmed. In the 81 remaining cases the primary tumor location was not identified by PET/CT. **Conclusions:** From the initial population of 159 patients with unknown primary tumor site, 20.7% were correctly identified by ¹⁸F-FDG PET/CT and confirmed later by histology, analysis of the pleural effusion and biopsy of the metastasis. From the same initial population, 28.3% remained with undetermined primary tumor localization, although the PET/CT scans provided a primary tumor location that was never confirmed. In the remaining 50.9% of this population, the primary tumor location was not detected by PET/CT. The acquired data of the present work, with 20.7% of clear identification of the unknown primary tumor site among the studied population, supports the valuable diagnostic contribution of FDG-PET/CT in the evaluation of patients with metastatic cancer from unknown primary origin.

P548**The value of FDG PET/CT in the evaluation of patients with metastatic carcinoma of unknown primary**

G. Tan¹, G. U. Vural², B. E. Akkas², U. Topal²; ¹Ankara Oncology Research and Training Hospital department of Nuclear Medicine, Ankara, TURKEY, ²Ankara Oncology Research and Training Hospital Department of Nuclear Medicine, Ankara, TURKEY.

Treatment and management of patients with metastatic carcinoma of unknown primary is a clinical problem. ¹⁸F-fluoro-2-deoxy-D-glucose (FDG) Positron Emission Tomography/Computed Tomography (PET/CT) is a well established diagnostic tool in the clinical oncology practice. The aim of this study is to evaluate the value of FDG PET / CT in detecting primary tumor site in patients with metastatic cancers of unknown origin and its role in the patient management. **Method:** In 2009, 41 patients with a biopsy proven metastatic disease and negative conventional diagnostic procedures underwent FDG PET/CT for the localization of the primary tumor site. Metastatic tumor sites were located in neck (n: 18, 43.9%), brain (n: 6, 14.7%), soft tissue (n: 4, 9.7%) and in other regions (n: 13, 31.7%). 4 patients lost on follow up was excluded and 37 patients were included in this study. The efficacy of FDG PET/CT was evaluated in combination with histopathological findings. **Results:** PET/CT has detected primary tumor site in 16 patients (39%). The primary tumor was detected in nasopharynx (n:5, 31%), lung (n:3, 19%), thyroid (n:2, 13%), larynx (n:1), stomach (n:1), liver (n:1), pancreas (n:1), tongue root (n:1) and in colon (n:1). Besides, in 7 patients (19%) additional metastatic sites which changed the treatment strategy were detected by PET/CT. **Conclusion:** Whole body FDG PET/CT has a high rate of detecting primary tumor sites that were undetected by other modalities in patients with carcinoma of an unknown origin. Also by detecting additional metastatic sites, PET/CT has important contribution to clinical management. Above all, to optimize the management, PET/CT has to be considered as a powerful method in the early phase of diagnostic work up of patients with carcinoma of an unknown primary particularly when the metastatic site is located in the head and neck region.

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Oncology Clinical Science: Melanoma**P549****False Negative and False Positive Findings with 18F-FDG PET/CT in Malignant Melanoma**

G. Liszskay¹, M. Kasler¹, K. Gilde¹, Z. Fejos¹, Z. Lengyel², K. Borbola¹, E. Schmidt¹, K. Borbely¹; ¹National Institute of Oncology, Budapest, HUNGARY, ²Positron Diagnostic LTD, Budapest, HUNGARY.

Purpose. The incidence of malignant melanoma has increased more rapidly than that of any other cancer, recently. Several studies have focused on the usefulness of PET/CT in staging or early evaluation of metastases. In our study we tested the sensitivity, specificity and accuracy of 18F-FDG PET/CT in patients with malignant melanoma. **Methods.** PET/CT was performed in 158 Stage II-IV melanoma patients (80 males, 78 females; mean age: 58.2 years) for staging and restaging between 2005 and 2008. Regarding the indications 4 different groups were analyzed, respectively. Group I (n=27) included patients who underwent operations due to the primary tumor. Group II (n=16) presented patients with lymph node metastases before regional lymph node dissection. Group III (n=17) included patients after the intervention. Additionally, group IV (n=82) presented patients with findings of distant metastases by conventional imaging techniques. True negative (TN), True positive (TP), false negative (FN) and false positive (FP) cases, additionally sensitivity, specificity and accuracy of the method were assessed. **Results.** True negative and true positive findings were found in 68 (43.0%) and 68 (43.0%) cases. Twelve (7.5%) FP and 10 (6.5%) FN cases were detected. Four PET/CT negative cases of cerebral

metastases, 2 cases of liver metastases were confirmed by MRI. In one patient with pulmonary propagation PET/CT was negative; however it was visualized by CT. In 2 additional patients' cutaneous manifestations were detected by physical examination, in one patient the dissemination of the disease was confirmed by conventional imaging. There were 5 false positive findings of pulmonary metastases, 1 liver, 2 lymph node, 2 cutaneous, and 2 gastrointestinal metastases by PET/CT. Sensitivity, specificity, and accuracy of the method differed by groups.

Group	Sensitivity (%)	Specificity (%)	Accuracy (%)
Group I	87.5	92.0	93.7
Group II	100.0	50.0	93.7
Group III	71.4	90.0	82.3
Group IV	84.7	86.1	85.3

Conclusions. PET/CT can improve the management of patients with malignant melanoma. However, it is very important to analyse the causes of false negative and positive results, and to combine the patient's thorough investigation with conventional imaging modalities in order to improve the precise diagnosis of the disease.

P550**Clinical impact of FDG-PET/CT scan in the initial staging and restaging of malignant melanoma**

P. Medina-Quiroz, I. Martinez-Rodriguez, I. Banzo, R. Quirce, J. Jimenez-Bonilla, M. de Arcocha, H. Portilla-Quatrococchi, A. Rubio-Vasallo, R. del Castillo, J. M. Carril; Hospital Universitario Marqués de Valdecilla. Servicio de Medicina Nuclear. Universidad de Cantabria., Santander, SPAIN.

AIM: Accurate staging evaluation has therapeutic implications in patients with malignant melanoma. In this context, conventional imaging techniques (CIT) such as ultrasound, CT or MRI have known limitations. The role of FDG-PET/CT (FDG) scan for the management of these patients is not well established. Our purpose was to evaluate the clinical impact of the FDG scan in the initial staging and restaging of patient with malignant melanoma. **MATERIALS AND METHODS:** The study group included 43 patients with malignant melanoma (22 women/21 men, mean age: 56.4 +/- 12.2 years, Breslow index: 0.2-7.8 mm and Clark level: II-IV). Location of lesions was head (7 patients), upper extremities (5 patients), trunk (13 patients) and lower extremities (18 patients). Patients were referred to FDG scan for initial staging (18 patients) and restaging (25 patients). Patients were at least 6 hours fasted and received an intravenous injection of 8 MBq/kg 18F-FDG. Blood glucose levels were <200 mg/dL in all cases. FDG scan was acquired 90 minutes after FDG administration. A visual analysis of images was performed. All patients had CIT staging with CT and/or MRI previous to FDG scan. **RESULTS:** In 29 of the 43 patients (67.4%), FDG scan did not change the CIT staging. Of these 29 patients, in 21 FDG and CIT showed the same lesions, in 7 (16.2%) FDG showed more lesions (mainly in lymph nodes and bone) and in 1 patient FDG showed less pulmonary lesions. In the other 14 patients (32.5%) FDG scan determined a change in the CIT staging. Five patients were correctly upstaged: 3 had lymph node involvement in a different nodal stations and local recurrence and 2 patients unsuspected bone metastasis. Understaging occurred in 9 of that 14 patients accordingly to FDG. FDG correctly discarded metastasis in an adrenal gland in 1 case (adrenal adenoma histologically confirmed), lung nodule in 1 case (CT follow-up) and lymph node enlargement in 3 (CT follow-up). However, FDG did not detect liver metastases in 1 patient, pulmonary metastases (<1 cm in size) in 2 patients and lymph node involvement in 1 patient. **CONCLUSION:** FDG and CIT staging agree in two third of patients with malignant melanoma. FDG scan correctly changed the CIT staging and restaging in 23.2% of patients. FDG scan detected more metastatic lesions especially bone and lymph node. Careful attention should be taken into account to the false negative FDG results obtained in liver, lung and lymph node metastases.

P551**The role of 18F-FDG-PET CT in malign melanome and comparison with conventional imaging modalities**

E. Ozkan, M. Araz, C. Soydal, M. Filik, O. N. Kucuk; Ankara University, Medicine Faculty, Ankara, TURKEY.

AIM: The aim of this study is to analyse the value of PET/CT in malign melanoma patients for preoperative staging or postoperative / posttreatment restaging and to compare with the conventional imaging modalities. **METHOD:** A total of 38 PET/CT findings of 36 malign melanoma patients (24M, 13F, mean age:53.78) performed in our clinic between years 2007-2010 were retrospectively analysed. 2 patients were examined for preoperative, 19 patients for postoperative staging and 15 patients for posttreatment restaging. **RESULTS:** In 27/36 patients a comparison with conventional imaging methods (USG, CT, MRI) was made. PET/CT was compatible with conventional imaging tools in 13/27 patients. In 5/14 patients no FDG uptake was seen in the areas radiologically shown (millimetric lung nodules in 4 patients and brain metastasis in 1 patient). In 9/27 patients, PET/CT revealed additional pathological FDG uptake in the liver, spleen, bone, lymph node, skin and soft tissue metastasis, recurrences and incidental thyroid lesions. In 4 patients, histopathological confirmation could be made (2 lymph nodes, 2 thyroid). In the 2 patients with pathological lymph node uptake, 1 of them (SUVmax:10.8) was reported as metastatic and the other (SUVmax:4.3) as reactive. In the other 2 patients, incidental thyroid uptake was detected. The results of the biopsies showed colloid nodule (SUVmax: 4.2) and papillary cancer (SUVmax: 16.9) respectively. **DISCUSSION:** It was found that PET/CT is superior to conventional methods in detecting local recurrences, secondary foci in the skin, distant metastasis and incidental pathologies like thyroid. However it has of limited value in the evaluation of millimetric lung nodules and brain metastasis.

P552**Is 0,75mm Breslow thickness the right cut-off point for performing sentinel node biopsy in patients with melanoma?**

A. Doumas¹, A. Dionyssopoulos¹, T. Christoforidis¹, D. Boundas², I. Iakovou¹, D. Lopresti¹, S. Georga¹, V. Nikos¹, N. Karatzas¹; ¹3rd Department of Nuclear Medicine, Aristotle University of Thessaloniki, Thessaloniki,

GREECE, ²⁴Hippokrates" Nuclear Medicine Laboratory, Thessaloniki, GREECE.

AIM: Currently, there is no clear cut-off point of Breslow thickness in order to avoid unnecessary lymph node excision surgery, without missing metastatic nodes, in patients with malignant melanoma. **METHODS:** We retrospectively studied a cohort of 64 patients, with pathologically proven malignant melanoma, who underwent lymph node scintigraphy and surgical resection of the sentinel node, during the last two years. The patients were divided into 5 groups: - Group 1: Ten patients, mean age 46+/- 6 years (range 40-55 years), with Breslow thickness of the lesion 0.51-0.75 mm - Group 2: Eleven patients, mean age 41+/- 9 years (range 31-61 years), with Breslow thickness 0.76-1mm. - Group 3: Twelve patients, mean age 59+/- 12 (41-76 years), with Breslow thickness 1.01-1.25mm. - Group 4: Fourteen patients, mean age 61+/- 8 (38- 74 years), with Breslow thickness 1.26- 1.5 mm - Group 5: Seventeen patients, mean age 56 +/- 10 (32- 71 years), with Breslow thickness >1.5mm **RESULTS:** Seven positive (infiltrated) lymph nodes were found. From these, 3 patients belonged to the 5th group (Breslow > 1.5mm) , two patients belonged in the 4th group (Breslow 1.26 -1.5 mm) one patient belonged in the 3rd group (Breslow 1.01- 1.25mm) and one patient belonged in the 2nd group (Breslow 0.76- 1mm). **CONCLUSION:** Sentinel node biopsy in patients with Breslow thickness less than < 0,75 mm isn't useful and must not be carried out, except in high risk cases such as melanomas with ulceration, high mitotic rate and vertical growth phase.

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The use of PET-CT for staging and restaging purpose in malign melanoma: Preliminary results

Y. Sanli¹, D. Has¹, F. Geçer¹, E. Yılmaz¹, S. Ekmekci¹, C. Türkmen¹, I. Adalet¹, S. Unal¹, E. Sağlam², F. Tas², S. Kurul², A. Mudun¹; ¹Istanbul University, Istanbul Faculty of Medicine, Department of Nuclear Medicine, Istanbul, TURKEY, ²Istanbul University, Istanbul Faculty of Medicine, Department of Oncology, Istanbul, TURKEY.

Objectives: Malign melanoma of the skin is one of the lethal cancers that may spread regionally and to distant sites. Accurate staging and restaging of disease is required for appropriate treatment protocol. In this study, we aimed to review our experience with FDG-PET/CT in the management of melanoma. **Methods:** In the present report, 23 (mean age 55.3±12.4 years) patients with melanoma who had whole-body PET/CT at our institution from April 2009 to January 2010 were retrospectively reviewed. Nine patients were female and 14 patients were male. FDG-PET scans were obtained for staging and restaging in 3 and 20 patients respectively. PET/CT scan was performed between 60 min following 10-15 mCi F-18 -FDG on a Siemens LSO HD system. FDG-PET findings were interpreted and classified as positive and negative or inconclusive. **Results:** Primary tumor locations were head and neck in 9 patients, trunk in 5 patient and extremity in 9 patients. PET scans were positive in 12 patients, negative in 10 patients and inconclusive in 1 patient. Of 15 patients with available complete data for Breslow Index (BI), 5 had BI 1-4mm and 10 had BI 4-8 mm. Positive scans were confirmed with biopsy whenever feasible or with conventional radiologic imaging methods. In 10 patients with locoregional and 2 patients with distant metastasis of primary lesions, appropriate therapy regimens according to their stage were planned. Among the 10 patients with negative PET results, 1 false negative result was found. In this patient, FDG-PET could not demonstrate the primary lesion in choroid plexus, which was shown by MRI imaging. The remaining PET negative patients were accepted as true negative by using clinical examination and other radiologic methods. These patients were free of disease after a mean follow-up of 5.2 months (2-8 months). One patient with suspicious metastatic uptake in axillary lymph node was accepted as positive and this patient received chemotherapy protocol. **Conclusion:** The pattern of distant spread of disease in melanoma is highly unpredictable. Despite low power of the study, our preliminary experience confirms the favorable results of FDG-PET/CT for staging and recurrence detection or metastatic spread.

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Lymphoscintigraphy for surgical planning: A new protocol to optimize surgical time slots and staff schedule in sentinel lymph node biopsy (SLNB) in malignant melanoma of the trunk.

M. Danús¹, B. Intriago¹, N. Calvo¹, M. Montero¹, J. Vaño², P. Mejina², D. Mejina², F. Martínez-Madueño², T. Azón², F. Rius², E. Baeta²; ¹DIMATGE, Reus, SPAIN, ²SAGESA HOSPITAL SANT JOAN, Reus, SPAIN.

INTRODUCTION: Small hospitals lacking of enough surgical resources require cost-effective scheduling of staff and surgical times. Patients with Malignant Melanoma (MM) of the trunk undergoing a sentinel lymph node biopsy (SLNB), can show variable drainage regarding the number and location of the lymph node basins. This variability requires different surgical approaches. Based on the good reproducibility of lymphoscintigraphy, we could plan a number of days before SLNB, the exact surgical fields, and organize the surgical time slots. **METHOD:** We underwent a prospective study, including consecutive patients candidates for SLNB in MM of the trunk. We perform two lymphoscintigraphies in each patient, the first one for surgery planning and the second one to perform the SLNB the following day. The interval between lymphoscintigraphies was more than 24 hours. Both lymphoscintigraphies were performed applying the same protocol and after the resection of the primary lesion. **RESULTS:** Up to date, we have included five patients. In all cases we found 100% reproducibility regarding the nodal basin location. We could avoid the inclusion of at least two potential surgical fields in each patient, saving a minimum of 50% scheduled surgical time slots. The results are summarized in the following table.

Patient	Days between lymphoscintigraphies	Lesion localization	Potential surgical fields	Drainage zone
1	21	Midline lumbosacral	Both axillae, Both groins	Both groins
2	28	Left Supra-escapular	Both axillae, Both supraclavicular areas	Supraclavicular area ipsilateral
3	1	Left lumbar site	Both axillae, Both groins	Both axillae

4	12	Inter-escapular	Both axillae Both supraclavicular areas	Both axillae
5	7	Right hypochondrium	Both axillae, Both groins	Right axilla

CONCLUSION: By performing lymphoscintigraphy for surgical planning in patients with MM of the trunk we were able to improve the cost-effectiveness of the surgical SLNB scheduling and the allocation of resources. Comparing two lymphoscintigraphies in the same patients, the reproducibility was 100%. This reproducibility allows a flexible scheduling of SLNB procedure regardless of the availability of a gamma camera, just needing the tracer injection.

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Oncology Clinical Science: Soft Tissues & Sarcoma

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Utility of FDG PET/CT in Childhood Rhabdomyosarcoma

F. Ricard¹, S. Cimarelli², E. Deshayes³, T. Mognetti², P. Thiesse⁴, F. Giammarile⁵; ¹Université de Lyon - Centre Léon-Bérard, Département de Médecine Nucléaire, Lyon, FRANCE, ²Centre Léon-Bérard, Département de Médecine Nucléaire, Lyon, FRANCE, ³Université de Lyon - Hôpital Edouard Herriot, Département de Médecine Nucléaire, Lyon, FRANCE, ⁴Centre Léon-Bérard, Département de Radiologie, Lyon, FRANCE, ⁵Service de Médecine Nucléaire, CHLS, Hospices civils de Lyon and Faculté de Médecine, EA 3738, UCB Lyon 1, Pierre Bénite, FRANCE.

Aim: Rhabdomyosarcoma is the most common soft tissue sarcoma in children and adolescents. Its prognosis has increased over the last decade but remains poor in disseminated forms. The therapeutic management of sarcomas requires reliable imaging for appropriate assessment of disease extent. This study aimed to evaluate 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) as an adjunct to conventional imaging techniques (CIMS) in the staging and restaging of paediatric rhabdomyosarcoma. **Materials and methods:** Thirteen consecutive children and adolescents (12 males and 1 female; mean age: 9.6 years) with histopathologically proven rhabdomyosarcoma (10 alveolar and 3 embryonic), in whom FDG PET/CT was performed at staging with less than a 15-day interval between CIMS and FDG PET/CT, were retrospectively included. Eight patients had one or more restaging assessments. In total, 35 FDG PET/CT were compared with CIMS (MRI, CT and Bone Scintigraphy). Histological data, the final judgement of a multidisciplinary tumour board and follow-up (mean: 27.7 months) were considered as the standard for result interpretation. **Results:** At staging, FDG PET/CT revealed a rhabdomyosarcoma of the prostate missed by CIMS, and found 19 true positive lymph node territories in 4 patients and 11 bone metastases in 3 patients, versus 12 and 3, respectively, with CIMS. Conversely, FDG PET/CT was inferior for detecting infracentimetric lung nodules in 1 patient. FDG PET/CT modified staging in 6/13 (46%) patients (N upstaging in 3 patients, N downstaging in 1 patient, M(bone) upstaging in 2 patients) and changed treatment plan in 2/13 (15%) patients at staging. During follow-up, both FDG PET/CT and CIMS revealed local recurrences in 3/8 patients. In 4 patients with focal cortical bone and/or widespread bone marrow involvement, treatment monitoring was more effective using FDG PET/CT. **Conclusion:** FDG PET/CT can be useful in assessing paediatric rhabdomyosarcoma. Its adjunction to conventional imaging seems to be significantly superior to CIMS alone especially for evaluating lymph node and bone involvement, with potential TNM changes at staging and restaging. FDG PET/CT can also be useful for detecting unknown primary site and can alter the therapeutic strategy.

P556

¹⁸F-FDG PET findings of elastofibroma dorsi

K. Koyama¹, T. Okamura², Y. Hamazawa³, H. Seura², Y. Miki¹; ¹Osaka City University Graduate School of Medicine, Osaka, JAPAN, ²PET center, Saiseikai Nakatsu Hospital, Osaka, JAPAN, ³Department of Radiology, Saiseikai Nakatsu Hospital, Osaka, JAPAN.

Objectives: The elastofibroma dorsi is often diagnosed incidentally by CT scanning as a characteristic shaped mass, because it is asymptomatic in most cases. Recently, incidental detection of this tumor has been reported in the PET medical checkup and there is also reported a possibility of misinterpreting such FDG uptake of this tumor as a malignant tumor. The purpose of this study is to retrospectively examine the FDG PET findings of elastofibroma dorsi. **Methods:** Of the 6000 patients performed dual-time-point FDG PET or PET/CT scanning in the PET center of Saiseikai Nakatsu Hospital from February 2005 to May 2008, 6 patients with 11 lesions who were diagnosed clinically to have elastofibroma dorsi were investigated in this study (age ranged from 63 to 72). Seven patients were performed FDG PET/CT scanning and the other 3 patients were performed FDG PET scannings and multi-detector CT scanning performed within 1 week before or after FDG PET scanning. Early and delayed images were acquired at 1 and 2 hours after FDG injection, respectively. FDG PET/CT images were examined visually and statistically. **Results:** On CT imaging, all tumors showed crescent shape, and the tumor major axis ranged from 37 to 150 mm. By visual analysis of PET images, all tumor lesions in early and delayed images showed abnormal but not strong FDG uptakes. By quantitative analysis of PET images, standardized uptake values (SUVs) in early images ranged from 1.1 to 2.7 (mean, 1.94 ± 0.59), and those in delayed images ranged from 1.2 to 2.8 (mean, 1.95 ± 0.54). The SUVs on delayed images were higher in 6/11 lesions (56%) and the SUV was lower in 5/11 lesions (44%) compared to those of early images. There was no significant difference in SUVs between early and delayed images. **Conclusions:** All elastofibromas showed abnormal FDG uptakes, however, SUVs show no significant difference in between early and delayed images.

Poster Presentations

P557 PET/CT with ¹⁸F-FDG in the evaluation of Sarcomas

R. Jover-Diaz¹, A. Vicente-Bártulos¹, D. Lourido-García¹, L. Gorospe-Sarasúa¹, A. Montero-Navas¹, J. García-Poza¹, E. Ortiz², M. Pozo³, R. Núñez-Miller¹, J. Alfonso-Alfonso¹; ¹Instituto Tecnológico de Servicios Sanitarios, MADRID, SPAIN, ²Centro MD Anderson-España, MADRID, SPAIN, ³Instituto Pluridisciplinar-Univ Complutense, MADRID, SPAIN.

PURPOSE: We aim to assess the importance of the PET/CT with ¹⁸F-FDG scans in staging and re-staging patients with pathologic proven sarcoma performed at our institution. **MATERIALS AND METHODS:** We retrospectively reviewed 75 PET/CT studies, in 40 patients with biopsy-proven sarcoma. All patients underwent at least one ¹⁸F-FDG PET/CT (GE ST 4) scan. The CT scan was performed with oral contrast in all patients and with intravenous iodinated contrast in selected cases. PET images were acquired in 2D mode (BGO), 45-60 minutes after the intravenous injection of ¹⁸F-FDG (0.15 mCi/Kg). Visual and semi-quantitative analysis was used to evaluate the PET images (SUV_{max}). All the studies were read and reported simultaneously by a nuclear medicine physician and a radiologist. **RESULTS:** 40 patients (26 women). Age: 52 years (20-84) There were 5 (12.5%) osseous and 35 (87.5%) extraosseous sarcomas. In this later group, the predominant tumors were uterine leiomyosarcomas (10 patients) and liposarcomas (11 patients). Also, the most frequent location for tumor involvement was in the soft tissues of the lower limbs. 28 patients underwent previous surgery, 16 patients were treated with chemotherapy and 12 with radiotherapy. The scans were performed for the initial staging in 10 patients; with all the other cases being for re-staging. Of the initial staging PET/CT scans, 9/10 patients showed local and/or regional involvement, with only one showing, distant spread of disease. Of the re-staging PET-CT scans, 25/30 had abnormal findings; 11 with local or regional involvement and 14 with distant metastases. In the post-treatment and follow-up assessment, PET/CT studies we found the following responses: -Complete Response: 4 patients -Partial Response: 1 patient -Post-surgical changes: 4 patients -Stability or progression: 31 patients CT scans demonstrated additional findings such as: pulmonary nodules, adenopathies and tumour implants that were metabolically inactive in PET. Therefore, only radiological follow-up was recommended for these non-FDG avid lesions **CONCLUSION:** In most PET/CT scans done for initial staging in patients with sarcoma, the disease is localized. By contrast, in re-staging studies the disease is considerably more extensive, with most cases having either local or distant metastasis. Unfortunately, very few (10%) patients demonstrate complete response by FDG PET/CT in our group of patients.

P52 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Oncology Clinical Science: Miscellaneous

P558 Renal parenchyma and collecting system imaging at PET/CT-scans in normal and impaired kidneys. Patterns of FDG-uptake and correlation to diuretic renography (MAG-3).

B. Intriago¹, M. Danús¹, C. Trampal², Y. López³, N. Calvo¹, M. Montero¹, L. Millá¹; ¹DIMATGE HOSPITAL SANT JOAN, REUS, SPAIN, ²IAT, Barcelona, SPAIN, ³SAGESA HOSPITAL SANT JOAN, REUS, SPAIN.

INTRODUCTION The aim of this study was to assess the information on renal function, that may be gained from renal images obtained from a standard oncologic diagnostic PET/CT-scans. **METHODS** We compared the findings from a diuretic-renography-MAG3 (DRMAG3) with those gained from a standard 18F-FDG-PET-scan performed for oncologic diagnostic purposes regarding degree of FDG-uptake at the renal parenchyma, collecting systems and ureters. A visual assessment was performed as well as measurements of the distribution and grade of FDG-uptake in the renal parenchyma (correlated to mediastinal blood-pool and liver), collecting systems and ureters in all patients. The CT-portion of PET/CT-scan and any available contrast-enhanced-CT were used to evaluate the dilatation of the collecting systems and ureters. DRMAG3 was used to evaluate any obstructive signs, the differential renal function (DRF) and the global and individual effective renal plasma flow (ERPF). Creatinine and urea blood levels from the same time period, were also reviewed. **RESULTS:** We studied 18 kidneys (9 patients). Two patients were already known as suffering from renal disease and 7 presented no clinical or analytical signs of renal impairment. The DRMAG3 detected 3 kidneys to be non functional (DRF< 15%) (belonging to the group of patients without previous history of renal impairment) and 4 kidneys showed pathological DRF (<40%) and ERPF. On the PET-scan, all kidneys showed similar parenchymal FDG-uptake (SUVmedian:4.4mg/L), without statistical difference (p<0.01) between the normal ones (SUVmedian:4.4mg/L) and the non-functional annulated kidneys (DRF<15% ; SUVmedian:3.9mg/L). All kidneys showed also correct parenchymal enhancement at contrast-CT-scans and their FDG-uptake was in all cases similar or higher than their liver and mediastinum correspondent uptake. In 4/18 kidneys, no FDG-activity was detected neither within the collecting system, nor in the ureters. Coincidentally these 4 kidneys were non functional at the DRMAG3, showing also variable degrees of pelvi-caliceal or ureteral dilatation (hydronephrosis grade II up to III) on CT images. **CONCLUSIONS:** Although the small studied sample can not reach statistical significance, our results showed that on conventional oncological PET/CT-studies, and in patients even without previous renal impairment history: -Visual absence of FDG excretion within collecting systems and ureters (associated in some cases to additional variable pelvi-caliceal or ureteral dilatation), should arouse awareness of an underlying non functional kidney, even if the parenchyma FDG-uptake seems non-altered. -Symmetrical parenchyma FDG-uptake, with a degree of uptake similar or higher than liver, does not preclude renal impairment.

P559 Sarcoidosis and sarcoid-like disease incidentally diagnosed in PET/CT studies. Clinical settings and patterns of 18F-FDG uptake.

B. Intriago¹, M. Danús¹, C. Trampal², N. Calvo¹, F. Marimon³, E. Etxebarria³, L. Millá¹; ¹DIMATGE, Reus, SPAIN, ²IAT, Barcelona, SPAIN, ³SAGESA HOSPITAL SANT JOAN, Reus, SPAIN.

INTRODUCTION: Incidental findings like Sarcoidosis and sarcoid-like granulomatous lesions are not uncommon in the diagnostic workup of oncologic diseases. These entities are important pitfalls interfering in the staging of disease. We intend to study the role of PET/CT in incidentally diagnosed sarcoidosis/sarcoid-like disease and to find out if any particular imaging pattern of FDG-uptake could be detected. **METHODS:** We retrospectively reviewed all patients referred to our institution in the last two years, to perform a PET/CT-scan for oncological staging purposes, who incidentally were diagnosed of sarcoidosis or sarcoid-like disease, either as single entity or as a concomitant disease. **RESULTS:** 6 patients were selected (1 male, 5 females), age (range: 31-60years). Two patients underwent a PET/CT-scan for staging/restaging of an already known neoplasm (endometrial and esophageal carcinoma) and the other 4 to exclude malignancy, that was suspected because of severe chronic anemia of unknown origin, retroperitoneal mass, pathological vertebral fracture and atypical lupus erythematosus. 5/6 patients had a histological confirmation of noncaseating granuloma compatible with sarcoidosis or sarcoid-like disease, whereas in 1 case the diagnosis was established after clinical follow up. In all cases tuberculosis was excluded (Lowenstein test negative) and in 0/3 showed pathological ECA levels. Three patients presented disease limited just to the pulmonary area (all showing the "lambda" sign), whereas 3 presented multiorgan involvement [multiple osseous lesions (n=2), multiple lymphatic areas(n=2), hepatic foci (n=2), splenic foci (n=1), pancreatic focus (n=1)]. PET/CT detected lesions not described on CT or MRI in the following locations: spleen, pancreas, breast, bone and small lymph nodes. PET/CT changed the staging category of endometrial carcinoma of one patient. PET/CT-scan was able to select the most accessible and successful biopsy site in 4/6 patients (laterocervical, subcarinal lymph node, vertebral body and breast). **CONCLUSIONS:** The diagnosis of sarcoidosis or sarcoid-like-disease is a combination of histological, clinical and radiological features, after excluding other inflammatory/infectious diseases. PET/CT is able to offer unique information for the following clinical purposes: - Raising the awareness of this entity as a concomitant disease in patients suffering from cancer or suspected malignancy, especially those who present a "lambda" sign. -Selecting the best biopsy site, based on the detection of accessible lesions not considered on conventional imaging. - Changing the staging of some cancer patients based on the detection of atypical pathological unexpected uptake-sites, which lead to a confirmation by biopsy.

P560 Incidental lesions detected with PET/CT

S. Yasuda¹, K. Kobayashi², Y. Miyatake², M. Ono², T. Kato², M. Takechi¹, T. Kojima², W. Ko², T. Ushimi²; ¹Tokai University School of Medicine, Kanagawa, JAPAN, ²Yotsuya Medical Cube, Tokyo, JAPAN.

Objective: Miscellaneous lesions are incidentally detected during FDG PET/CT study including carcinomas, and this fact has potential to increase the value of PET/CT. The aim of the study was to determine the types and frequency of incidental lesions detectable with PET/CT. **Methods:** The study group was consisted of 1634 asymptomatic subjects (939 men, 695 women, 54.9±10.7 years old) who underwent PET/CT study for cancer screening between May 2005 and December 2009 at our institution. PET/CT study was performed 60 minutes after injection of 140-200 MBq of FDG (Discovery ST, GE Healthcare, WI). PET/CT images were visually interpreted by 2 physicians and recorded prospectively. The recorded findings were compared with final diagnoses obtained by other imaging modalities and laboratory studies carried out later. **Results:** Malignant tumors were detected in 12 of 1634 subjects (0.7%); colon and rectum (3), lung (3), thyroid (2), breast (2), esophagus (1), and ovary (1). All 12 subjects underwent potentially curative treatments. Carcinomas except for 3 lung carcinomas were PET-positive. The 3 lung carcinomas were less than 1.5cm in size and detected by CT; 52 pulmonary nodules (>5mm) were found on CT images, and 3 of 52 nodules (5.8%) were revealed to be carcinomas. A total of 178 clinically meaningful nonmalignant lesions were found in 167 of 1634 subjects (10.2%); diffuse thyroidal FDG uptake compatible with chronic thyroiditis (75), cholecystolithiasis (48), urinary tract stone (>5mm) (21), maxillary sinusitis (16), adrenal tumor (7) including one case with Cushing syndrome, aneurysm (5), colonic adenoma (3), and atypical mycobacteriosis of the lung (3). As a result, carcinomas and clinically meaningful benign lesions were found at a rate of 0.7% and 10.2%, respectively in our study group. **Conclusion:** Because miscellaneous lesions can be discovered including carcinomas at potentially curative stage, careful attention should be paid in interpreting PET/CT images.

P561 Performance profile of FDG-PET and PET/CT for cancer screening on the basis of a Japanese nationwide survey between 2005 and 2008.

R. Minamimoto¹, M. Senda², T. Terauchi³, K. Uno⁴, S. Jinnouchi⁵, H. Fukuda⁶, T. Inoue⁷; ¹National Center for Global Health and Medicine, Tokyo, JAPAN, ²Institute of Biomedical Research and Innovation, Kobe, JAPAN, ³National Cancer Center, Tokyo, JAPAN, ⁴Nishidai Clinic Diagnostic Imaging Center, Tokyo, JAPAN, ⁵Atsuchi Memorial Clinic PET Center, Kagoshima, JAPAN, ⁶Institute of Development, Aging and Cancer, Tohoku University, Sendai, JAPAN, ⁷Yokohama City University, Yokohama, JAPAN.

Objective "FDG-PET for cancer screening" is defined as FDG-PET (including PET/CT) scan with or without combination of other tests for cancer screening of healthy subjects. This survey is aiming at investigating the current status of "FDG-PET for cancer screening" in Japan and to evaluate its performance profile. **Methods** This survey was based on the questionnaires sent to 290 facilities, in which FDG-PET scans were performed between 2005 and 2008. We evaluated 162427 subjects from 107 PET centers, who were positive by FDG-PET and/or by one or more combined screening tests and were referred for further evaluation. **Results** On analyzing 162427 cases who underwent FDG-PET cancer screening at 107 PET centers, thorough examination was indicated for 11.0% (9.8% for dedicated PET, 11.8% for PET/CT) of the cases as a result of positive findings in PET and/or combined test. Among those, 1483 cases of cancers (1.18 % of total cases, positive predictive value of 30.8%) were found, of which 0.92% were PET positive and 0.26% were PET negative, resulting in the relative sensitivity of PET being 77.6%. Cancers of the colon/rectum,

thyroid, lung, and breast were most frequently found (407, 355, 328, and 155 cases, respectively) with high PET sensitivity (86%, 90%, 84%, and 88%). Conclusions Although the sensitivity may not be sufficiently high for some cancers, the advantage of 'FDG-PET for cancer screening' is to be able to detect a variety of cancers at a single test.

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Frequency of The Second Primary Detected by PET/CT in a Cohort of 2500 Patients

N. Can¹, M. Unlu²; ¹MEDICANA International Hospital, Ankara, TURKEY, ²Gazi University Medical Faculty Nuclear Medicine Department, Ankara, TURKEY.

We retrospectively analysed our PET/CT data pool between January 2009 and February 2010 to find the frequency of the second primary among oncology patients. **Material-method:** There were 2500 patient administered for diagnosis, staging, restaging or evaluation of treatment response. Patients coming more than once were counted just one time unless they had 2nd primary. Distribution of patients according to malignancy was as follows: 702 patients were lung-pleural - mediastinal cancer (ca), 418 pancreaticohepatobiliary-gastrointestinal tract ca, 347 lymphoma, 295 breast ca, 253 genitourinary ca, 204 head and neck ca, 58 malignant melanoma, 50 soft tissue and bone ca, 102 cancer of unknown primary and 71 with other. **Results:** The frequency of second primary was %3 overall, (n: 81; 45 male, 36 female). There was synchronised cancer in 29 cases out of 81 (35%), synchronised malignancy and second primary were observed most commmly in lung cancer group (n: 18 and n: 15 respectively). Number of patients according to the groups are shown in table 1. The second primary was developed most commonly in lung ca group. Colorectal ca in 12 patients (10 male, 2 female), head-neck ca in 9 (9 male), urinary system-prostate ca in 6 (6 male) patients were developed as the secondary or synchronised. Secondly breast cancer group developed second primary most (n: 12) : 5 case with gynecological cancer, 4 case with colorectal cancer. The frequency of secondary cancer in groups was as follows: in lung cancer %4.7, in pancreaticohepatobiliary-gastrointestinal cancer %4.4, in breast cancer %4, in genitourinary cancer %3.5, in melanoma %3.5, in head- neck cancer % 3 and in lymphoma %1.5. The diagnosis was confirmed with histopathology in all cases. **Conclusion:** PET/CT successfully detects the secondary or synchronised cancer earlier which has bad prognosis. The patient cohort is under the follow up in respect of prognosis.

Table of Contents	Head-neck cancer (n:12)	Lung cancer (n: 7)	Gynecological cancer (n: 7)	Urinary system-prostate cancer (n:10)	Colorectal cancer (n: 24)	Esophagogastric cancer (n: 2)	Breast cancer (n: 5)	Lymphoma (n: 10)	Malignant melanoma (n:0)	Hepatobiliary-pancreatic cancer (n: 4)
Second Primary Cancer										
Second Primary Cancer										
Head-neck cancer (n: 6)	1	3	0	1	1	0	0	0	0	0
Lung cancer (n: 33)	9	0	0	6	12	1	1	3	0	1
Gynecological cancer (n: 7)	0	0	0	1	2	0	2	2	0	0
Urinary System- prostate cancer (n: 2)	0	0	0	0	0	0	0	1	0	1
Colorectal cancer (n:7)	0	3	1	0	0	0	1	1	0	1
Esophagogastric cancer (n: 5)	1	0	1	0	2	0	1	0	0	0
Breast ca (n: 12)	0	1	5	0	4	1	0	1	0	0
Lymphoma (n: 5)	1	0	0	1	2	0	0	0	0	1
Malignant melanoma (n: 2)	0	0	0	0	1	0	0	1	0	0
Hepatobiliary-Pancreatic cancer (n:2)	0	0	0	1	0	0	0	1	0	0

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Experience with 18F-FDG-PET/CT in oncologic paediatric patients

A. P. A. Cistaro¹, S. Asafei², M. Pagano², V. Barat², E. Basso², M. Bianchi², F. Saglio², P. Fania³, F. Fagioli²; ¹IRMET S.p.A., Turin, ITALY, ²Oncology Department, Regina Margherita Infant Hospital, Turin, ITALY, ³Positron Emission Tomography IRMET S.p.A., Turin, ITALY.

Aim: To assess the role of FDG-PET/CT in paediatric patients. **Materials and Methods:** 75 patients (age 2-20 years) have been analysed: 12 for metabolic characterisation of lesions of unknown origin suspected for malignant disease, 11 for staging and 52 for re-staging. Whole body PET/CT images were obtained 60 min after the administration of 18F-FDG (3.7 MBq/kg) with Discovery ST (GE Medical Systems). CT was performed with adequate acquisition parameters for paediatrics. **Results:** no patient needed sedation during the procedure. In patients analysed for suspected malignant tumour, PET-CT resulted positive in 7 pts (final diagnosis: 2 Autoimmune Lymphoproliferative Syndromes (ALPS) caused by Fas mutation, 2 HL, 2 NHL, 1 ALL), and negative in 5 pts (2 lung aspergillosis, 1 spondilodiscitis, 1 eosinophilic granuloma, 1 lymphadenitis). In positive cases, PET-CT resulted able to indicate the most active and accessible site guiding biopsy. It allowed to avoid biopsy in patients with a PET-CT negative for disease in patient analysed for tumour staging (7 HL and 4 NHL), in 4 cases PET/CT confirmed previous clinical-radiological staging. In 7 cases improved previous staging modifying clinical and therapeutical approach, finding occult tumour sites. SUV measured on first PET/CT exam is important to evaluate chemotherapy effectiveness and for patient's follow-up. We also analysed 52 patients for re-staging (13 Ewing's sarcoma, 12 osteosarcoma analysed for suspected lung recurrence, 6 rhabdomyosarcoma, 5 NHL, 5 HL, 2 neuroblastoma, 1 Wilm's tumour, 1 sarcoma of kidney, 3 pNET, 1 adrenal gland carcinoma, 1 undifferentiated hepatic sarcoma, 1 synovial sarcoma, 1 epithelioid sarcoma). In 35/52 patients PET/CT correctly confirmed malignancy recurrence, 2

patients resulted false positives (lung flogosis in 2 osteosarcoma patients), 1 false negative (small lung lesion in Ewing's Sarcoma patient) and 14 true negatives. The PET/CT exam has modified the therapeutic approach in the 14% of this group of patients. **Conclusions:** in paediatric patients 18F-FDG-PET/CT seems to be useful in metabolic characterization of suspected tumour and it finds the more accessible active sites for biopsy. In our experience, in patients affected by lymphomas, PET/CT was able to improve staging in 7/11 cases. It seems also useful in re-staging modifying the therapeutic approach. Nevertheless, because of the high variety of tumour types and the low number of patients analysed, it is necessary to perform further investigations to support these results.

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18F-FDG PET in the management of patients with solitary pulmonary nodules: correlation to lesion size

S. Kommata; University Clinic of Nuclear Medicine, Vienna, AUSTRIA.

Aim of the study: We aimed to review the 18F-FDG PET scans of patients with indeterminate pulmonary nodules and to correlate the validity of the outcome with the size of the lesions. **Materials and Methods:** Ninety-five patients (47 male, 48 female, mean age 60±12.5 years) with solitary pulmonary nodules who had FDG PET scans were included in the present retrospective study. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Final diagnosis concerning malignancy was made from histology from tissue biopsy/surgical intervention or a two-year follow-up. The lesion-size (maximal diameter) was determined from CT images in 66 patients. These patients were divided according to their lesion-size in group I (30 patients): lesions <1.5 cm and group II (36 patients): lesions ≥1.5cm. **Results:** For all 95 patients FDG PET was true positive in n=52, true negative in n=29, false positive in n=9 and false negative in n=5. Overall, sensitivity of 18F-FDG-PET was 91%, specificity 76%, PPV 85% and NPV 85%. In group I - small lesions - sensitivity was 78% and specificity 71% (true positive n=11, true negative n=12, false positive n=3 and false negative n=4). In group II the sensitivity was 100% and specificity 61% (true positive n=25, true negative n=7, false positive n=4 and false negative n=0). **Conclusion:** According to our results 18F-FDG PET is a valuable tool for the characterisation of pulmonary solitary lesions. For lesions ≥1.5cm FDG-PET a negative PET scan excluded malignancy in our patients. For lesions <1.5cm and negative FDG-PET scan, a two years follow-up with CT has to be performed (Fleischner society criteria, Radiology 2005). The sensitivity of FDG PET for small pulmonary nodules is affected by respiratory movement. Our first results using respiratory gating in this group of patients suggest a significant improvement for the sensitivity by this technique. FDG PET positive results had a high predictive value for malignancy in both groups. However, specificity was moderate for small and large lesions. This drawback can be partly overcome using the good anatomical information from the CT part of PET/CT studies.

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Dynamic F-18 FDG PET for Evaluating Tumor Vascularity

N. Shuke, T. Onishi, A. Ando, K. Yamamoto, Y. Nomura, K. Saito; Kushiro Kojinkai Memorial Hospital, Kushiro, JAPAN.

Objective: Dynamic F-18 fluorodeoxyglucose (FDG) PET with 3D list mode acquisition could provide images in early blood flow phase. The objective of this study was to assess the usefulness of this method to evaluate tumor vascularity. **Methods:** To determine appropriate frame time for dynamic FDG PET images, a phantom study was performed using cylindrical phantom that had radially separated chambers filled with FDG solutions of different concentrations (0.5 - 55 KBq/ml). Using this phantom, 3D list mode data acquisition was performed using a PET-CT system (Discovery STE, GE). PET images of different frame time (1-3 sec) were reconstructed using 3D OSEM and FORE-FBP methods to evaluate uniformity and quantitativity in relation to frame time. As clinical applications, 3D list mode data acquisition was performed for 10 min right after bolus injection of FDG (200-300 MBq) in 7 patients with hypervascular tumors (hepatocellular carcinoma, 2; renal cell carcinoma, 3; carotid body paraganglioma, 2). Using acquired raw data, serial dynamic PET images in 64 x 64 matrix with frame time of 2 sec were reconstructed using 3D OSEM method. Dynamic PET images in early blood flow phase was visually evaluated for tumor vascularity and compared with contrast-enhanced X-ray CT (CE-CT). **Results:** The phantom study revealed that frame time of 2 sec at shortest was appropriate to obtain acceptable uniformity (constant of variation: 20%) and quantitativity (fractional error: 20%) with 3D OSEM. In clinical applications, Tumor blood flow was well-appreciated by visual evaluation on the initial blood flow phase images of serial dynamic PET images and the findings were concordant with those of CE-CT in all cases. **Conclusion:** Dynamic FDG PET with 3D list mode data acquisition in early blood flow phase was useful for evaluating tumor vascularity, although field of view was limited to the detector length in longitudinal direction. This method could be useful particularly for patients with renal failure or allergies to contrast media.

P53 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized Nuclear Medicine: Endocrinology

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A complex method for a visualization and localization of hyperfunctioning parathyroid glands including subtraction technique of planar scintigraphy and SPECT-CT

M. Garcheva, I. Kostadinova, N. Temelkova, G. Ganchev; Medical University-Sofia, Sofia, BULGARIA.

The scintigraphy of the parathyroid glands is based on the fact, that only the hyperfunctioning glands could be visualized. It is very helpful for their pre-and intraoperative localization. **The aim** of the study was to introduce and evaluate a complex radionuclide method for a precise localization of hyperfunctioning parathyroid glands. It combined 2 steps for their visualization: the first included application of subtraction technique of planar scintigraphy with sequential

images with ^{99m}Tc -pertechnetate and ^{99m}Tc -tetrofosmin (with an activity of 37 MBq and 740 MBq respectively) and the second - SPECT-CT technique. The thyroid, visualized with ^{99m}Tc -pertechnetate was subtracted (step subtraction) from the early (30 min.p.i.) ^{99m}Tc -tetrofosmine image, followed by low-dose SPECT-CT of the neck and upper part of the thorax for an exclusion of an ectopic parathyroid gland. The whole examination was in the range of 60 minutes. The method was applied in 17 patients with a proven hyperparathyroidism (parathormone was in the range of 97–1312 pg/ml). In four of them there was a concomitant thyroid problem (2-with partial resection, 2-with nodular goiter). In all of the patients an increased focal uptake in the hyperfunctioning parathyroid glands was detected (in 21 glands), which scintigraphic localization was proved surgically. The step-subtraction technique was very useful especially in cases with a changed thyroid gland, where a differentiation of the parathyroid from a thyroid tissue with unclear size and morphology was needed. SPECT/CT additionally helped in cases with doubtful results from the first step (small glands), for detection of multi-gland disease (found in 2 patients) and especially in cases with ectopic glands (in 2 patients with retrosternal and mediastinal localization, respectively). **We could conclude**, that the applied complex method for the visualization and localization of the hyperfunctioning parathyroid glands is very promising but further confirmation of the results are needed.

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Increased Metabolic Activity of ^{18}F -FDG in the Thymus Gland of Patients with Graves' Disease

S. Wang, Y. Chen; Shin Kong Wu Ho-Su Memorial Hospital, Taipei, TAIWAN.

PURPOSE: The aim of this study was to analyse the patterns of thymic ^{18}F -FDG uptake in patients with Graves' disease and the relationship between standard uptake value (SUV) level of 2-[Fluorine-18] fluoro-2-deoxy-D-glucose (^{18}F -FDG) uptake (in thyroid and thymus) and serum levels of T_3 , T_4 , TPO Ab, TSH R Ab and thymulin in patients with Graves' disease. **MATERIALS AND METHODS:** The subjects consisted of 65 patients with newly diagnosed Graves' disease without anti-thyroid drug treatment. In the control group, 30 examinees with history of Graves' disease after medical treatment was recruited, whose thyroid functions were normal. Whole-body ^{18}F -FDG Positron Emission Tomography (PET) was performed on all patients. The intensity of ^{18}F -FDG uptake in the thyroid and thymus region was graded subjectively on a five-point scale and semi-quantitatively using the SUV in the patient. Serum T_4 , T_3 , TSH, TPO Ab, TSH R Ab, and thymulin were measured by immunoassay. **RESULTS:** Among the 65 patients with Graves' disease, only 30 (46.2%) cases showed thyroid uptake of ^{18}F -FDG, and 39 (60%) cases showed thymus uptake of ^{18}F -FDG. The correlation coefficient between the serum thymulin and SUV level of ^{18}F -FDG uptake in thyroid was good ($r=0.74$, $p<0.001$). In the control group, 10 of the 30 examinees (33.3%) showed thyroid uptake of ^{18}F -FDG. In thymus, there was no substantially increased ^{18}F -FDG uptake in control group examinees. **CONCLUSION:** In Graves' disease patients, thyroid uptake of ^{18}F -FDG was not uniformly increased. Regrowth of thymus with focal midline uptake was the most common pattern of ^{18}F -FDG uptake in patients with Graves' disease. The relationship between SUV level of thyroid ^{18}F -FDG uptake and serum thymulin was good. T_3 and T_4 may be two important physiological factors regulating the uptake of ^{18}F -FDG in thymus.

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Usefulness of in vivo counting in parathyroid radioguided surgery

P. García-Talavera¹, C. González², E. Martín², M. E. Martín², A. Gómez², J. R. García-Talavera², ¹Hospital Clínico de Valladolid, Valladolid, SPAIN, ²Hospital Universitario de Salamanca, Salamanca, SPAIN.

Aim. In our hospital, radioguided surgery is performed in patients with primary hyperparathyroidism (pHPT). The aim of this study is to determine the optimal cut-off value for in vivo counting in order to distinguish between normal tissue and pathological glands. Furthermore, we evaluate the possibility of using this parameter to differentiate between unilobular and multiglandular disease. **Material and methods.** We included 63 patients with pHPT who were operated at the University Hospital of Salamanca between 2002 and 2009. All resected specimens were analyzed by frozen section. To plan the surgery, a double phase ^{99m}Tc -MIBI scintigraphy was performed with a Skylight (Philips) gammacamera, acquiring planar images 10-minutes and 2-hours after intravenous (i.v.) tracer administration (740 MBq). Between 30 minutes and 3 hours before the surgery, a new i.v. dose of ^{99m}Tc -MIBI (370-740 MBq) was injected. In vivo measurements were taken with a gamma probe of CdTe (Europrobe), using as background (Bkg) an additional measurement taken in the thyroid midline. Results were analyzed by means of ROC curves and non-parametric tests (Kruskal-Wallis and Mann-Whitney) using SPSS version 15.0. **Results.** A minimally invasive radioguided parathyroidectomy was performed in 30 cases; unilateral neck exploration in 18 cases; and, bilateral approach in 15 cases. In total, 54 solitary adenomas, four double adenomas, two cases of hyperplasia and three carcinomas were found. Besides, 9 pathological ectopic glands were localized: two paraesophageal, three retroesophageal, one paratracheal, one in superior mediastinum, one retroclavicular, and one retrosternal. There were statistically significant differences ($U=268.5$; $p=0.000$) between the in vivo/Bkg index for pathological glands ($n=70$; $x=1.77$; $SD=0.8$) and for normal tissue ($n=37$; $x=0.98$; $SD=0.13$). Using a ROC curve analysis, the optimal cut-off to detect pathological tissue was set to 1.15 (sensitivity=87%; specificity=95%; PPV=97%). Comparing the in vivo/Bkg index in different groups of glandular pathology (Kruskal-Wallis test), statistically significant differences were found ($\chi^2=16.13$; $p=0.001$). The best cut-off to distinguish between a single affected gland (carcinoma/adenoma) and a multiglandular disease was 1.51 (sensitivity=67%, specificity=87%, PPV=95%). **Conclusions.** The gamma probe was found to be a very useful tool in parathyroid surgery, helping to localize ectopic glands and permitting to differentiate between normal and pathological glands (accuracy=90%) by setting a cut-off of 1.15 in the in vivo index. However, although the in vivo index (cut-off=1.51) is as well somehow helpful to identify uniglandular disease (PPV=95%), one should take into account that there are a large number of solitary adenomas (33%) not fulfilling the criterion.

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3D subtraction of ^{99m}Tc -MIBI SPECT vs. ^{99m}Tc - TcO_4^- SPECT images as the fundamental part of comprehensive protocol for

hyperfunctioning parathyroid glands localization.

J. Trnka¹, J. Kubinyi¹, S. Adamek²; ¹General University Hospital, Praha, CZECH REPUBLIC, ²Motol University Hospital, Praha, CZECH REPUBLIC.

INTRODUCTION: Detection and localization of hyperfunctioning parathyroid glands or its adenomas is not an easy task due to many reasons (tiny size, which is similar to spatial resolution of a gamma scanner; complicated metabolism; lack of a high specific radiopharmaceutical which would be trapped in parathyroid tissue only, etc). Currently several methods are used but none of them providing sufficient diagnostic accuracy. Traditional planar imaging does not reflect current imaging possibilities, and therefore it should be replaced by tomo-imaging. Common protocols using combination of planar and subsequent single SPECT image suffer from possible washout of ^{99m}Tc -MIBI in time of SPECT acquisition. Dual-phase ^{99m}Tc -MIBI imaging itself cannot detect small lesions with fast washout. 3D subtraction of early ^{99m}Tc -MIBI vs. $^{99m}\text{TcO}_4^-$ should detect also lesions with fast washout which cannot be visible in the late ^{99m}Tc -MIBI image. The subtraction is supposed to increase the sensitivity and to have no relevant effect on specificity regarding the solely dual-phase ^{99m}Tc -MIBI examination. **METHOD:** We proposed a combination of dual-phase ^{99m}Tc -MIBI SPECT followed by $^{99m}\text{TcO}_4^-$ SPECT. All three images (early + late ^{99m}Tc -MIBI + $^{99m}\text{TcO}_4^-$) were compared visually to each other using volume rendering method. Early ^{99m}Tc -MIBI vs. $^{99m}\text{TcO}_4^-$ was also evaluated semi-quantitatively by 3D subtraction method after spatial registration and normalization. Subtraction step was aimed to locate parathyroid glands with fast washout, and it also supported unconvincing visual findings. A group of 135 patients was analyzed by an experienced physician and compared with consecutive surgical findings. Each of four particular parathyroid glands was considered separately into calculation of sensitivity and specificity. **RESULTS:** Overall sensitivity = 93% and specificity = 95% (diagnostic accuracy = 94%) regarding the surgical findings. 3D subtraction discovered almost all the lesions found independently by visual dual-phase ^{99m}Tc -MIBI + $^{99m}\text{TcO}_4^-$ analysis. In 12 cases, the subtraction determined true positive lesions which had been missed by these visual analyses. It represents a sensitivity improvement of 8 percentage points regarding the whole visual examination. **CONCLUSION:** The proposed combined protocol is very efficient and should be used in clinical practice, although it is quite time and manpower consuming. Tomographic 3D subtraction, as an essential part of this protocol, is very useful and contributing tool.

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The Role of the Experience of Nuclear Medicine Physician on Selection of Patients for Minimally Invasive Parathyroidectomy: Institutional Experience

O. Ozdogan¹, S. Ayhan¹, B. Akinci², R. Bekis¹, G. Capa Kaya¹, A. Comlekci², B. Degirmenci¹, M. A. Kocdor³, E. Derebek¹, T. Canda¹, H. Durak¹; ¹Dokuz Eylul University School of Medicine Department of Nuclear Medicine, Izmir, TURKEY, ²Dokuz Eylul University School of Medicine Department of Internal Medicine, Division of Endocrinology and Metabolism, Izmir, TURKEY, ³Dokuz Eylul University School of Medicine Department of Surgery, Izmir, TURKEY, ⁴Dokuz Eylul University School of Medicine Department of Pathology, Izmir, TURKEY.

Purpose: The experience levels of the interpreters for diagnostic studies are important for correct diagnosis. The literature is missing studies evaluating the possible role of the reporting nuclear medicine physician's experience level on the results of the parathyroid scintigraphy, for which this study was designed. **Method:** One hundred and fifty-seven patients with primary hyperparathyroidism who were cured with surgery were included to this retrospective study. The parathyroid scintigraphies and neck ultrasonographies were evaluated retrospectively. The reports were classified according to the results-conclusion section as an adenoma, a washout adenoma, indeterminate adenoma, a double adenoma or hyperplasia or hyperplasia. The experience levels of the nuclear medicine physicians were ascertained from the patient files according to the date of the reports and the reporting physicians were grouped as residents and specialists. The statistical analyses were performed using the final pathology results. **Results:** The parathyroid scintigraphies were negative for any lesion in 23 patients. The final diagnosis was an adenoma in 19 and hyperplasia in 4 cases. The ultrasonography which was performed in 21 of them was localized lesions in 7 of them. There were 113 true positive cases among 134 MIBI positive patients. There was not any statistically significant difference between reviewers in the whole group according to the experience. There were 108 patients diagnosed to have an adenoma or washout adenoma (adenoma group). In this subgroup the results were true positive in 91.6% and 72.2% of the patients reported by the specialists and the residents respectively and the results were significantly different ($p<0.007$). **Conclusion:** The surgeon can localize the parathyroid adenomas in about 92% of the patients with a minimally invasive surgery when the PS reports were confirming an adenoma and the report was evaluated by a nuclear medicine specialist.

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Diagnostic accuracy of ^{99m}Tc -Sestamibi dual-phase parathyroid scintigraphy and integrated imaging of thyroid in patients submitted to video-assisted minimally invasive parathyroidectomy

I. Bruno¹, A. Collarino¹, G. Perotti¹, D. Di Giuda¹, A. Cannarile¹, M. Negri¹, G. D'Angelo¹, M. Raffaelli², R. Bellantone², A. Giordano¹; ¹Institute of Nuclear Medicine, Catholic University of Sacred Heart, Rome, ITALY, ²Division of Endocrine Surgery, Catholic University of Sacred Heart, Rome, ITALY.

AIM: in the last few years there has been an increasing use of video-assisted techniques for parathyroidectomy in selected patients, partly due to progressive improvement of scintigraphic techniques. Italian guidelines suggest the combined use of ^{99m}Tc -pertechnetate imaging of the thyroid together with ^{99m}Tc -Sestamibi dual-phase scintigraphy to overcome interpretative difficulties. We aimed to verify whether or not it is appropriate to select patients for video-assisted minimally invasive parathyroidectomy (MIVAP) by means this "integrated" scintigraphic technique (PS). **MATERIALS and METHODS:** we retrospectively evaluated 40 patients (34 females, 6 males; mean age: 58 yrs, range: 34-78 yrs) with primary hyperparathyroidism submitted to PS

in our Institute between June 2006 and December 2007. Images of the neck and mediastinum were acquired using a pin-hole collimator at 5 and 120 minutes after injection of ^{99m}Tc -Sestamibi (370 MBq); at 170 minutes thyroid scintigraphy was performed (^{99m}Tc -pertechnetate, 148 MBq) using the pin-hole collimator. An enlarged parathyroid was identified and located on the basis of standard dual phase criteria and/or discrepancy at visual comparison between early ^{99m}Tc -Sestamibi and ^{99m}Tc -pertechnetate imaging. Inclusion criteria for MIVAP were: elevated iPTH (>100 pg/ml), and serum calcium (>10.5 mg/100 ml) values, at least one enlarged parathyroid gland at PS. MIVAP was performed according to the technique described by Miccoli et al. (1998). PS results were compared with surgical and histopathologic findings. Follow-up lasted for at least 2 years. RESULTS: a total of 48 parathyroid glands were surgically removed in the patient group. PS correctly identified site and number of the enlarged parathyroids in 35/40 patients (87.5%); in 2/40 patients (5%) PS detected one enlarged parathyroid while surgical exploration found two enlarged parathyroids; in 2/40 patients (5%) PS identified two hyperfunctioning parathyroids while surgical exploration discovered only one enlarged parathyroid; in the remaining patient (2.5%) PS identified but not correctly localised an adenoma. In 44/48 removed glands (91.6%) PS correctly identified site and number of hyperfunctioning parathyroids; in 2/48 (4.2%) PS failed to reveal an adenoma, because of its small size while in 2/48 (4.2%) a normal parathyroid and a follicular thyroid nodule showed increased uptake at PS. No patients showed persistent or recurrent hyperparathyroidism after two years of follow-up. CONCLUSION: in our study PS correctly identified number and site of hyperfunctioning parathyroids with a high sensitivity (91.6%); if performed in "scintigraphically" selected patients, MIVAP may be able to assure an excellent surgical outcome, with a reduction of cost and length of hospitalisation.

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Hybrid SPECT with Low-dose CT in Preoperative Localization of Ectopic Mediastinal Parathyroid Glands in Patients with Hyperparathyroidism

J. Kubinyi, S. Adámek, P. Libánský, P. Broulík; Charles University Prague, Praha, CZECH REPUBLIC.

Localization of ectopic parathyroid glands requires registration of SPECT and either diagnostic CT or MR images. The aim of this study was to assess potential role of low-dose CT in preoperative localization of mediastinal parathyroid glands in the patients with hyperparathyroidism. METHODS: 137 consecutive patients examined in our department between Oct 2007 and Dec 2009 with subsequent surgery have been included in the study (120 women 18–82 yrs and 17 men 19–76 yrs). All of them had high levels of calcium and parathormone. In each patient, short (3 min) planar scout scan followed by 2 SPECT studies covering an area from face to diaphragm were performed: early one starting 7 min and late one starting 2 hrs after injection of 700 MBq ^{99m}Tc -MIBI. Data were recorded and reconstructed on Infinia-Hawkeye / Xeleris (GE) using standard acquisition and reconstruction protocols. The late SPECT was completed by low-dose CT. In case of ectopic lesion visible on the scout scan, low-dose CT was performed with early SPECT, too. Additional SPECT has been performed on another day after injection of 200 MBq ^{99m}Tc -pertechnetate. The result of each SPECT examination was assessed visually as (1) rotating 3D reconstructed data (volume rendering), (2) tomographic slices in 3 planes, and (3) 3D subtraction of pertechnetate from early MIBI SPECT data. RESULTS: In 14 patients, mediastinal localization of ectopic parathyroid gland has been confirmed by a surgeon. Glands were removed and histologically verified. In all patients, the levels of parathormone and calcium normalized after surgery demonstrating that ectopic lesion was the only source of hyperparathyroidism. SPECT/low dose CT correctly localized 12 mediastinal parathyroid adenomas and 2 hyperplasias of size 12–70 mm. Twelve of 14 glands were localized in anterior mediastinum surrounded by the thymus tissue. In order to remove 5 of them, partial sternotomy was necessary while the remaining 7 glands were approached from supraclavicular incision. Two glands were localized in posterior mediastinum behind trachea and were removed through lateral incision on the neck. SPECT alone made possible to detect all ectopic glands and localize their approximate position. A crucial role of low-dose CT was to define relation of the ectopic glands to the surrounding tissues. CONCLUSION: SPECT/low-dose CT provides the surgeon with sufficient information required to decide on surgery and a suitable strategy to approach the lesions. In our group of patients, diagnostic CT was not necessary.

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Results with Dual Phase Histopathology of Tc 99m MIBI Parathyroid Scintigraphy Relationship Between Retention Indices

S. Yildirim¹, G. Koca¹, S. Kuru², K. Demirel¹, A. Baskin¹, M. Korkmaz¹, ¹Health of Ministry, Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara, TURKEY, ²Health of Ministry, Ankara Training and Research Hospital, Department of General Surgery, Ankara, TURKEY.

AIM: Dual phase Tc 99m MIBI scintigraphy has proved method to locate the hyperfunctioning parathyroid tissue, particularly adenomas. Its false positive results related to coexistent thyroid pathology. Our aim was to evaluate histopathological results of Tc 99m MIBI retention of patients in neck region with dual-phase Tc 99m MIBI scintigraphy. MATERIAL METHOD: 29 patients with suspected solitary parathyroid adenoma from laboratory and ultrasound imaging methods were evaluated with dual-phase Tc 99m MIBI scintigraphy. Scintigraphy was performed by injection of the tracer at a total dose 15 mCi and images were taken at 10 minutes and 2 hours after injection. All patients had Tc 99m MIBI retention values and histopathologic diagnosis. RESULTS: Parathyroid histopathologic results were 24 adenomas, 3 parathyroid hyperplasia and 2 normal parathyroid tissues in 29 patients. In terms of distribution of thyroid pathologies 3 cases were thyroiditis, 8 cases had nodular thyroid, and 18 were normal. Average MIBI activity retention was 70.49 ± 14.01 in parathyroid adenomas, 63.53 ± 24.56 in parathyroid hyperplasias and 55.16 ± 18.60 in patients with normal parathyroid tissues. Among these 3 groups in terms of activity retention values did not reveal a statistically significant difference. In patients with nodular thyroid Tc 99m MIBI retention was 81.65 ± 8.50, in patients with thyroiditis the value was 70.44±14.51 in terms of activity retention was no statistically significant differences between groups. CONCLUSION: By dual-phase Tc 99m MIBI scintigraphy, the distinction between parathyroid and thyroid pathologies could not be drawn in patients with Tc 99m MIBI retention in neck region.

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Correlation of preoperative ^{99m}Tc -sestamibi parathyroid scintigraphy to the size of enlarged parathyroid glands in patients undergoing surgery for hyperparathyroidism

D. Kustić, A. Drašković, A. Smokvina; University Hospital of Rijeka, Clinical Department of Nuclear Medicine, Rijeka, CROATIA.

AIM: To establish sensitivity of preoperative parathyroid planar scintigraphy comparing scintigraphic findings to the size of surgically removed enlarged parathyroid glands. METHODS: We studied 40 consecutive patients who underwent parathyroidectomy at the Surgery Clinic of our hospital, 32 of them with primary hyperparathyroidism, and 8 with secondary hyperparathyroidism. All patients were preoperatively administered 555 MBq ^{99m}Tc -sestamibi intravenously. Planar images of the neck were obtained at 15 minutes and again at 1 and 3 hours. Scintigraphy was considered positive in the presence of the focal area retaining activity on delayed images. Preoperative scintigraphic and sonographic findings were compared to the size of surgically removed nodes, subsequently pathohistologically diagnosed either as parathyroid adenomas or nodular hyperplasia. RESULTS: Among 32 patients with primary hyperparathyroidism, 27 of them (84%) had positive scintigraphy in terms of retaining activity focus at the location where node was removed during surgery, and pathohistologically diagnosed as parathyroid adenoma. The largest diameters of those nodes were equal to or greater than 10 mm. All of those were seen by preoperative sonography, except 2 substernally located and found during surgery owing to their increased activity. In 5 of 32 patients with primary hyperparathyroidism scintigraphic findings were equivocal (16%). In 4 of those pathohistology of the removed node verified parathyroid adenoma measuring less than 10 mm. Two of those were seen by sonography. In one patient with negative both scintigraphic and sonographic findings, no parathyroid tissue in surgically extirpated sample was histologically found. In the group of patients with secondary hyperparathyroidism, more parathyroid glands with nodular hyperplasia were removed, scintigraphic results were positive for all except two larger than 10 mm (86%), and were equivocal for all measuring less than 10 mm. Enlarged parathyroid glands were seen by sonography in 7 of 8 patients with secondary hyperparathyroidism. CONCLUSION: Preoperative scintigraphy approved absolute sensitivity (100%) in detection of parathyroid adenomas in primary hyperparathyroidism if their size was equal to or larger than 10 mm. For adenomas measuring less than 10 mm scintigraphy was mostly equivocal. Scintigraphy had high sensitivity (86%) also in detection of parathyroid glands with nodular hyperplasia measuring more than 10 mm in patients with secondary hyperparathyroidism, while for those measuring less than 10 mm sensitivity was poor (<10%).

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Aminoterminal propeptide of type 1 procollagen and bone densitometry in assessing fracture risk in postmenopausal women with thyroxine-induced subclinical hyperthyroidism; efficacy of antiresorptive treatment

P. Valsamaki¹, A. Zanglis¹, A. Chatzipetrou¹, C. Vlachou¹, G. Fountos², S. Gerali¹; ¹"PAMMAKARISTOS" General Hospital, Athens, GREECE, ²Technological Education Institute of Athens, Athens, GREECE.

AIM: To evaluate the effects of antiresorptive treatment (bisphosphonate±calcium and vitamin D supplementation) of 1.5–3years duration on bone metabolism, in conjunction with the presence of thyroxine-induced subclinical hyperthyroidism (TI-SCH). Serum thyrotropin (TSH) values and the surrogate markers of fracture risk, i.e. serum aminoterminal propeptide of type 1 procollagen (P1NP) and bone mass density (BMD) measurements, were correlated. MATERIALS-METHODS: 55 postmenopausal women receiving thyroxine for benign thyroid disease were randomly selected. Patients were subjected to BMD measurements (hip and/or lumbar spine) and divided into four groups (A₁, A₂, B₁, B₂) based on their serum TSH levels (normal limits: 0.4–4.04 μU/mL) and intake of bone antiresorptive medication (BARM)- Table 1. Serum TSH and P1NP levels were measured with the Elecsys analyzer (Roche Diagnostics, Basel, Switzerland). The Dual-Energy-X-Ray-Absorptiometry (DEXA) technique (Hologic QDR-4000) was applied for bone densitometry. Data statistical analysis was performed using the MedCalc™ software package.

	Group A ₁ TSH WNL+ BARM	Group A ₂ TSH WNL No BARM	Group B ₁ TI-SCH No BARM	Group B ₂ TI-SCH+ BARM
Number of patients	9	19	16	11
Age (yrs)	68.8±5.7	63.4±10.2	64.4±7.3	65.3±9.4
TSH NP (mg/dL)	20.3±12.9	30.82±15.53	34.92±19.13	28.81±21.44
PTH (μU/mL)	1.240±0.790	1.292±0.939	0.119±0.91	0.110±0.097
BMD (T score %)	80.7±20.2	93.5±14.1	88.69±11.00	80.97±7.75
PTH (pg/mL)	37.3±19.45	53.5±24.72	38.84±19.30	52.92±37.0

Table 1. Patient data and results. Values presented as mean±standard deviation of the mean(SD). WNL: within normal limits, PTH: Parathyroid hormone RESULTS: P1NP values were normally distributed (D' Agostino-Pearson test, without log-transformed-data) in all groups. Statistically significant differences of mean P1NP values appeared only between group A₁vsB₁ (p=0.033, Welch test). The difference in mean P1NP values between groups A₁vsA₂ (p=0.075) and B₁vsB₂ (p=0.456) failed to reach statistical significance. The comparison of BMD values of groups A₁vsA₂ and B₁vsB₂ (p=0.096 and p=0.045, respectively), showed a clear tendency for lower BMD values in BARM-receiving patients, although this difference reached statistical significance only in the group of patients with TI-SCH. While not statistically significant, PTH values also appeared to follow the observed group-corresponding-trend as the P1NP levels (A₁vsA₂: p=0.075 and B₁vsB₂: p=0.266). CONCLUSIONS: According to our data, BARM for 1.5–3years causes depression of serum P1NP levels, thus decreasing bone turnover, in all postmenopausal patients receiving thyroxine for benign thyroid disease. Patients with TI-SCH and without BARM, exhibit significantly higher mean P1NP levels, thus significantly increased bone remodeling, in comparison with patients presenting normal TSH, who receive BARM. Therefore, in postmenopausal women with TI-SCH, careful thyroxine-dose-adjustment seems mandatory, besides the appropriate BARM, for BMD stabilization/or increase. 1

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The usefulness of double - phase ^{99m}Tc - MIBI scintigraphy for preoperative localization of enlarged parathyroid glands

N. Ristevska¹, D. Pop Gjorceva¹, S. Stojanoski¹, L. Ivkovski², M. Angeleska¹, S. Miceva Ristevska¹, B. Antevski³; ¹Institute of Pathophysiology & Nuclear Medicine, Skopje, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF, ²Institute of Oncology & Radiotherapy, Skopje, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF, ³Clinic of Thoraco - Vascular Surgery, Skopje, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF.

Introduction: The diagnosis of hyperparathyroidism (HPT), primary (pHPT) or secondary (sHPT), is most often based on serum laboratory test findings (calcium, phosphates and parathyroid hormone-pth level). **Aim:** of this study was to evaluate the usefulness of ^{99m}Tc-MIBI scintigraphy in localization of enlarged parathyroid glands (pgs). **Materials and Methods:** 46 patients were examined with pHPT or sHPT, who visited our department during the year 2009. 34/46 patients (74%) were female and 12/46 were male (26%); the patients were ageing from 18 to 70 years (mean age of 49yrs). 14/46 patients (30%) were going on haemodialysis, 13/46 (28%) had kidney stones, 10/46 patients (22%) were diagnosed with osteoporosis, and 9/46 patients (20%) had hypercalcemia as their first finding. **Results** of the study are presented on the table given below:

	ultrasonography	parathyroid hormone	^{99m} Tc-MIBI scintigraphy	histological findings
positive (+) / ↑	22/46 (48%)	35/46 (76%)	27/46 (59%)	18/18 (100%)
negative/normal	17/46 (37%)	5/46 (11%)	19/46 (41%)	
no data available	7/46 (15%)	6/46 (13%)	/	
	operated pts with posit. scint.	not operated pts with posit. scint.	no data available	
	18/27 (67%)	4/27 (15%)	5/27 (18%)	

In 16/18 operated patients the histological findings confirmed existing of parathyroid adenoma, in 1/18 p histology confirmed hyperplasia of pgs, and in 1/18 p histology showed parathyroid carcinoma. In 23/27 p (85%) both scintigraphy and ultrasonography findings were positive; 2/19 p (10%) with negative scintigraphy showed positive ultrasonography (suspicious for enlarged pgs). In 2 p with scintigraphy for parathyroid adenoma, additional positive accumulation of the tracer was found in the region of left breast and left axilla. The examination of these findings in the first patient confirmed - fibroadenoma of the breast (pgs scintigraphy was positive), and carcinoma of the left breast in the second one (pgs scintigraphy was negative). **Conclusion:** Our study confirmed the well known strategy that ^{99m}Tc-MIBI scintigraphy and ultrasonography imaging modalities are supplementary and most often are used for preoperative localization of enlarged parathyroid glands. Not less important is the fact of possibility for additional findings following the pgs scintigraphy, as finding of breast carcinoma in female p.

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Correlation of subtraction parathyroid scintigraphy with weight, histopathologic finding and oxyphil cell content of parathyroid glands in parathyroid hyperplasia

S. R. Dugonjic, Z. Jankovic, B. Ajdinovic, D. Pucar; Military Medical Academy, Belgrade, SERBIA.

Parathyroid hyperplasia (PHP) is defined as an absolute increase in mass of parenchymal cells of the parathyroid gland. PHP is classified as primary, secondary and tertiary. The enlargement of parathyroid glands (PG) is usually asymmetric, resulting in a "dominant" gland. At least two glands should be examined histologically to confirm the diagnosis. Subtotal parathyroidectomy, removing three PG and leaving small remnant of forth, is the treatment of choice. High percent of recurrence, especially in primary PHP, imposes need for preoperative localizing procedures with high sensitivity. Parathyroid scintigraphy localizes about 60% of hyperplastic glands. **AIM:** The aim of this study was to correlate findings of subtraction parathyroid scintigraphy (SPS) with weight, histopathologic finding and oxyphil cell (OC) content of PG in patients with parathyroid hyperplasia. **MATERIALS and METHODS:** Twenty seven patients with primary/secondary PHP underwent SPS before surgery. Static scintigrams of neck and chest were performed, 15min, and 2h after iv. inj. of 740MBq of Tc99m-MIBI/tetrofosmin. Four hours latter, after iv. inj. of 185MBq Tc99m, thyroid scintigraphy was performed. After normalization and motion correction, subtraction Tc99m from Tc99m-MIBI/tetrofosmin scintigrams was done. Scintigraphic results were graded from 1-5, in relation to degree of uptake. SPS graded 3, 4 and 5 were considered positive. Number and weight of operated PG was evaluated macroscopically. On standard stained hematoxylin-eosin slides, histopathologic and cellular types were defined. OC content were defined as <10%, ≥10% and ≥20% of OC. **RESULTS:** All SPS findings were positive; sensitivity per patient was 100%. SPS localized 51 from 73 abnormal PG; sensitivity per gland was 70%. PG weighed 0.1 to 6.7g (median-1g). Between SPS and PG weight, significant positive correlation was found, (p<0.0001). Significant positive correlation was found between PG weight and OC content, (p=0.0002). No significant correlation was found between SPS and OC content. Thirty eight PG had < 10% of OC, 32 PG ≥10% and 3 PG ≥20% of OC. Four patients had diffuse PHP, and 23 patients nodular PHP. There was no significant statistical difference between SPS and hyperplasia type, and between OC content and hyperplasia type. Between PG weight and hyperplasia type significant positive correlation was found, p=0.00159. **CONCLUSION:** Sensitivity of SPS per patient was 100%, and per gland was 70%. High positive correlation was found between: SPS and PG weight, PG weight and OC content and PG weight and hyperplasia type. Between SPS and OC content, and SPS and hyperplasia type, no significant correlation was found.

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Nuclear Medicine Algorithm for Evaluation and Staging of Sporadic Medullary Thyroid Carcinoma (MTC) Associated with High Concentrations of Serum Calcitonin

K. Zaplatnikov¹, V. Soukhov²; ¹Nuclear Medicine Clinic MAZ Nuernberg, Nürnberg, GERMANY, ²Hospital of Military Academy Nuclear Medicine Department, St. Petersburg, RUSSIAN FEDERATION.

Purpose: Routine radioimmuno analysis (RIA) of serum calcitonin concentrations often used for detection of MTC in patients with ultrasonography (US) detected nodular thyroid diseases. We evaluated Calcitonin screening in patients with presence of hypoechoic nodes for further diagnostic/therapeutic strategy choice. **Methods:** Routine radio immunological measurements of serum calcitonin concentrations were performed in 1,548 patients (415male; 1,133 female) with US revealed nodular thyroid diseases and repeated Pentagastrin stimulation in patients with mild or moderate elevation of serum Calcitonin levels. The average age was 44 years (range 8-86 years). Additional examination included thyroid Tc-99m-Perchnetat scan, measurements of thyroid hormones, TSH and antithyroid autoantibodies. Patients suspected for lymph nodes (LN) mts at neck region undergone MRI (45 pts), among them 4 pts were evaluated using MRI/Octreo-Scan Fusion. **Results:** We found that 44 (2,8%) of patients with nodular thyroid diseases by US had serum calcitonin level by RIA above 10 pg/ml. Among them 10 patients (22,7%) presented histologically confirmed MTC. 6 of 10 patients with MTC had basal serum calcitonin level above 100 pg/ml. The remaining 4 patients had moderate elevation of basal serum calcitonin (range, 12-66 pg/ml). Serum calcitonin concentrations increased to more than 100 pg/ml after administration of Pentagastrin in all patients with MTC (2.4x to 47.7x increase). These findings referred to next diagnostic modalities. All pts with MTC and high Calcitonin have cold lesion in thyroid scan. 40 pts demonstrated enlarged LN by MRI that matched with foci of increased Octreo-SPECT-Scan uptake in 4 of them. The rest pts with Calcitonin levels from 10-33 pg/ml and negative Pentagastrin stimulation had C-cell hyperplasia, renal failure or other diseases. All pts with high Calcitonin that were positive for MTC and mts have undergone another surgical strategy. **Conclusions:** These results suggested that routine RIA measurements of serum Calcitonin w- or w/o Pentagastrin stimulation test, thyroid scan, MRI/SPECT-Octreoscan is useful for early detection of MTC among patients with nodular thyroid diseases, especially in presence of hypoechoic nodes. This allow to choose right diagnostic algorithm and prescribe adequate therapy.

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Advanced Reconstruction Algorithms For Simultaneous Tc-99m-sestamibi/I-123 SPECT/CT Parathyroid Studies

S. Shcherbinin¹, A. Celler¹, S. Cosyn², S. Chamoiseau³; ¹The University of British Columbia, Vancouver, BC, CANADA, ²GE Healthcare Technologies, Buc, FRANCE, ³Centre Hospitalier de Bigorre, Tarbes, FRANCE.

Aim: This study aimed at improving of the diagnostic sensitivity of localization of parathyroid lesions from simultaneous dual-isotope SPECT/CT scans. To this end, we applied the most advanced (and validated in phantom experiments) image reconstruction algorithm for simultaneous dual-isotope Tc-99m-sestamibi/I-123 parathyroid SPECT/CT studies and examined the importance of physics-based image degradation factors such as attenuation, resolution loss, collimator septal penetration, scatter, and cross-contamination, for image quality. **Materials and Methods:** Our data processing included: (1) reconstruction of both Tc-99m and I-123 images with and without corrections for aforementioned factors; (2) delineation of the thyroid (ROI) in I-123 image; (3) copying this ROI to Tc-99m image, (4) normalization of both images to the common level using ROI activities; (5) subtraction of the normalized I-123 image from the normalized Tc-99m image. We applied this technique to one phantom experiment and five patient studies. In phantom experiment, four cylindrical containers were placed inside a 7L cylinder filled with Tc-99m. While the containers filled with both Tc-99m and I-123 isotopes mimicked thyroid, the source with Tc-99m only imitated an adenoma. In patient studies, 9.25MBq of I-123 was injected 4 hours and 740MBq of Tc-99m-sestamibi - 10 minutes before SPECT/CT scan. All studies used Infinia Hawkeye (GE Healthcare) SPECT/CT system equipped with LEHR collimator. Separated and wider energy windows [126-147keV] / [151-175keV] were set in patient studies and narrower and adjacent ones [129-149keV] / [150-170keV] - in the phantom experiment. **Results:** With clinically used doses and non-overlapping energy windows, the 3D distance-dependant resolution recovery and CT-based attenuation correction were the main factors to improve the performance of the subtraction technique. However, in controversial cases (i.e. tiny or deeply or mediastinal located adenomas), advanced reconstruction with corrections for collimator septal penetration, scatter, and cross-contamination may be necessary. Especially, in one study, they considerably enhanced detection of the left lobe adenoma. Additionally, sophisticated algorithms can be utilized for optimization of the imaging protocol. For example, while using advanced reconstruction the decreased dose or shorter scanning time may be compensated by establishing wider and/or adjacent energy windows. The phantom experiment showed that these unfavourable situations practically did not affect accuracy of the recovered absolute activity (errors around 10%) and subtraction images. **Conclusions:** The subtraction technique based on advanced image reconstruction may (i) improve diagnosis in controversial cases and (ii) be used to decrease the injected dose and/or duration of the scan.

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Basal Glucose Metabolism of hepatic, muscular and adipose tissues in obesity.

W. Yao¹, C. Wu², Y. Tsai³; ¹Department of Nuclear Medicine, National Cheng-Kung University, Tainan, TAIWAN, ²Department of Family Medicine, National Cheng-Kung University, Tainan, TAIWAN, ³Institute of Clinical Medicine, National Cheng Kung University, Tainan, TAIWAN.

Objectives: Obesity is closely related to insulin resistance and abnormalities in glucose metabolism. The aim of this study is to investigate the alterations of basal glucose metabolism in the liver, muscles, and fat tissues in obese subjects and its relationship with insulin resistance using FDG PET/CT. **Methods:** Fourteen obese subjects (BMI 32.4 ± 6.5 kg/m²) and 14 lean healthy subjects (BMI 20.4 ± 1.4 kg/m²) were studied with dynamic and whole body FDG PET/CT.

Standardized uptake values (SUVs) were measured over the liver, muscles (psoas and medial thigh) and fat tissues (abdominal subcutaneous and visceral). Amount of abdominal visceral and subcutaneous fat was measured from CT. Serum glucose and insulin levels were measured before injection of radiotracer. **Results:** There were significantly higher SUVs in the muscles (psoas 0.92 ± 0.16 vs. 0.63 ± 0.07 , $P < 0.001$; medial thigh 0.66 ± 0.14 vs. 0.56 ± 0.11 , $p = 0.039$) and the liver (2.57 ± 0.26 vs. 2.04 ± 0.35 , $p < 0.001$) in obese patients than in lean subjects, while fat tissues showed no significant difference between groups. Across groups, muscular glucose uptake was positively correlated with BMI, visceral fat amount and insulin levels. **Conclusions:** Different from resistance of muscular glucose uptake in hyperinsulinemia studies, the obese subjects have higher basal muscular glucose uptake, which is positively correlated with visceral fat amount and insulin resistance.

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Diagnostic Fidelity of MIBI-SPECT/CT and/or MRI-Fusion Compared to Methionine-PET/CT in Patients with Hyperparathyroidism

K. Zaplatnikov¹, W. Wiedemann¹, V. Soukhov²; ¹Clinic for Nuclear Medicine MÄZ, Nürnberg, GERMANY, ²Hospital of Medical Military Academie, St. Petersburg, RUSSIAN FEDERATION.

PURPOSE: To find out if single-photon emission computed tomography (SPECT) with CT and/or MRI-Fusion or 11C-Methionine-PET/CT in addition to (99m)Tc-methoxyisobutylisonitrile (MIBI) planar scintigraphy by Subtraction with Perchnetat or Dual Phase Examinations have greater fidelity in finding of parathyroid adenomas in Hyperparathyroidism **METHOD:** Among the 136 consecutive patients who underwent planar (99m)Tc-MIBI scintigraphy for hyperparathyroidism (HPT), 90 underwent delayed SPECT and CT (and/or MRI) (Fusion works at Software Fa. Mediso). 49 pts. underwent additional (Tc-99m)-Perchnetat-subtraction examination. In 7 pts with glands size of 5 mm 11C-Methionine-PET/CT studies were performed. Two independent experts made neck US and scored the topographical localization, diagnostic confidence, and impact of each diagnostic modality on the therapeutic strategy. **RESULTS:** Planar Tc-MIBI scintigraphy in Dual Phase mode had a sensitivity of 89% with a positive predictive value (PPV) of 92% in pts with glands ≥ 1 cm. SPECT/CT and/or MRI Fusion did not affect these values, but it increased the diagnostic confidence in more than 50% of the patients. (Tc-99m)Perchnetat-subtraction increased the sensitivity only in multinodal thyroid goiter from 64% to 67%, but decreased the PPV from 89% to 67%. In hyperplastic glands < 1 cm, (99m)Tc-MIBI scintigraphy had a sensitivity of 65% and a PPV of 73%. When (99m)Tc-MIBI scintigraphy was combined with SPECT/CT/MRI-Fusion or Tc-99m Subtraction, the results were 96%/94% and 79%/64%, respectively. For very small adenomas the results of 11C-Methionine-PET/CT gave sensitivity of 95% and a PPV of 97%. **CONCLUSIONS:** Adding SPECT/CT and/or MR-Fusion to planar (99m)Tc-MIBI scintigraphy improved the finding of parathyroid adenomas in all cases. (Tc-99m)Perchnetat-subtraction was of limited value. However, for all hyperplastic glands < 1 cm we recommend effective combination of MIBI-SPECT/CT/MR-Fusion. 11C-Methionine-PET/CT seems to be of no-greater accuracy, but it need to be verified.

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Do Pre-Surgical Serum Calcium Levels Predict Lesion Weights and Numbers of Lesions Detected by MIBI Imaging in Patients with Primary Hyperparathyroidism?

K. J. Nichols, G. G. Tronco, M. B. Tomas, C. J. Palestro; North Shore - Long Island Jewish Health System, Manhasset & New Hyde Park, NY, UNITED STATES.

Aims: This investigation was undertaken to determine whether, in patients with primary hyperparathyroidism (PHP), there are correlations between the preoperative serum calcium (Ca) level and (1) the number of abnormal glands, and (2) test sensitivity. **Methods:** The study population consisted of 618 patients with biochemically confirmed PHP, who underwent MIBI imaging and subsequent surgery. MIBI imaging included early & late planar pinhole neck imaging, ^{99m}TcO₄ pinhole thyroid imaging, image subtraction & SPECT from mandibular angle to heart base. One experienced nuclear physician, blinded to other test results & final diagnoses, graded studies on a 5-point scale from "0" (definitely normal) to "4" (definitely abnormal). Ca values were obtained from pre-surgical laboratory reports and lesion weight (wt.) was obtained from pathology reports. **Results:** 815 parathyroid lesions were resected from the 618 pts. 489 pts. had single gland disease (SGD) and 129 pts. (326 lesions) had multigland disease (MGD). Lesion wts. were significantly lower for MGD than for SGD [$\log(\text{wt/gm}) = -1.55 \pm 1.16$ versus -0.62 ± 1.08 , $p < 0.0001$]. In MGD, lesion wt. decreased significantly with increasing lesion number ($r = -0.41$, $p < 0.0001$). The sum of lesion wts. per pt. in MGD was similar to lesion wt. per pt. in SGD [$\log(\text{wt/gm}) = -0.68 \pm 1.19$ versus -0.62 ± 1.08 , $p = 0.59$], regardless of the number of lesions involved. Despite similar total lesion wt. per pt., Ca levels were significantly lower in pts. with MGD than in pts. with SGD (10.9 ± 1.0 versus 11.1 ± 0.9 , $p = 0.003$). Contingency table analysis of Ca level quartiles versus lesion wt. quartiles yielded $\chi^2 = 107.4$ ($p < 0.0001$) and Ca quartiles versus lesion number yielded $\chi^2 = 72.7$ ($p < 0.0001$), indicating significant associations of Ca levels with lesion wts. and lesion numbers. Progressively lower Ca quartile levels were significantly correlated ($r = 0.92$, $p = 0.001$) with progressively lower MIBI sensitivity values of 88%, 89%, 82% and 71%, respectively, from highest to lowest Ca quartiles. **Conclusions:** These data suggest that in pts. with PHP, who present with lower serum calcium levels, MIBI studies should be reviewed carefully for subtle abnormalities that might indicate smaller lesions and/or multigland disease.

P583

Diagnostic 131-I Whole Body Scan in the Evaluation of Patients with Differentiated Thyroid Cancer and Serum Thyroglobulin Levels < 1 ng/mL: Seven Years of Clinical Experience.

I. Lucena, L. Costa, J. Teixeira, R. Martins, J. Couto, F. Lopes, H. Duarte, O. Soares, L. Bastos; IPOFG-E.P.E., Oporto, PORTUGAL.

Aim: To investigate the influence of diagnostic radioiodine whole body scan (DxWBS) and low blood levels of thyroglobulin (< 1 ng/mL) on the need for repeat radioiodine therapy after total thyroidectomy and initial ablation therapy of patients with differentiated thyroid cancer (DTC). **Material & Methods:** 648 cases of DTC treated between 2003 and 2009 were studied retrospectively. All patients were submitted to 131I ablation therapy (3,7 GBq) less than 2 months after total thyroidectomy. Six months after ablation therapy they all had DxWBS and concomitant blood measurements of thyroid stimulating hormone (TSH) and thyroglobulin (Tg) after 4 weeks of thyroid hormone withdrawal. Recombinant thyroid-stimulating hormone (rTSH) was only used in 5 patients. All patients had: a) histologically proven DTC; b) low or intermediate risk of recurrence according to the 2009 American Thyroid Association (ATA) guidelines; c) 131I DxWBS performed 6 months after radioablation; d) TSH and serum Tg levels measured at the time of the 131I DxWBS; e) no local or distant metastasis known prior to or at time of the 131I DxWBS. The number (n) and percentage (%) of patients who required repeated radioablation were recorded. We also evaluated the percentage of patients who had thyroid remnants detected by DxWBS despite very low levels of Tg (< 1 ng/mL). **Results:** 121 (18,7%) of the 648 patients studied were submitted to repeat radioiodine therapy based on the following: a) presence of remnant thyroid tissue on 131I DxWBS and Tg < 10 ng/mL (n = 65; 53,7%); or b) serum Tg > 10 ng/mL and negative DxWBS (n = 27; 22,3%); or c) positive 131I DxWBS for remnant thyroid tissue and serum Tg > 10 ng/mL (n = 29; 23,9%). Forty two (34,7%) of these 121 patients required repeat radioiodine therapy, despite their blood Tg level $< 1,0$ ng/mL. Cervical ultrasonography (US) performed in 12 of these 42 individuals was negative in 8 cases. **Conclusion:** Repeat radioiodine therapy was more frequently required when DxWBS was positive for thyroid remnants, independently of the blood levels of Tg. More than one third of the repeat radioiodine therapies were performed when Tg was lower than 1 ng/mL (DxWBS positive).

P584

The role of imaging techniques in the follow-up of secondary hyperparathyroidism patients after renal transplantation in treatment with cinacalcet

C. Villen Garcia, F. Perez Angel, A. J. Montellano Fenoy, L. Mohamed Salem, J. Sanchez Catalicio, M. I. Castellon Sanchez, F. Nicolas Ruiz, L. Jimeno Garcia, D. Sanz Garcia, M. A. Claver Valderas; Hospital Universitario Virgen de la Arrixaca, MURCIA, SPAIN.

Introduction: Chronic kidney disease is associated with a cascade of events that adversely affect mineral metabolism and lead to renal osteodystrophy. Included in this group is secondary hyperparathyroidism (SHPT). When renal failure is responsible for SHPT we might expect that the best treatment is a renal transplant together with the normalization of the renal function. However, the degree of improvement is frequently incomplete. The primary abnormalities that can persist after transplantation are hyperparathyroidism and hypercalcemia. For these reasons, effective control of persistent SHPT is an important therapeutic goal after renal transplantation. As hypercalcemia limits the use of vitamin D analogs, the use of cinacalcet (mimpara®), a calcimimetic drug, is being increasingly studied. For patients with chronic renal failure who develop SHPT, imaging techniques can be useful, especially to evaluate the location, size and functional status of parathyroid glands. **Aim:** To evaluate the usefulness of cervical ultrasound and technetium-99m-methoxyisobutylisonitrile (^{99m}Tc-MIBI) parathyroid scintigraphy in the follow-up of SHPT patients after renal transplantation in treatment with cinacalcet. **Material and methods:** We revised retrospectively 14 patients (6 females and 8 males), aged 37-70 years (average mean age 53.1) with renal transplantation between October 2004 and November 2007, who developed SHPT. In our hospital all the patients were evaluated with cervical ultrasound and scintigraphic studies ^{99m}Tc-MIBI including non-standard image acquisition techniques (Pinhole), pre-mimpara and post-mimpara, starting from the year that the treatment was initiated. The hormone parathyroid was determined in all patients, by RIA method at the time of ^{99m}Tc-MIBI scanning. **Results:** The ^{99m}Tc-MIBI was positive in 13 patients, negative in 1 (pre-mimpara) and positive in 10, negative in 3 and inconclusive in 1 (post-mimpara). The cervical ultrasonography was positive in 9 patients, negative in 3, inconclusive in 2 (pre-mimpara) and positive in 8, negative in 3 and inconclusive in 3 (post-mimpara). The hormone parathyroid was elevated in all patients showing values between 88-1314 pg/ml (pre-mimpara) and 36-300 pg/ml (post-mimpara).

	^{99m} Tc-MIBI Eco cervical PTH (pg/ml)					
	+	-	?	+	-	?
PRE-mimpara	13	1	0	9	3	2
POST-mimpara	10	3	1	8	3	3
						36-300

Conclusion: In our study, we consider ^{99m}Tc-MIBI scintigraphy to be the preferred option to identify hyperfunctional parathyroid glands in patients with SHPT after renal transplantation in treatment with cinacalcet. The combination ^{99m}Tc-MIBI scintigraphy with eco cervical shows a higher sensitivity to determine the location and size of PTGs allowing the use of cinacalcet in these patients, avoiding unnecessary surgery processes and reducing the associated comorbidity.

P585

Value of the TC99m-Sestamibi scintigraphy in the assessment of pancreas transplant

J. Sanchez Catalicio, A. J. Montellano Fenoy, C. Villena Garcia, F. Perez Angel, L. Mohamed Salem, M. I. Castellon Sanschez, J. Contreras Gutierrez, F. Nicolas Ruiz, L. Jimeno Garcia, M. A. Claver Valderas; Hospital Universitario Virgen de la Arrixaca, MURCIA, SPAIN.

Introduction: The pancreas transplantation is performed usually simultaneously and in combination with kidney transplantation in patient with DM type-1 and terminal renal disease. The majority of post-transplant complications, especially acute rejection and vascular complications appear during the following three months. **Objective:** To evaluate the utility of scintigraphy in the study of vascularization and viability in of pancreatic transplant. **Material and methods:** Material y métodos. We revise retrospectively 48 scintigraphic studies carried out in 20 patients (9 females and 11 males) aged between 29 and 50 years with DM type-2 and terminal renal disease during the period between 2000 and 2010 who underwent a pancreatico-renal transplantation. The scintigraphic study is performed after the administration of 20 mCi of Tc99-

Septamibi acquiring images in dynamic mode (2 seconds/image during 2 minutes followed by one minute/image during 30 minutes) and static of 5 minutes/image getting the activity/time curve. The basal study is achieved during the 1st week post-transplantation and is repeated depending on the clinical context of the patient. The clinical histories of the 20 patients are revised before the scintigraphy and the posterior follow up taking as a reference biochemical blood markers and clinical situation. We consider a normal scintigraphic pattern when the graft is observed since early images, the peak time of pancreatic activity in relation to aortic peak time is less than 6 seconds and when the uptake is homogenous with good definition in static image. The scintigraphic pattern of earl acute rejection is presented with decreased vascular flow (peak time pancreatic activity to aortic is > 6 seconds) together with heterogenous hypoactivity in static image. In case of vascular thrombosis the scintigraphic pattern shows absence of flow-uptake in the graft. **Results**

	Normal scintigraphy	Nonconclusive scintigraphy	Rejection scintigraphy	Trombosis scintigraphy
Good clinic control/Normal blood markers.	23	4	2	1
Bad clinic control/altered blood markers.	7	3	8	0
TOTAL	30	7	10	1

Conclusions The scintigraphy is noninvasive imaging method useful in assessing vascularization and viability of pancreatic transplant. The best control of transplant is obtained by the combination of clinical data and noninvasive methods including scintigraphy, as there is no blood biochemical marker nor imaging method sensitive or specific enough.

P586

The role of ^{99m}Tc-DMSA(V) and ¹⁸FDG-PET/CT in patients with medullary thyroid carcinoma. Preliminary results.

F. Perez Angel, C. Villena Garcia, L. Mohamed Salem, J. Sanchez Catalicio, A. Montellano Fenoy, M. I. Castellon Sanchez, L. Frutos Esteban, F. Nicolas Ruiz, J. M. Rodriguez, M. A. Claver Valderas; Hospital Universitario Virgen de la Arrixaca, MURCIA, SPAIN.

Introduction: Medullary thyroid carcinoma (MTC) is an uncommon tumour accounting for less than 10% of all thyroid malignancies. The inherited forms account for 25% and includes multiple endocrine neoplasias (MEN) types 2A and 2B, while the remaining 75% are sporadic. Serum calcitonin is the most sensitive and specific marker of MTC for primary diagnosis and follow up. Nuclear medicine can play an important role when tumor recurrence/metastases are suspected on the basis of elevated tumor marks and the initial radiological evaluation is inconclusive. **Aim:** The purpose of this prospective study was to determine the diagnostic value of ^{99m}Tc-DMSA(V) and ¹⁸FDG-PET/CT for detecting metastases/recurrence in MTC with elevated serum calcitonin levels and negative imaging test. **Material and methods:** We studied 15 patients (8 female and 7 male) with histological diagnosis of MTC (5 sporadic and 10 MEN2A), age range 33-68 (mean 49.3) years. All patients underwent ¹⁸FDG-PET/CT according to usual protocol and ^{99m}Tc-DMSA(V) scanning 120 minutes after intravenous injection of 370 MBq of ^{99m}Tc-DMSA(V) with both planar imaging methods and SPECT-CT. The serum calcitonin was determined according RIA laboratory methods at moment of DMSA scanning. **Results:** All fifteen patients were asymptomatic, with elevated serum calcitonin levels (117-23000 pg/ml). ^{99m}Tc-DMSA(V) scintigraphy was positive in 10 patients and negative in 5 patients. ¹⁸FDG-PET/CT scan was negative in 12 patients and positive in 3 patients. Sensitivity of ^{99m}Tc-DMSA(V) scintigraphy for detecting recurrence/metastases was 66.7% using calcitonin levels as the reference, and the sensitivity of ¹⁸FDG-PET/CT was 20%.

AGE (years)	SEX	CALCITONIN LEVELS (pg/ml)	DMSA (V)	¹⁸ FDG-PET/CT
1 49	F	>1000	+	-
2 49	M	514	-	-
3 41	M	318	+	-
4 50	M	3110	+	+
5 57	F	238	+	-
6 48	M	404	+	-
7 46	M	272	-	-
8 68	F	325	+	+
9 50	F	23000	+	-
10 42	F	117	+	+
11 67	F	1380	+	-
12 53	F	3630	-	-
13 41	F	824	-	-
14 33	M	180	+	-
15 46	M	2073	-	-

Conclusion: In our study there was no correlation between calcitonine levels and ¹⁸FDG-PET/CT and ^{99m}Tc-DMSA(V) findings. ^{99m}Tc-DMSA(V) scan is a cheap, readily, available and highly sensitive imaging agent. We concluded that there is no imaging modality which alone is able to diagnose reliably recurrent and metastatic MTC in case of elevated serum calcitonine, therefore the combination of different imaging modalities must be considered the method of choice in the follow-up of the disease. The final results of the rest of this prospective study are expected to confirm this conclusion.

P54 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized Nuclear Medicine: Thyroid

P587

Late follow up results after radioiodine and surgery treatment of toxic thyroid adenoma

Z. Petrovski, K. Trajkovska; Clinical Hospital-Bitola, Bitola, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF.

Objectives: The aim of the study was to evaluate late follow-up results in surgery and radioiodine treatment of toxic thyroid adenoma and compare incidence of hypothyroidism and recurrence hyperthyroidism in treated patients. **Methods:** We observed 93 treated patients (77 female, 26 male, age range 18 - 76 yrs) with adenoma toxicum. 29 (32,2%) pts underwent surgery (adenectomy), while 64 (67,8%) pts received J-131 therapy (555 - 1100 MBq). The long term results of the treatment were followed 1 - 15 years after therapy (median 9,2 yrs). **Results:** Recurrent hyperthyroidism occurred in 4/29 (13,8%) pts after surgery adenectomy in comparison to 5/64 (7,8%) pts with radioiodine therapy. The patients after enucleation of autonomous nodule of the thyroid show increase incidence of late recurrent hyperthyroidism. These results are likely to be due to persistent functional autonomy in the parenchyma surrounding the autonomous adenoma. Apparently this persistent autonomy could be successfully removed by radioiodine. Appearance of hypothyroidism was observed in 6/64 (9,3%) pts treated with J-131, while after surgery had in 3/29 (10,3%) pts. Incidence of hypothyroidism between operated patients and radioiodine treated patients was approximately the same. **Conclusions:** Radioiodine therapy is useful, economical and affective treatment of autonomous thyroid adenoma that provides a safe protection in preventing late recurrent hyperthyroidism and is more successful therapy than surgery treatment.

P588

Determination of the thyroid function after administration of ¹³¹I-Na in patients with hyperthyroidism

C. de Gracia González, B. Martínez de Miguel, R. Pérez Pascual, M. Martín Fuentes, E. Martínez Montalban, S. Rodado Marina, M. D. Marín Ferrer, J. Coya Viña, L. M. Martín Curto; Hospital Universitario la Paz, MADRID, SPAIN.

Introduction: ¹³¹I-Na is administrated in hyperthyroidism situations due to persistent hormonal hypersecretion. ¹³¹I-Na has the same metabolic cycle that the stable form, is taken up by thyroid tissue and is used for the synthesis of hormones. ¹³¹I emits β particles and γ, β particles (0.606 MeV) have a penetration of 1-2 mm in soft tissue, which produces a radiation that damages the cytoplasmic structures and the core. This decreases the cell reproductive capacity which leads to thyroid tissue destruction and fibrosis and gland volume reduction. **Aim:** Determine the percentage of patients with persistent hyperthyroidism after antithyroid that, after undergoing treatment with ¹³¹I-Na, reach hypothyroidism or euthyroidism state, and the time lapse. **Patients and methods:** 49 patients with persistent hyperthyroidism have been studied in our Hospital (Universitario la Paz), 80% women and 20% men. 19 of these patients (41%) with Toxic Multinodular Goiter were treated with doses of ¹³¹I-Na of 555 MBq. While 30 patients with Graves Disease (59%) received doses of ¹³¹I-Na of 370 MBq. The doses of ¹³¹I-Na were set according to the hospital protocol. Antithyroid treatment were temporarily suspended in all patients a week before the dose of ¹³¹I-Na, patients were followed up by measurement of T4, T3 and TSH levels with revisions a month and then every 3-6 months. **Results:** The results are shown in the table below. The time represents the period from the dose of ¹³¹I-Na up to the diagnosis of hypothyroidism or euthyroidism.

	Hypothyroid (%)	Euthyroid (%)	Time (months)
Toxic Multinodular Goiter	41.7%	58.3%	6.5
Graves Basedow	100%	0	4.2
Hyperthyroidism (all cases)	75.5%	24.5%	5.1

Conclusion: A high percentage of patients with an hyperthyroidism history were diagnosed hypothyroidism in about 5 months after administration of the dose of ¹³¹I-Na. 58.3% of the patients with Toxic Multinodular Goiter achieved an euthyroid state after 6.5 months, and all studied patients with Graves Disease reached a state of hypothyroidism in about 4 months.

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Post-therapeutic ¹³¹I whole body scan: qualitative and semiquantitative comparison between early and late images

R. Mazza¹, M. Salvatori¹, P. Castaldi¹, G. Perotti¹, M. L. Maussier¹, L. Indovina², M. Negri¹, A. Giordano¹; ¹Institute of Nuclear Medicine, Catholic University of Sacred Heart, Rome, ITALY, ²Institute of Health Physics, Catholic University of Sacred Heart, Rome, ITALY.

AIM. Until now there is still no consensus for the optimal time for performing the post-therapeutic ¹³¹I whole body scan (TxWBS). The aim of this study was to compare TxWBS scans performed 3 (3-TxWBS) and 7 (7-TxWBS) days after radioiodine therapy (RAIT) in patients with differentiated thyroid cancer (DTC), to establish the best time for TxWBS execution. **MATERIALS AND METHODS.** We prospectively studied 69 DTC patients (50 women and 19 men, mean age 46 yrs) submitted to RAIT between April 2008 and April 2009 (54 pts for remnant ablation and 15 pts. for evidence or suspicion of relapse and/or distant metastases). TxWBS was performed three and seven days after RAIT; qualitative evaluation was performed by 3 expert nuclear medicine physicians. For each study number and localization of ¹³¹I avid lesions were recorded. Each pair of images was classified by the following score: 0, if 3 and 7-TxWBS provided same data; 1, if 3-TxWBS provided more data than 7-TxWBS; 2, if 7-TxWBS provided more data than 3-TxWBS; 3, if data provided by 3- and 7-TxWBS resulted complementary. The nature of the lesions was confirmed by histopathology (11 cases) and clinical follow-up at 6 months (58 cases). **RESULTS:** 3-TxWBS showed 53 thyroid remnants, 29 lymph-nodes metastases, 6 bone metastases, and 17

lung metastases; 7-TxWBS showed 53 thyroid remnants, 25 lymph nodes metastases, 7 bone metastases, and 21 lung metastases. Statistical analysis did not show any significant difference between 3 and 7-TxWBS regarding the number of lesions. Score 0 was assigned to 56/69 (81%) pts., score 1 to 5/69 pts. (7%; 3 with lymph nodes and 2 with distant metastases); score 2 to 7/69 pts. (10%; 2 with lymph nodes and 5 with distant metastases); score 3 to 1/69 pt (1%). Semi-quantitative analysis revealed a mean $T_{1/2}$ of 1.43 days for thyroid remnant, 1.68 for lymph-node metastases, 1.83 for bone mts. and 1.97 for lung mts, respectively. TNM modification was performed in 7/69 pts. (10%) and clinical management was modified in 9/69 pts (13%). On the whole, more lymph nodes metastases were observed at 3-TxWBS, while more distant metastases were recorded at 7-TxWBS. CONCLUSION. Our data suggest that in low risk patients only 3-TxWBS could be performed, without loss of important information. On the contrary, in high risk patients both studies could be performed to obtain complete data and to plan the correct clinical management.

P590

131I Whole Body Scan (WBS) and Urinary Iodine Excretion (UIE) in Follow up of Patients (Pts) with Differentiated Thyroid Cancer (DTC): Considerations in Pts in Thyroid Hormone Withdrawal (THW) and after Recombinant Human TSH (rhTSH)

L. Bertolazzi, V. Barbetti, L. Di Ciolo, C. Cananzi, M. Gaffuri, C. Motta, E. Piccardo, G. Agnese; ASL2 SV Ospedale Santa Corona, Pietra Ligure, ITALY.

Aim. The purpose was to compare WBS and urinary iodine excretion of Pts in THW and after rhTSH; and also to study relationship and significant effects between UIE rate in both groups. **Methods.** 186 Pts (128 females and 58 males, mean age 48) who underwent thyroidectomy for DTC and radioiodine ablation, undergo diagnostic assessment with WBS after six months. They followed a low iodine diet for two weeks. 80 Pts in THW (TSH > 40 uU/ml), 106 Pts after rhTSH (TSH > 100 uU/ml). UIE was performed before administration of 5 mCi of 131I. After 48 hours WBS was performed with a gamma camera Siemens e-cam; appropriate anatomic markers were settled on Pts in the same position (100.000 counts/view was required). **Results.** In 80 Pts in THW: 48 Pts (60%) had UIE below of the reference range (80 - 120 ug/l); the median UIE was 46 ug/l. In 29 Pts (36 %) UIE was in the reference range, whilst in 3 Pts (4%) UIE was in the upper limit of the reference. In 106 Pts after rhTSH: 30 Pts (28 %) have UIE lower than the reference range; the median UIE was 65 ug/l. In 71 Pts (67 %) was in the reference range whilst in 5 Pts (5 %) was in the upper limit of the reference. WBS of all Pts has been negative for presence of thyroid tissue. As for scintigraphy counts only anterior and posterior views of the chest of Pts having UIE under 120 ug/l (maximum rate in reference range) were considered. In 77 Pts in THW 100.000 counts in 210" were collected, while in 101 Pts after rhTSH the same counts were collected in 530". **Conclusion.** Pts in THW have demonstrated low or normal UIE, as effect of iodine depletion regimens and decreasing iodine intake associated to a high rate of radioiodine uptake (with best compliance of Pts and removing any movement artefact). This is mainly due to the kinetics of radioiodine in rhTSH Pts that are quite different from the kinetics of 131I in THW Pts. In THW renal function and clearance of iodine are markedly decreased, resulting in about a 50% decrease in renal clearance of 131I and 50% increase in bio-availability of 131I as compared with euthyroid Pts receiving rhTSH. In Pts rhTSH the administration of therapy with thyroxine (containing iodine, 60-100 ug per day) might determine higher iodine content.

P591

Importance of personalized follow-up in thyroid cancer

M. A. Balsa Breton, S. I. Vasquez Tineo, A. Mendoza Paulini, A. Mariana Monguia, C. Paniagua Correa, M. P. Garcia Alonso, A. Ortega Valle, L. Castillejos Rodriguez, F. J. Penin Gonzalez, C. Pey Illera; Hospital Universitario De Getafe, Getafe (Madrid), SPAIN.

Objective: To retrospectively assess different prognostic factors in patients with differentiated thyroid cancer (DTC) and 3 or more treatments with 131-I. **Material:** During the last 10 years we have administered 620 treatments with 131-I in 431 patients with DTC diagnosis (325 women and 106 men): 295 papillary cancers, 78 follicular type of papillary, 44 follicular cancers, 3 poorly differentiated cancers and 11 Hurtle's carcinomas. Forty eight patients (32 men and 16 women) have needed 3 or more doses of 131-I (11%), due to persistence of remains, local recurrence, lymph node involvement and / or metastases. **Results:** *) 15% of males, compared to 9.87% women, needed more than 2 doses. *) 28 patients older than 45 years and 20 younger than 45 needed more than two 131-I doses. *) Histology: Papillary cancers 35/48 (11.8%), 6/48 follicular type of papillary (7.7%), 3/48 follicular cancers (6.8%), 3/48 Hurtle's carcinomas (27%) and 1/48 poorly differentiated cancer (33.3%). *) There was extrathyroidal extension in 14 patients. *) There was locoregional lymph node involvement in 27 of the 41 papillary cancers, 2 of the 3 follicular cancers and in 1 of the 3 Hurtle's carcinoma. *) There was found lung metastases, at diagnosis or evolution, in 13/41 papillary cancers, 1/3 follicular cancers, 1/3 Hurtle's carcinoma and in the poorly differentiated cancer. Bone metastases were found in 3/41 patients with papillary carcinoma. *) MACIS scoring in the 41 papillary cancers: Low risk (<6) in 15 patients and high risk (>6) in 26 patients. *) TNM stage: >45 years: 5 patients stage IV, 17 stage III, 5 stage II and 1 patient stage I. <45 years: 15 patients stage I and 5 stage II. Regarding prognostic factors described in the literature, we have to attract attention about the fact that 20 patients (41.6%) that required 3 or more doses of 131-I were <45 years old (15 of them stage I) and 12 patients with papillary cancer MACIS scoring was <6. **CONCLUSION:** Although the prognostic factors should always be assessed at baseline staging, the personalized follow-up must set the standard therapeutic guide, especially in young patients because of their greater potential morbidity, although they are theoretically included in low-risk group.

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Non-visualized Thyroid gland by Tc-99m MIBI scan with Normal Thyroid Scan

G. Koca, A. Baskin, K. Demirel, H. I. Atilgan, M. Korkmaz; Health of Ministry, Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara, TURKEY.

Parathyroid scan is a non-invasive method, frequently used in determining parathyroid adenoma. Several methods and radiopharmaceuticals, Tc-99m MIBI and Tl-201 chloride/ Tc-99m pertechnetate (Tl-201/ TcPO⁴⁻) subtraction, are commonly used for this purpose. In our case there was no accumulation in thyroid gland in Tc-99m MIBI scan, whereas in Tl-201 image of the subtraction scan we observed decreased accumulation in thyroid gland than it is expected and TcPO⁴⁻ scan of the thyroid gland was quite normal. Case: 21 year old male with osteoporosis and growth-development retardation, was referred for MIBI parathyroid scan, because of high blood levels of intact parathormon (PTH) and bone specific alkalen-phosfatase (ALP) levels which were 219.4 (PTH normal range: 15-88 pg/ml) and 355 (ALP normal range: 21-58 U/L), respectively. Either in early or in late images with Tc-99m MIBI parathyroid scan thyroid gland was not visualized. Therefore he also had Tl-201 /TcPO⁴⁻ subtraction scan method. However Tl-201 accumulation in thyroid gland was not sufficient for assessment of subtraction method. In his thyroid ultrasonography, thyroid gland was in homogenous echo and there was neither solid nor cystic lesion. The physical examination of his neck was normal. Other laboratory findings which are all normal, as follows TSH: 3.03 (Normal range: 0.35-5.6 IU/ml), free T3: 3.66 (N: 2.5-3.9 pg/ml), free T4: 0.90 (N: 0.59-1.3 ng/dL), Anti TPO:0.3 (N: 0-40 IU/ml), Anti-TG-Ab: <2.2 (n:0-+) u/L, TSH receptor Ab: 1.0 (N: 0-14 U/L), osteocalcine: 9.13 (N: 1.5-15 ng/dL), growth hormone: 1.3 (N: 0.014-5.21), calcitonin:17 (N: 0-150 ng/mL), sedimentation: 6 (N: 0-15 mm/h). There was no significant symptom of acute or chronic thyroiditis. The discordant uptake in thyroid gland with Tl-201 and Tc-99m MIBI scan could not be explained with clinical or laboratory examinations. To our knowledge and results of our search of the published literature, there is no case like this before. **Conclusion:** Even though Tc99m MIBI is habitually used in imaging parathyroid gland and suppressed thyroid gland, it should be taken into account that sometimes we may not be able to visualize even the normal thyroid gland and we might encounter suboptimal visualization in these cases with Tl-201 subtraction method as well.

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Survival analysis of patients with differentiated thyroid carcinoma based on the risk stratification

G. Farmakis, E. Gouverneur, J. Thiele, D. Hellwig, C. Kirsch; Saarland University Medical Center, Homburg, GERMANY.

Objectives: The management of differentiated thyroid carcinoma is dependent on the initial stage of the disease. The terms "(very) low risk disease" implying a Stage I/II disease, and "high risk disease" implying a Stage III/IV disease being based on the AJCC/IUCC classification are widely used in the clinical routine. The aim of this retrospective study was to perform a survival analysis of patients with differentiated thyroid carcinoma based on the risk stratification. **Methods:** In a retrospective analysis 836 patients of the institutional database were evaluated. Patients with follow-up of at least one year were included. Data on clinical and histological characteristics were processed. Survival distributions were calculated using Kaplan-Meier curves and differences were compared by the Cox regression. **Results:** The median follow-up was 6.6 ± 6.0 years. 589 patients (70 %) suffered from papillary carcinoma (319 high risk, 270 low risk), whereas 247 patients (30 %) suffered from follicular carcinoma (161 high risk, 86 low risk). The overall survival showed a poorer survival rate of patients with follicular compared to those with papillary carcinoma (p<0.01). The comparison of risk groups showed poor survival rates for follicular high risk patients compared to papillary high-risk patients ((p<0.01), while the best survival rates were presented in follicular low risk patients. However, the comparison to papillary low-risk patients yielded no statistically significant results (p=0.33). **Conclusion:** The overall survival of patients with follicular carcinoma was poorer compared to those with papillary carcinoma. Follicular high risk patients presented reduced survival rates. In contrast, follicular low risk patients had the best survival rates, although statistically not significant compared to papillary low risk patients.

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Inpatient Treatment of Thyroid Disease in Germany 2008

R. Lorenz, C. Reiners; University of Würzburg, Würzburg, GERMANY.

Aim: The aim of this study was to report numbers about diagnosis and treatment of all inpatients with the diagnosis of thyroid disease in Germany in the year 2008. **Material and Methods:** Analysis was done with the latest available database for the year 2008 from the "Institut für das Entgeltssystem im Krankenhaus" (InEK) with ICD-diagnoses and treatment procedures for all inpatients in Germany. The patient treatment data from 1661 out of 2083 hospitals in Germany (79.7% completeness) were included in the database. The database is public available from the internet site www.g-drug.de. Data selection was performed for diagnostic codes of thyroid disease and thyroid specific procedure codes. **Results:** In 2008 154,144 patients with a thyroid disease were treated stationary. This corresponded to 0.8% of all 19,622,738 inpatient treatment cases and to 188 treatments per 100,000 inhabitants. The 3 most frequent ICD-diagnosis codes were E04 (nontoxic goiter) with 75,359 cases, E05 (hyperthyroidism) with 48,442 cases and C73 (thyroid cancer) with 21,576 cases. A surgical therapy was carried out 104,609 times and a radioiodine therapy 45,282 times. The age distribution of all thyroid patients resulted in the following portions: Age group 0-19 years 1.0%; 20-39 years 13.5%; 40-59 years 43.4%, 60-79 years 37.5%, and 80 years and older 4.6%. **Conclusion:** A numerical overview to the stationary care of thyroid disease patients in Germany in 2008 could be provided. The most frequent reason for an inpatient therapy was the diagnosis of nontoxic goiter. The surgical treatment of stationary thyroid disease patients was about twice as frequent than the conservative treatment. The largest patients group was at the age between 40 and 59 years.

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Identification of optimal radioactive iodine dose for radioactive iodine treatment in the patients with benign thyroid disease associated with hyperthyroidism

D. Yüksel, I. D. Uguz, O. Yaylali, S. Kirac, F. Akin, B. Akdag; Pamukkale University, Denizli, TURKEY.

Aim: The present study aimed to examine the effectiveness of our fixed low dose I-131 in the patients with benign thyroid disease that received a fixed low dose of I-131 in our institution for the treatment of hyperthyroidism. **Material & Methods** Medical records of 140 patients that received a fixed low dose of I-131 treatment in our institution between July 2002 and February

2008 were retrospectively reviewed. A total of 103 patients that had received radioactive iodine treatment (RIT) for hyperthyroidism with available complete follow-up data were included: 15 patients (10 F, 5 M) with Graves' disease (GD), 36 patients (29 F, 7 M) with toxic adenoma (TA), and 52 patients (32 F, 20 M) with toxic multinodular goiter (TMNG). Age, sex, concomitant conditions other than thyroid disease, antithyroid medications, I-131 dose administered, and the presence and duration of response to RIT were recorded for each patient. Development of hypothyroidism or euthyroidism following RIT was considered as complete response to treatment for patients with GD, whereas development of euthyroidism was a sign of treatment response for patients with toxic nodular goiter. **Results:** Of 103 patients, 71 were female and 32 were male (mean age: 60 ± 12 years). The mean I-131 doses administered to patients with GD and toxic nodular goiter were 333 ± 74 MBq and 666 ± 148 MBq, respectively. Based on our treatment response criteria, our cure rates for GD, TA, and TMNG were 73.3%, 55.6%, and 65.4%, respectively. The mean duration of follow-up was 9 ± 6 months (range: 6 to 48 months). Ninety patients received single dose and 13 patients received twice I-131 treatment. Hypothyroidism developed in 10 patients with GD and TA, and in 13 patients with TMNG. The mean time of achieved to hypothyroidism following a single dose was 3 ± 1 months for patients with GD and TA, and 4 ± 1 months for TMNG patients. Cumulative cure rates following the second doses were as follows: 93.3% for GD, 63.9% for TA, and 71.2% for TMNG. **Conclusion:** We suggest that the fixed low dose of I-131 used in our institution for the ambulatory treatment of the patients with benign thyroid diseases associated with hyperthyroidism is effective. Optimal doses of I-131 to reach complete cure are 185 - 370 MBq for patients with GD and 740 - 925 MBq for patients with TA or TMNG.

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Can we use TC-99m MIBI scintigraphy for the differentiation of malignant and benign thyroid nodules?

M. Caglar, C. Kapulu Akca, N. Ersoz Gulcelik, G. Guler Tezer, A. Usman; Hacettepe University, Ankara, TURKEY.

Technetium-99m-methoxyisobutylisonitrile (MIBI) has been proposed to characterize thyroid nodules preoperatively. The aim of this study was to find out which thyroid nodules retain MIBI and whether preoperative detection of malignancy is possible. Methods: Over a period of 36 months, 48 patients (36 women, 12 men; aged 47 ± 12.8 (mean ± S.D.) (24-75.yr) with thyroid nodules were studied. All patients underwent thyroid ultrasonography with 7 MHz transducer, 99mTc-pertechnetate thyroid scanning and single injection-dual-phase (30 min and 2 hr) tumor scintigraphy with 99mTc-MIBI. MIBI scans were considered positive if there was focal tracer retention in the thyroid nodule on the delayed SPECT image. Results: In the following months 21 patients underwent surgery. Histopathological diagnoses revealed a total of 8 thyroid carcinomas. 6 were MIBI positive and 2 were MIBI negative (one papillary microcarcinoma and one patient with Multi Drug Resistance (MDR) positive tumor). 6 and 2 patients had papillary and follicular carcinoma respectively. Thirteen patients had benign adenomas on histological examination. Of these, 5 and 8 were MIBI (+) and (-) respectively. 25 patients who did not have surgery were followed up for a mean period of 12 months (3-24). Twelve of them were MIBI positive and 13 were negative. Control physical exam and USG did not reveal any evidence of enlargement of the nodule or malignant characteristics on USG. The positive and negative predictive values of MIBI scintigraphy for the detection of thyroid cancer was 26 % and 95 % respectively. Conclusion: These results indicate that although MIBI accumulation and retention in the thyroid nodule is not tumor specific, absence of Tc-99m MIBI retention drastically reduces the probability of malignancy, however, papillary microcarcinoma or tumors with MDR protein cannot be excluded.

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Utility of serum thyroglobulin, TC-99m thyroid scintigraphy, neck I-131 uptake and ultrasonography for the evaluation of patients with thyroid cancer after surgery

M. Caglar, B. Temelli, N. B. Kanat, M. Tuncel, S. Erhan Vargol; Hacettepe University, Ankara, TURKEY.

The correlation between remnant thyroid mass after surgery and the percentage of neck uptake is controversial. Aim : To evaluate the correlation between ultrasonography (USG), Tc-99m thyroid scintigraphy (TS), 24 hour radioiodine I-131 uptake (RAIU) and serum thyroglobulin (Tg) in patients with differentiated thyroid carcinoma (DTC) after surgery. Methods : We prospectively studied 29 patient with a mean age of 45.89±11.85 years (range 15-74) with DTC treated with total thyroidectomy. Patients with metastases and anti-Tg antibodies were excluded. After optimal endogenous thyroid-stimulating hormone stimulation (> 30 mU/ml), TS, RAIU, USG and serum thyroglobulin and antithyroglobulin antibody measurements were done for all patients. Results : Out of 23 patients with papillary, 2 patients with follicular and 4 patients with mixed tumors, 6 had thyroiditis on the histological examination (21%). The mean remnant thyroid volume was 0.283 ml (0-1.89 ml). Tg values after surgery were in the range of <0.2 and 84 ng/ml (median:4.93). RAIU varied between %0.1 to %16.4 (median2.9, mean:4.42). USG and TS detected residual tissue in the neck in 18 and (%62) and 25 patients (%86) respectively. TS was significantly more sensitive than USG for the detection of remnant thyroid tissue (P < 0.005). When RAIU was ≥ 0.9 %, all patients had tracer uptake in the thyroid bed on TS. The correlation between thyroid bed iodine uptake and remnant volume was poor. (r =0.26 =p<0.05). The RAIU in patients with thyroiditis was not different than those without thyroiditis. In 4 patients whose Tg values were above 25ng/ml extrathyroidal uptake was seen on the postablation scan. Conclusions: For the postoperative evaluation of patients with well differentiated thyroid cancer 1) The sensitivity of TS is higher than USG for the detection of residual thyroid tissue 2) When remnant volume does not correlate with Tg levels, metastases are likely 3) Postoperative RAIU correlates poorly with remnant volume 4) No relation was found between IU and presence of thyroiditis on the surgery specimen.

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Meningocele mimicking a metastasis of papillary thyroid carcinoma

A. Campenni¹, M. A. Violi, M. Moleti, G. Sturmiolo, D. Cardile, R. Paratore, A. Blandino, F. Trimarchi, F. Vermiglio, S. Baldari; Università di Messina, Messina, ITALY.

Aim: ¹³¹I whole body scan (WBS) is a sensitive procedure for detecting metastases in differentiated thyroid carcinomas (DTC). Nevertheless, a wide spectrum of potentially misleading readings has been reported following its use. Herein we describe for the first time a case of ¹³¹I accumulation in a meningocele due to a closed spina bifida (CSB). **Material and Methods:** A 69-year-old woman underwent near-total thyroidectomy for a large multi-nodular goiter. Histopathological reports revealed a 3 cm (maximum diameter) large papillary carcinoma of the thyroid. Five months later, after conventional L-T4 withdrawal, the patient underwent: (a) Radioiodine Thyroid Uptake (RTU) measured 24 hours after ¹³¹I tracer activity (1.8 MBq) oral administration; (b) Radiolodine Therapy (RIT) with ablative activity (3700 MBq). WBS was performed five days after RIT using dual-headed gamma-camera equipped with high-energy low-resolution parallel-hole collimator (HELPRAR). The scan revealed the persistence of residual thyroid tissue (11% of the administered tracer activity of ¹³¹I), along with a focal ectopic radioiodine concentration mimicking vertebral metastasis at the level of L5. At the time WBS was performed, serum TSH and Tg were 54.2 UI/ml and 10.6 ng/ml, respectively. In the absence of TgAb, Tg levels were consistent with the persistence of thyroid remnants only. Magnetic Resonance Imaging (MRI) revealed a "pouch-like" image at the level of the L5-S1 vertebrae corresponding to a meningocele caused by a CSB. Our patient was unaware of this malformation, which at clinical examination appeared to be as a small and soft mass covered by skin. **Results:** Its likely NIS-independent radioiodine retention might be the result of intracavitary accumulation of ¹³¹I, or of increased vascularity and capillary permeability, or on both factors combined. **Conclusion:** Due to the high frequency of CSB, this malformation (often clinically silent) should be taken into account in DTC patients with lumbosacral ¹³¹I accumulation and inconsistent Tg values.

P599

Intrathyroid metastasis of malignant melanoma: a case report

M. Punda, M. Franceschi, S. Roncevic, N. Matesa, Z. Kusic; Dpt. of Oncology and Nuclear Medicine, UH "Sestre Milosrdnice", Zagreb, CROATIA.

Aim: Metastases to the thyroid gland are rare, especially in the case of intrathyroid metastasis of malignant melanoma. The aim of our case report is to present results of incidentally found focal pathological intrathyroid FDG-uptake detected in patient with malignant melanoma who underwent staging using FDG-PET/CT scanning. **Materials and methods:** A 67-year-old female patient underwent staging of malignant melanoma of the skin on the right shoulder using F18-FDG-PET/CT scanning. Pathological FDG-uptake was detected in thyroid nodule (19 x14 mm) in the lower left thyroid lobe that required further investigation. Another hypodense lesion of 9 mm in diameter was detected in the right lower lobe, but without pathological FDG accumulation. The patient underwent further examination including determination of thyroid hormones, thyroid ultrasonography (US), thyroid scintigraphy using ^{99m}Tc-pertechnetate and fine-needle aspiration cytology (FNAC). **Results:** The patient showed no clinical or hormonal signs of thyroid dysfunction. US of the thyroid confirmed nodules that were already detected on PET-CT and showed additional two nodules. Thyroid scintigraphy registered an inhomogeneous accumulation of radiopharmaceutical in the right lower lobe and a "hot" nodule in the left lower lobe. An US guided FNAC of the nodule in the left lower lobe showed follicular changes of thyroid cells (differential diagnosis of adenomatoid nodule and follicular tumor). An additional FNAC, from the right lower lobe, detected cellular changes typical for metastatic melanoma. Based on these findings, the patient was referred for total thyroidectomy. Postoperative pathological diagnosis confirmed diagnosis of metastatic melanoma in the nodule in right lower lobe, but also revealed foci of metastatic melanoma within the adenomatoid nodule in the left lower lobe that was not found on FNAC. **Conclusion:** An intrathyroid metastasis from malignant melanoma was determined in the FDG positive and scintigraphic "hot" nodule in the left thyroid lobe, but also in the other nodule without increased FDG uptake. False-negative FDG-PET result of the intrathyroid metastatic melanoma could be explained by limitations of this method to detect micrometastases and lesions smaller than 1 cm. Presented case suggests that all intrathyroid nodules detected by F18-FDG-PET/CT, not only those with pathological FDG uptake, should undergo further investigation.

P600

The Assessment of the Effect of Auto Antibodies Positivity in Autoimmune Thyroiditis on the Salivary Glands Functions

O. Vural Topuz, A. Caliskan, R. Kaya, C. Onsel, K. Sonmezoglu, H. Sayman, L. Kabasakal, B. Kanmaz, M. Hallac, I. Uslu; Istanbul University, Cerrahpasa Medical Faculty, Nuclear Medicine Dept., Istanbul, TURKEY.

Aim: Previous studies have suggested that Hashimoto thyroiditis may cause various degrees of salivary gland involvement. In this study we aimed to determine if the auto antibodies positivity in autoimmune thyroiditis can cause the salivary gland's functions impairment and the xerostomia. **Materials and methods:** Fifty four autoimmune thyroiditis patients (49 F, 5M, mean age 45,3) who require routine thyroid scintigraphy and 11 healthy controls (8F, 3M mean age 48,1) (Group 0) were included in the study. The patients with any other diseases causing xerostomia such as diabetes mellitus and Sjögren's Syndrome were excluded from the study. Among the 54 patients; 31 who have xerostomia (group 1) and 23 without xerostomia (group 2) constituted 2 subgroups. Dynamic imaging of the anterior head including thyroid gland, bilateral parotid and submandibular glands was started after intravenous injection of 10 mCi of Tc-99m pertechnetate. Sequential images were obtained at 25c/frame for 1 minute and thereafter 1min/frame for 40 minutes. At twenty minutes after injection of the tracer saliva secretion was stimulated by lemon juice given into the mouth of the patients. Time-activity curves of both parotid and submandibular glands were generated by taking area of interest. E₃% was calculated by dividing the count value taken at 5 minutes after the maximum count value (E₃) of a gland to the maximum count value of the same gland (T_{max}). The determined E₃% values of each salivary gland of each group were compared with each other by using Anova and T tests. Results: In group 0 the mean E₃% values of parotid and submandibular glands were 51,4±16,4 and 69,4±8,72 respectively. There were no significant differences between Group 0 and Group 1 when the values of Group 0 compared with Group 1 of the mean E₃% values of parotid glands 55,5±9,6 and submandibular glands 71,7±12,6 (p>0,05). Likewise, there were no significant differences between Group 0 and Group 2 when the values of Group 0 compared with Group 2 of the mean E₃% values of parotid glands 58,9±13,9 and submandibular glands 71,2±10,7 in the same values (p>0,05). **Conclusion:** Although, poorer salivary gland function can be seen in autoimmune thyroiditis patients with xerostomia, this impairment was not significant from those of the normal subjects.

P601**Bone Mineral Density Assessment with DEXA in Hyperthyroid Patients who had Received Radioiodine Treatment**

H. T. İlçe, M. E. Yıldırım, M. E. Erkan, A. N. Korkmaz, S. Ataoğlu, A. S. Doğan; Medical School of Düzce University, Düzce, TURKEY.

Aim: Hyperthyroidism is one of the most common endocrine pathologies in adults. Hyperthyroidism affects bone resorption and formation and enhances calcium reabsorption from the bone tissue. Therefore hyperthyroidism causes loss of bone mineral density. One of the choices for treatment of hyperthyroidism is radioiodine treatment. There is not enough data the current literature regarding the effects of radioiodine treatment on bone mineral density in hyperthyroid patients who had received radioiodine treatment. In this study, the effects of radioiodine treatment on bone mineral density were evaluated by DEXA. **Material and Methods:** Thyroid scintigraphy, thyroid functions, and DEXA results of hyperthyroid patients who had received radioiodine treatment in our department were evaluated before and after therapy. Hyperthyroidism was diagnosed by clinical examination, ^{99m}Tc pertechnetate scintigraphy, thyroid sonography and measurement of thyroid hormones. Thyroid function tests and bone mineral density results were calculated before and after radioiodine treatment. **Results:** Forty six patients (31 female, 15 male), with a mean age of 58.4±11.1 were studied. Among in 24 patients (52%), and 19 of them suffered from toxic multinodular goiter (%41). Before radioiodine treatment mean TSH was 0.005 IU/ml, FT₃ was 12.33 pmol/L, and FT₄ was 17.38 pmol/L, baseline mean lumbar spine T score was (-)1.15, lumbar spine Z score was 0.33, lumbar spine bone mineral density 0.99 g/cm², mean femur T score was (-)1.30, femur Z score was 0, femur bone mineral density was 0.83g/cm². After one year of radioiodine treatment the results were as follows: TSH 1.19 IU/ml, FT₃ 3.44 pmol/L, FT₄ 11.33 pmol/L, lumbar spine T score (-)0.85 lumbar spine Z score 0.04, lumbar spine bone mineral density 1.03 g/cm², femur T score (-)1.0, femur Z score 0.30 and femur bone mineral density were 0.87 g/cm². **Conclusion:** Radioiodine treatment can be used successfully in chosen hyperthyroid patients. The decrease that occurs in bone mineral density during hyperthyroidism improves after radioiodine treatment. hyperthyroidism patients; 3 patients had Graves' disease (%7), toxic nodular goiter was found

P602**Early Prediction of Graves' Disease Course Using Thyroid Doppler Ultrasonography**

K. Zaletel, S. Gaberšček, E. Pirnat, S. Hojker; University Medical Centre Ljubljana, Ljubljana, SLOVENIA.

Aim. Our aim was to evaluate the significance of thyroid volume and thyroid vascularity measured at presentation of Graves' disease (GD) in prediction of thyroid disease outcome after long-term treatment with methimazole. **Methods.** We investigated 57 patients with GD, aged between 20 and 77 years (mean, 38.8 ± 11.7). At the disease presentation thyroid hormones and thyroid antibodies were determined, including thyroglobulin antibodies, thyroid peroxidase antibodies and TSH receptor antibodies (TSI). Thyroid volume was measured, colour flow Doppler sonography (CFDS) pattern (I, II or III) was estimated and peak systolic velocity (PSV) of intrathyroid arteries was calculated by using a 7.5 MHz linear transducer. All patients were treated with methimazole for 11.0 ± 3.2 months and then followed after discontinuation of treatment or treated with radioiodine, if euthyroidism was not restored. **Results.** In 25 patients (group 1) remission was achieved for at least one year, while in 32 patients (group 2) the disease recurrence or aggravation was observed 4.3 ± 5.59 months after methimazole cessation. In group 1 the levels of T4, T3 and TSI at presentation were significantly lower compared to group 2 (p = 0.002, p = 0.0003 and p = 0.012, respectively). Similarly, the mean thyroid volume was smaller in group 1 (19.7 compared to 33.5 ml, p = 0.002). PSV was also significantly lower in group 1 (22.3 compared to 28.2 cm/s, p = 0.0001), while a significantly higher proportion of patients in group 2 presented with CFDS pattern III (p = 0.03). **Conclusions.** Our results indicate that remission after long-term methimazole treatment is plausible in GD patients with smaller thyroid volume and lower thyroid vascularity at the disease presentation. Therefore, both thyroid volume and thyroid vascularity are very good early predictive factors that may help us identify patients with heavier course of GD.

P603**The evaluation of radioiodine therapy outcome after ten years in patient with Graves disease**

S. S. Abdelrazek, F. Rogowski, A. Parfienczyk, M. Frackiel, P. Szumowski, A. Ostasz-Sokolik, A. Kociura-Sawicka; Medical University of Bialystok - Department of Nuclear Medicine, Bialystok, POLAND.

The aim of our study was to evaluate the long term (10 years) effect of radioiodine (¹³¹I) therapy on the achievement of euthyroidism and prevention the relapse of hyperthyroidism. **Material and Methods:** We treated 750 patients aged 18-65 years, 85% of them were female and 15% male. Qualification of these patients was based on clinical features, high levels of serum FT3 and FT4, low levels of serum TSH and characteristic appearance on thyroid scans and ultrasound. All the patient were treated unsuccessfully with antithyroid drugs for 6-24 months. Antithyroid drug treatment was used in patients with overt hyperthyroidism to induce euthyroidism prior to radioiodine treatment and was discontinued 5 days before ¹³¹I therapy. Malignant changes were excluded in patients with nodules by fine needle aspiration biopsy. Serum levels of TSH was more 0.1 and the serum levels of FT4 and FT3 were within normal ranges before the radioiodine therapy. Effective T-half measured by the use of T24 and T48 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 200-800 MBq. The absorbed dose ranged between 80 and 200 Gy. Follow up control was done every 6 weeks in the first year, then every 6 months for 9 years. Repeated radioiodine therapy was given after 6 months of the first dose if indicated. **Results:** The success of treatment was: after 1 year 70% of patient achieved euthyroidism, 20% develop hypothyroidism and 10% of the patients has persistent hyperthyroidism and need more than one dose of ¹³¹I. After 3 years of radioiodine therapy 68% of patient achieved euthyroidism and new 12% of teh patients develop hypothyroidism (32% of all patients); after 5 years of ¹³¹I therapy 66% of patient still in euthyroidism, 2% more develop hypothyroidism (34% of all patients). after 8 years of radioiodine therapy 63% of patient still in euthyroidism and 37% of the patients develop hypothyroidism.

After ten years of ¹³¹I therapy 61% of patient still in euthyroidism and 39% of the patients develop hypothyroidism. **Conclusions:** The achievement of euthyroidism and the low percent of hypothyroidism were due to good diagnosis, well preparation of the patients; accurate measurement of administered activity, effective half-life, and well-organised follow up.

P55 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized	Nuclear	Medicine:
Gastroenterology		

P604**Reliability of the presenting symptoms in predicting the outcome of gastric emptying scintigraphy**

L. I. Sonoda, M. Y. Z. Halim, C. Solanki, N. Bird, S. Middleton, K. Balan; University of Cambridge, Cambridge, UNITED KINGDOM.

PURPOSE: In patients presenting with upper gastrointestinal (GI) symptoms, clinical impression of rapid or delayed gastric emptying (GE) may be misleading. This study was undertaken to determine the frequency of rapid/delayed GE compared to clinical presentation in patients referred for GE scintigraphy. **METHODS AND MATERIALS:** A retrospective review of 642 (234 males, 408 females, mean age 45 years old) consecutive GE studies was performed. Each patient received a standard solid meal containing two large eggs labelled with 12 MBq of ^{99m}Tc-tin colloid and a glass of water. Static imaging in upright position (anterior and posterior 60 second) every 15 minutes was performed for 150 min. using a large field of view gamma camera fitted with a low energy collimator and a computer system. GE was classified as normal, rapid and delayed based on half-emptying time and percentage retained at 150 min. **RESULTS:** Seventy (11%) patients with suspected rapid and 572 (89%) with suspected delayed GE were studied. Normal, rapid and delayed GE respectively were observed in 11(16%), 54(77%) and 5(7%) patients with the clinical suspicion of rapid GE and 178 (31%), 215(37%) and 178(31%) patients with suspected delay in GE. One patient with suspected delay had a biphasic GE pattern. Positive Predictive Value (PPV) of clinical suspicion for rapid GE was 77% while PPV of clinical suspicion for delayed GE was 31%. **CONCLUSION:** Our experience demonstrates that clinical impression is often an unreliable predictor of the outcome of GE scintigraphy, especially in patients suspected of having a delayed GE. GE scintigraphy using solid egg meal is a very useful investigation in the management of patients presenting with complex upper GI symptoms.

P605**Evaluation of Liver Transplant Function by Nuclear Medicine Methods**

V. Artiko, D. Sobic-Saranovic, S. Pavlovic, E. Jaksic, M. Todorovic-Tirnanic, N. Petrovic, V. Obradovic; Institute for Nuclear Medicine, Belgrade, SERBIA.

Aim: The aim is evaluation of the perfusion, morphology and the biliary tree patency of the liver transplants by the two scintigraphic methods successively performed. **Material and Methods:** The study was performed in 20 controls and 20 patients after orthotopic liver transplantation (up to two years). "First pass" acquisition was performed with scintillation camera, after bolus injection of 360 MBq ^{99m}Tc-diethyl-IDA, (60 frames/60s), continued by 59 minutes (1 frame/min) slower dynamic study. From the liver and kidney activity during "first pass" study, hepatic perfusion index (HPI) was calculated using slope-analysis. Hepatobiliary scans obtained during second phase of the study were analyzed for morphology, and parenchymal and hepatobiliary TA curves were generated and analyzed according to the time to maximal activity (Tmax) and the time to half of maximum activity (T/2). **Results:** In comparison to the controls (HPI=0.66.5±0.07%) portal perfusion was slightly (0.69±0.08%), but not significantly (p>0.05) increased. In 6 patients, biliary phase of hepatobiliary scintigraphy showed increased accumulation of radiopharmaceutical in the left (n=2) or right (n=6) hepatic duct. Uptake of the radiopharmaceutical (Tmax =21.5±2.9min) was slightly, but not significantly (p > 0.05) delayed in comparison to the controls (16.2±3.7min). Excretion from the hepatocytes was significantly (p< 0.05) prolonged (32.5±4.1 min) in comparison to the controls (26.7±3.9 min) while extrahepatic flow was also significantly (p < 0.01) prolonged (93.0±17.3 min) than physiological (44.0±6.9 min). **Conclusion:** The single injection hepatic radionuclide angiography and hepatobiliary scintigraphy are noninvasive, sensitive and valuable for the follow up of the liver transplants.

P606**The diagnostic significance of hepatic parenchymal retention index parameter determined by hepatobiliary scintigraphy in liver transplant recipients**E. A. Gencoglu¹, G. Yaman¹, T. Bahceci¹, A. Cinar¹, K. Kavak¹, A. Aktas¹, M. Haberal²; ¹Baskent University Medical Faculty, Department of Nuclear Medicine, ANKARA, TURKEY, ²Baskent University Medical Faculty, Department of Surgery, ANKARA, TURKEY.

Aim: Hepatobiliary scintigraphy with Tc-99m iminodiacetic acid derivatives is a non-invasive, objective, and quantitative technique to evaluate the function and integrity of the hepatobiliary tree in liver transplant recipients. This method easily identifies many structural complications as well as functional complications related to hepatic perfusion, tracer uptake, and excretion. The aim of this study was to evaluate the value of hepatic parenchymal retention index parameter determined by hepatobiliary scintigraphy in the early diagnosis of functional complications in liver transplant recipients. **Material and method:** One hundred liver transplant recipients (64 men, 36 women of overall mean age 29.12 ± 14.2 years) were studied. Hepatobiliary scintigraphy was performed at 7-10 days after the transplantation immediately after intravenous injection of 1.85 MBq/kg of Tc-99m mebrofenin. A large field-of-view dual-head gamma camera was used for image acquisition. To test graft perfusion data were recorded every one second for one minute, to evaluate parenchymal function, data were recorded every 30 seconds for 40 minutes. The images were evaluated visually and quantitatively. The quantitative parameters used were

hepatocyte extraction fraction and hepatic parenchymal retention index. Scintigraphic findings were then correlated with biopsy results. **Results:** In the visual analysis, all grafts (100%) showed normal perfusion and normal hepatocyte extraction. In the quantitative analysis, hepatocyte extraction fraction values were within the normal range in all cases (mean value: $96.2 \pm 2.3\%$). According to the results of hepatic parenchymal retention, patients were divided into 3 groups. Group 1 consisted of 75 recipients, in whom hepatocyte excretion was seen as normal. In these patients, hepatic parenchymal retention index values were within the normal range (mean: $18.14 \pm 4.30\%$). Group 2 included 15 patients, whose liver grafts showed severely decreased hepatocyte excretion. In this group, hepatic parenchymal retention index values elevated severely (mean: $82.64 \pm 8.23\%$). Group 3 included 10 patients, in whom hepatocyte excretion decreased mildly-moderately and hepatic parenchymal retention index increased mildly-moderately (mean: $43.60 \pm 9.80\%$). The hepatic parenchymal retention index values were then statistically compared and significant differences were found among these 3 groups ($p < 0.001$). When the scintigraphic findings were compared with biopsy results, it was revealed that acute rejection in all Group 2 recipients and mild-moderate hepatocyte damage/cholestasis in all Group 3 patients. In the light of these findings, we conclude that, hepatic parenchymal retention index parameter determined by hepatobiliary scintigraphy may be valuable in the early diagnosis of functional complications in liver transplant recipients.

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Parametric comparison in evaluation of solid gastric emptying scintigraphy

L. I. Sonoda, M. Halim, C. Solanki, N. Bird, S. Middleton, K. Balan; University of Cambridge, Cambridge, UNITED KINGDOM.

Purpose: The results of gastric emptying scintigraphy (GES) have been commonly expressed as the time taken for the contents of the stomach to diminish by half (T1/2) and the percentage of the original volume remaining (GR) in the stomach at a specific time. We sought to ascertain the level of agreement between these two parameters in determining normal, rapid and delayed GE in patients undergoing GES using a solid test meal. **Methods and Materials:** GES using a ^{99m}Tc -tin colloid labelled solid egg meal in 642 consecutive patients referred to the Nuclear Medicine Department over a 10-yr-period was retrospectively reviewed. Gastric emptying (GE) T1/2 and GR at 150 min. of each study were subjected to careful scrutiny and statistical analysis. **Results:** There was good correlation between T1/2 and GR at 150 min. (Pearson's Correlation Coefficient = 0.554, $P < 0.001$) in assessing GE. Matching T1/2 and GR were present in 499/642 (78%) of studies. Discordant results with one parameter showing normal GE and the other abnormal GE were seen in 142/642 (22%) of studies. Truly biphasic GE with one index showing rapid GE and the other delayed GE was seen only in 1/642 of cases. The use of T1/2 alone yielded more normal results than GR alone (290/642, 45% vs. 230/642, 36%). **Conclusion:** Our results have shown a good correlation between T1/2 and GR in assessing GE using a solid meal. Concurrent use of T1/2 and GR by paying attention to the clinical details is probably the optimal method of reporting GE studies.

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Clinical profile of idiopathic rapid gastric emptying on gastric emptying scintigraphy

L. I. Sonoda, M. Niriella, M. Halim, N. Bird, S. Middleton, K. Balan; University of Cambridge, Cambridge, UNITED KINGDOM.

Aim: To investigate the incidence of idiopathic rapid gastric emptying (IRGE) during routine gastric emptying scintigraphy (GES). **Methods:** The results of a 2.5 h solid GES using a standardized scintigraphic technique were reviewed in 642 patients to see which patients met criteria for rapid gastric emptying, defined as $>50\%$ emptying of isotope-labelled solid meal in <70 minutes. When rapid gastric emptying occurred without an obvious cause or abnormal serum biochemistry, it was considered idiopathic (IGE). **Results:** Of total 642 patients, 70 (11%) had clinical suspicion of rapid GE. 182/642 patients (28%) had rapid GES, of which 144 (79%) were considered idiopathic. There were 97 (53.2%) males and 85 (46.7%) females whose mean (SD) HET were 43 (15.3) and 41(15.8) respectively. The pre-dominant symptoms were abdominal pain (29.6%), classical dumping symptoms (28.1%), vomiting (21.5%), bloating (17.8%), and diarrhoea (2.9%). Of 70 patients with clinical suspicion of rapid GE, 54 (77%) showed rapid and 5 (7%) delayed GE giving 77% positive predictive value for the test. **Conclusion:** The majority of patients with rapid GE confirmed by GES studies were idiopathic. IRGE was equally common among males and females. However, only a minority of these patients presented with classical symptoms of dumping syndrome.

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Duodeno-gastric reflux - an incidental finding during routine ^{99m}Tc -HIDA scintigraphy

L. I. Sonoda, M. Halim, C. Solanki, S. Middleton, K. Balan; University of Cambridge, Cambridge, UNITED KINGDOM.

Purpose: Duodeno-gastric reflux (DGR) is an incidental finding on ^{99m}Tc -HIDA studies but its detection often yields useful clinical information. Present study was carried out to determine the rate of detection as well as incidence of DGR in patients undergoing routine HIDA imaging over a 5-year-period. **Materials and Methods:** One hundred and eighty-three sequential patients (52 males, 131 females, mean age 46 years old) who underwent ^{99m}Tc -HIDA cholecystigraphy over a 5-year-period between 2004 and 2008 have been retrospectively reviewed. Age, sex, previous surgery, clinical indications for the study, presence or not of DGR and clinical reports were subjected to analysis. **Results:** Biliary dyskinesia ($n=135$; 74%), post-surgical symptoms ($n=33$; 18%) and sphincter of Oddi dysfunction ($n=15$; 8%) were the main indications for the study. 33/183 (18%) patients had DGR of which 21 (64%) were present in 117 patients with otherwise normal studies while 12 (36%) were seen in 66 patients with abnormal results ($p=0.87$). All except one case of DGR was detected and mentioned in the original clinical report. 25/132 (19%) and 8/51(18%) patients respectively with normal and abnormal biliary tract anatomy were found to have DGR ($p=0.76$). Occurrence of DGR had no significant relationship with age, sex or gall bladder ejection fraction. **Conclusion:** DGR is an easily detected common finding on routine cholecystigraphy and may be the cause of presenting symptoms in patients who may have an

otherwise normal HIDA study. The occurrence of DGR does not appear to have any significant relationship with age and sex of patients, biliary tract anatomy, or gall bladder function.

P610

Is gallbladder ejection fraction using fatty meal CCK cholecystigraphy useful for diagnosis of chronic cholecystitis?

V. Dabbagh Kakhki¹, D. Beiki²; ¹Mashhad University of Medical Sciences, Imam Reza Hospital, Nuclear Medicine Research Center, Mashhad, IRAN, ISLAMIC REPUBLIC OF, ²Tehran University of Medical Sciences, Research Institute for Nuclear Medicine, Tehran, IRAN, ISLAMIC REPUBLIC OF.

Introduction: A standard noninvasive imaging method to preoperatively confirm the suspected diagnosis of chronic calculous cholecystitis is desirable. S incalide or fatty meal cholecystigraphy can confirm the diagnosis of chronic acalculous cholecystitis. **Objective:** The goal of this study is to determine the gallbladder ejection fraction using a standard fatty meal in chronic cholecystitis and to compare it with subjects without biliary disease. **Methods:** In this study 36(46.2%) healthy subjects and 42(53.8%) patients with RUQ or abdominal pain after eating, with suspected chronic cholecystitis according to sonography and clinical findings, underwent cholecystectomy with ^{99m}Tc -BrIDA. After 1 hour injection of ^{99m}Tc -BrIDA, the subjects ingested the fatty meal (10 g fat of Humana formula). GBEF was calculated at 30 and 60 minutes after fatty meal ingestion. After cholecystectomy, postoperative pathologic evaluation was recorded. For control group, we studied patients who were referred for ^{99m}Tc -sestamibi myocardial perfusion imaging, with no signs, symptoms and history of cholecystitis. All of them had normal GB and liver ultrasonography. **Results:** Based on Gaussian distribution in normal group, threshold of GBEF for diagnosis of chronic cholecystitis at 30 and 60 minutes after fatty meal ingestion respectively was 27.46% and 61.44%. In comparison healthy volunteers and patients, GBEF at 30 minutes in patients (61.21%) was lower than normals (69.54%), but there was no statistically significant difference ($P > 0.051$). Also, GBEF at 60 minutes was lower in patients but statistically was not significant (GBEF in control group=84.26%, GBEF in patient group=80.22%, $P=0.144$). No significant difference was noticed in GBEF according to gallbladder wall thickness, lymphoplasmal cell infiltration, fibrosis and number of gallbladder stone and had not important effect. Area under the curve for GBEF was 0.655 at 30 and 0.601 at 60 minutes. Sensitivity and specificity for GBEF30 threshold:28 were 4.76% and 94.44% as well as for threshold:45 were 9.52% and 86.11%. For GBEF60:61 sensitivity and specificity were 9.52% and 97.22% while for 70 were 21.43% and 91.67%. Based on our study, Humana formula can be as an alternative to cholecystokin 8. **Conclusion:** We have described a lower limit of normal GBEF values using a standard fatty meal (120 ml of Humana formula including 10 g fat) as an alternative to sincalide. Final diagnosis must be upon both the clinical findings and GBEF, not just according to GBEF.

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Biliary Acids Absorption Measurement With ^{75}Se -SEHCAT In The Initial Diagnosis Of The Chronic Diarrhea

P. C. Notta, D. Ramal, S. Maisterra, M. Roca, Y. Ricart, J. Mora, A. Sabaté, R. Puchal, J. Martín-Comin; Hospital universitari de Bellvitge, Hospitalet de Llobregat, SPAIN.

Aim: To evaluate the usefulness of ^{75}Se HCAT test in the early diagnosis of patients with diarrheic syndrome. **Methods:** 37p that presented diarrheic syndrome of recent beginning were prospectively evaluated, (26 women, aged 25-80 years), within the first month of evolution. In all patients the abdominal retention of biliary acids 4 and 7 days after the oral administration of 0.01mCi of ^{75}Se HCAT was measured, once before initiating the treatment and in the patients with positive basal study the test was repeated 3 months later. The retention index is defined as the abdominal activity at 4 or 7 days divided for the abdominal activity 3h post-administration. The patients were visited at 3 and 6 months after the first study. Depending on the response they were classified as a) complete response: normalization of the stool frequency, b) partial response, decrease of the depositional frequency or no response. The test was considered to be positive when abdominal retention index was: $<25\%$ at 4th day and $<10\%$ at 7th day. **Results:** Group A: The abdominal retention of ^{75}Se -SEHCAT was normal in 21 patients. 6 of these patients were diagnosed of colonic diverticulosis, 8p of irritable bowel syndrome, 1p of lymphocytic colitis, 1p of post-gastroenteritis syndrome, 1p of celiac disease and 1p of cardias stenosis. 6p are still without a clinical diagnose. Group B: The abdominal retention of ^{75}Se -SEHCAT was decreased in the remaining 16 patients; all the patients but 1 showed pathological index of retention at 4th day and all of them at day 7. Following the administration of resicolestiramine 8p (50%) presented partial response and 8p (50%) showed complete response. In the 3rd month examination, the retention index had increased in 4 patients at 4th day and in 9 patients at 7th day.

	Group A (4 th día)	Group A (7 th día)	Group B(4 th día)	Group B (7 th día)
Initial examination	42,3% +/- 13,0 (23,6-71,4%)	19,6% +/- 7,9 (10-31,6%)	13,0% +/- 10,5 (0,3-31,9%)	2,8% +/- 2,5 (0,0-6,4%)
Re-test (3 months)	-	-	8,2% +/- 7,9 (0,7-17,6%)	2,2% +/- 1,7 (0,0-4,9%)

Conclusion: The measurement of the absorption of ^{75}Se -SEHCAT allows the early diagnosis of the biliary acids malabsorption in 43% of the patients with diarrheic syndrome, allows early treatment and subsequently improves the quality of life. The measurement at 7th day seems to be more precise than the one of the 4th day.

P612

Significance of SUV at the anastomosis of subtotal gastrectomy in follow-up F-18 FDG PET

S. Zeon, B. Choi, S. Kim, K. Won, I. Kim; Keimyung University School of Medicine, Daegu, KOREA, REPUBLIC OF.

Aim The aim of this study was to characterize the FDG uptake at the anastomosis site (A-site) of subtotal gastrectomy with Bilioth I (BI) or Bilioth II (BII) on PET. **Materials and Methods** From

February 2006 to October 2007, 22 patients (12 men, 10 women; age, 39–78 y; mean age, 59.0 y) who underwent BI (n=17) or BII (n=5) and two or more times of follow-up PET were enrolled this study. The patients with local recurrence and nodal or distant metastasis were excluded. The patients underwent CT and endoscopy within 1 month of referral. Nine patients had two times of follow-up PET, and 13 patients had three times. Among the patients who had three times of follow-up PET, 9 patients underwent BI and 4 patients underwent BII. The interval between operation and first follow-up PET was 12.8 months (n=22, 12–15 months), and the first and second was 12.3 months (n=22, 10–14 months), second and third was 11.7 months (n=13, 10–13 months). FDG uptake at A-site and F of remnant stomach (F) were measured by maximum standardized uptake value (SUVmax) using a region of interest technique. **Results** In patients with BI, mean SUVmax (mSUVmax) at the A-site was significantly higher than F on all of the follow-up studies (3.2±1.0 vs. 2.0±0.6, p=0.000; 2.9±0.8 vs. 2.2±0.6, p=0.003; 3.0±0.6 vs. 2.1±0.7, p=0.015), respectively. In patients with BII, there were no significant difference between the mSUVmax of A-site and F on first and third time of PET (2.2±0.4 vs. 2.8±0.9, p=0.080; 2.4±0.7 vs. 3.2±1.1, p=0.109), but mSUVmax at F was significantly higher than mSUVmax of A-site (2.6±0.4 vs. 2.0±0.6, p=0.042) on second follow-up PET. There were no significant difference of mSUVmax at A-site on three times of follow-up PET in patients with BI (p=0.458) and BII (p=0.232). mSUVmax of A-site in BI was significantly higher than those of BII on first follow-up PET (p=0.031), and there were no significant difference of SUVmax at the A-site in BII (p=0.058 and p=0.148, respectively). **Conclusion** This study shows that the SUV at the anastomosis would be same as that of fundus in second follow-up of F-18 FDG PET, 2 years after the subtotal gastrectomy with B-I or B-II procedure. Further more the SUV at the A-site could be a possible differential diagnostic point of physiologic response to anastomotic procedure from gastritis or local tumor recurrence at the anastomosis in follow-up study after stomach cancer surgery.

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Dysphagia and pneumonia risk following stroke: comparison between clinical and scintigraphic evaluation. Preliminary report.

V. Valenza¹, M. Lavalle¹, M. G. Cantone², M. C. Nosdeo¹, F. Iodice², G. Perotti¹, P. Profice², R. Urso¹, V. Di Lazzaro²; ¹Institute of Nuclear Medicine, Catholic University of Sacred Heart, Rome, ITALY, ²Department of Neuroscience, Catholic University of Sacred Heart, Rome, ITALY.

Background and aim: Swallowing abnormalities after stroke are common (50% of patients) and increase the risk of pulmonary infections, poor nutritional status and overall mortality. Therefore, early identification of the presence of dysphagia is important in the management of stroke patients. The “water test” (WT) and Gugging Swallowing Screen (GUSS) score are the most commonly used test to detect dysphagia/aspiration, but are not enough sensitive. We propose the use of the oro-pharyngeal scintigraphy (OPS) to complete the dysphagic assessment and to better detect the risk of pneumonia. **Methods:** 13 stroke patients (4 female and 9 male; mean age 66 yrs) were evaluated with WT, GUSS and OPS. WT was performed by sitting the patient upright and asking them to drink 2, 10 and 50 ml of cold water; GUSS also evaluated the semisolid and solid food swallowing. Dribbling of water back out of the mouth, failure to initiate the swallow, coughing, choking, alteration of voice quality were considered as an abnormal tests result. OPS is based on the sequential acquisition of 480 images after the administration of 10 ml of water containing 37 MBq of ^{99m}Tc-Colloid. The evaluation of scintigraphic images and the activity/time curves allow a qualitative (dribbling of water back out of the mouth, failure to initiate the swallow, bolus fragmentation with multiple swallowing, naso-pharyngeal or pharyngo-oral reflexes, premature ingestion of the bolus, laryngo-tracheal aspiration) and a quantitative [oral and pharyngeal transit times (OTT, PTT), retention indexes (ORI, PRI) and tracheal aspiration percentage (TAP)] analysis of swallowing disorders. **Results:** WT was positive in 9/13 pts (70%); GUSS score was <10 in 2/13 pts (15%), between 10 and 19 in 9/13 pts (70%) and 20 in 2/13 pts (15%). OPS quantitative analysis showed positive OTT in 8/13 pts (61%), PTT in 11/13 (85%), ORI in 13/13, PRI in 8/13 (61%), and aspiration in 3/13 pts (23%), respectively. OPS qualitative analysis showed presence of multiple deglutition in 10/13 pts (77%), early drop of bolus in 8/13 pts (61%), tongue propulsion deficit in 12/13 pts (92%), and pharyngeal peristalsis deficit in 9/13 pts (69%). One pt with negative WT and GUSS score 9, one pt with positive WT and GUSS score 14 and one pt with positive WT and GUSS score 12 presented aspiration at OPES. **Conclusion:** OPES, compared to clinical tests, is more sensitive to identify and quantify the aspiration in stroke patients, allowing to plan the correct nutrition program.

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Impact of splenic artery ligation after major hepatectomy on hepatocellular function or viability

J. G. Tralhao¹, A. M. Abrantes², A. C. Goncalves³, S. Tavares⁴, A. C. Mamede⁵, A. F. Brito⁶, D. Cardoso⁷, A. B. Sarmiento-Ribeiro⁸, M. F. Botelho⁹, F. Castro-Sousa⁹; ¹Surgical Department, Surgery III, HUC, Biophysics / Biomathematics Institute, IBILI, CIMAGO, Faculty of Medicine, Coimbra, Portugal, Coimbra, PORTUGAL, ²Biophysics / Biomathematics Institute, IBILI, CIMAGO, Faculty of Medicine, Coimbra, Portugal, Coimbra, PORTUGAL, ³Biochemistry Institute, Cimago, Faculty of Medicine, Coimbra, Portugal, Coimbra, PORTUGAL, ⁴Faculty of Sciences, University of Coimbra, Biophysics / Biomathematics Institute, IBILI, Faculty of Medicine, Coimbra, Portugal, Coimbra, PORTUGAL, ⁵Faculty of Health Sciences, University of Beira Interior; Institute of Biophysics and Biomathematics, IBILI-Faculty of Medicine, University of Coimbra, Coimbra, PORTUGAL, Coimbra, PORTUGAL, ⁶Biophysics / Biomathematics Institute, IBILI, Faculty of Medicine, Coimbra, Coimbra, Portugal, Coimbra, PORTUGAL, ⁷Nuclear Medicine Department, HUC, Coimbra, Portugal, Coimbra, PORTUGAL, ⁸Institute of Biophysics and Biomathematics, IBILI, CIMAGO -Faculty of Medicine; ICNAS, University of Coimbra, Coimbra, Portugal, Coimbra, PORTUGAL, ⁹Surgical Department, Surgery III, HUC, CIMAGO, Faculty of Medicine, Coimbra, Portugal, Coimbra, PORTUGAL.

Background: Liver failure after major hepatectomy(MH) is the main cause of mortality in hepatobiliary surgery. It is attributed to various factors including too small remnant liver to

support over-perfusion followed by secondary injuries in hepatic endothelial cells in small liver. It was reported that splenectomy induced significant reductions in excessive portal system pressure resulting in improved functions in the settings of living donor liver transplantation or MH. Aim: To investigate the impact of portal blood flow reduction by splenic artery ligation after MH in hepatocellular function or viability in a murine model. **Material and Methods:** Forty-two wistar male rats (8 weeks old) were divided in two groups:85% hepatectomy (Hx group) and 85% hepatectomy+splenic artery ligation (Hx+ASp group). Liver blood markers (aspartate-aminotransferase, alanine-aminotransferase, alkaline-phosphatase, gamma-glutamyl-transpeptidase, total-bilirubin and lactic-acid-dehydrogenase), hepatic extraction function (HEF) using ^{99m}Tc-mebrofenin were evaluated three days before and 24h (Hx group (n=5)/Hx+ASp group (n=7)), 48h (Hx group(n=6)/Hx+ASp group(n=3)), 72h (Hx group(n=8)/Hx+ASp group(n=3)) and 120h (Hx group(n=3)/Hx+ASp group(n=7)) after surgery. At each time(24, 48, 72 and 120 h) we have isolated hepatocytes from liver biopsy to evaluate by flow cytometry(FC) oxidative stress levels using the fluorescent probes DCFH2-DA, DHE and mercury orange, the cell viability and death using the Annexin-V/Propidium Iodide assay, and the mitochondrial membrane potential using the JC-1 probe. **Results:** 1)There are significant increase of blood markers before and after surgery, but without differences between groups Hx and Hx+ASp(ns); 3) HEF maintained normal values without differences between the groups(ns); 4) In isolated hepatocytes from animals we observe an higher decrease in cell viability statistically significant at 24h in Hx+ASp group compared with the Hx group (65% vs 84%). However, after 120h, in Hx group, a decrease in cell viability is detected, that may be related with the increase in peroxides and superoxide anion production and with the decrease in mitochondria membrane potential. On the other hand, in Hx+ASp group, an increase in cell viability and a decrease in cell death are observed when we compare with the other animal group (71% vs 31%). **Discussion:** Our preliminary results show that after splenic artery ligation had beneficial effects on MH showed by better results on FC evaluation related to the increase in cell viability in Hx+ASp group compared with Hx group. These results suggest that splenic artery ligation after hepatectomy support liver regeneration.

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How Reliable Are Scintigraphic Gastric Emptying Assessments of Gastroparesis Determined Via Manual Drawings of Gastric Regions?

K. J. Nichols, Z. Javaheri, M. B. Tomas, C. J. Palestro; North Shore - Long Island Jewish Health System, Manhasset & New Hyde Park, NY, UNITED STATES.

Objectives: Gastroparesis can be detected through scintigraphic imaging of the stomach following ingestion of a standardized radiolabeled meal (J Nucl Med Technol. 2008;36:44-54). Gastroparesis is defined as > 10% retention at 4 hrs. This assessment requires manually drawing regions around perceived stomach regions. This investigation was undertaken to determine variability of assessing gastroparesis by this means. **Methods:** This was a retrospective analysis of gastric emptying studies performed on 156 consecutive subjects, 63 men & 93 women (mean age 54±20 years). No subject was taking any medication at the time of the study likely to influence test results. Pts. ingested a standardized meal and underwent a standardized 4 hr. gastric emptying protocol consisting of anterior & posterior abdominal imaging at 0, 1, 2, 3 & 4 hrs. after meal ingestion. Algorithms enabled 5 observers to view paired anterior & posterior conjugate view scintigrams & draw stomach regions individually as needed on each of the 10 images in order to conform most closely to perceived stomach contours, and permanently recorded counts obtained for each region for each computation session, so that multiple re-computations for an individual pt. resulted in multiple entries in computer files. Frequencies with which the 5 observers felt it was necessary to perform multiple assessments, and the percent of times for which this changed study interpretation (pt. from having to not having gastroparesis, or vice versa), were computed. **Results:** The final assessment of gastroparesis, defined as the last computation for each pt. at 4 hrs. > 10% of initial activity, was observed in 18/156 (12%) pts. Observers performed more than 1 set of drawings in 50/156 (32%) pts., with session numbers distributed as: 106 pts. requiring only 1 computation session, 31 pts. needing 2 sessions, 16 pts. with 3 sessions, 1 pt. with 4 sessions and 2 pts. with 5 sessions. Among pts. requiring multiple computation sessions, 7/156 (4%) had discrepancies such that some sessions yielded gastric retention > 10% but for other sessions yielded retention < 10%. Thus, the percent of pts. with gastroparesis varied from 10%-14% depending on manual drawings. For the 7 discrepant cases, percent retention at 4 hrs. ranged from 1.1%-25.6%, with mean = 10.3%±4.2%. **Conclusions:** While scintigraphy offers an excellent means of assessing gastroparesis non-invasively, the variability associated with performing drawings manually suggests that data processing quality assurance is essential, and that technical improvements, such as automation of gastric region generation, warrants future investigations.

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The Assessment of the Parotid Gland Functions after the Superficial Parotidectomy Operations

E. Karaman¹, Ö. Vural Topuz², N. Kaya¹, O. Ozturk¹, C. Onsel², C. Yagriz¹, I. Uslu², O. Enver¹; ¹Istanbul University, Cerrahpasa Medical Faculty, Department of Otorhinolaryngology and Head Neck Surgery, Istanbul, TURKEY, ²Istanbul University, Cerrahpasa Medical Faculty, Nuclear Medicine Department, Istanbul, TURKEY.

Aim: The aim of this study was to evaluate the long term effects of the superficial parotidectomy operation on the functions of operated parotid gland and the effects of its functional changes on the other side gland's functions by using salivary gland scintigraphy. **Materials and Methods:** Eighteen patients (9F, 9M, mean age 46.6±9.0) operated between years 2004 and 2009 and a control group of 18 healthy subjects were included in the study. Seven patients with increased antiTg and antiTPO levels were excluded from the study because of the possibility of salivary gland disorders. The patients with diabetes mellitus and Sjögren disease which can cause salivary gland's impairments were also excluded. The mean age of the rest 11 patients (8F, 3M) was 48.1±11.8. After intravenous injection of 10 mCi Tc-99m pertechnetate, sequential images over the anterior view of the head that included bilateral parotid and submandibular glands were obtained at 2sc/frame for 1 minute and then 1min/frame for 40 minutes. At twenty minutes after injection of the tracer a lemon juice was given into the mouth of the patients for stimulation of saliva secretion. Time-activity curves were generated by taking area of interest in both parotid

glands. Also, $E_5\%$ was calculated by dividing the count value taken 5 minutes after the maximum count value (E_5) to the maximum count value (T_{max}) of the same gland. The $E_5\%$ values of operated 18 parotid glands, the non-operated glands of the same group and 22 parotid glands of controls were compared statistically by using Mann-Whitney U tests. $p < 0.05$ was considered significant. Results: The mean $E_5\%$ value of operated parotid glands and non-operated glands were 69.0 ± 17.4 and 51.4 ± 17.9 respectively. There was a significant difference between these values ($p = 0.013$). When the $E_5\%$ values of operated parotid glands (69.0 ± 17.4) were compared to the values of 22 parotid glands of control (51.5 ± 16.4) the difference was also significant ($p = 0.005$). On the other hand there were no differences between non-operated parotid glands of patients and all the parotids of controls ($p > 0.05$). Conclusions: Our data show that although superficial parotidectomy operation can cause to decrease in functions of operated parotid glands, it doesn't lead to any compensatory increase in the functions of the opposite site.

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Spect scintigraphy: precise and more sensitive method in detection of small lesions of hepatic hemangiomas

D. Pop Gjorceva, S. Miceva Ristevska, D. Miladinova, N. Ristevska, S. Stojanovski; Institute of Pathophysiology & Nuclear Medicine, Skopje, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF.

Aim: The aim of this study is to estimate the contribution of SPECT scintigraphy (sc) in diagnosing of hepatic hemangiomas (hh) especially in detecting of lesions less than 2 cm. **Subjects and methods:** 43 patients (pts) were included in the study, aging from 29 to 68yrs; 32 female (74%) and 12 male (26%). Findings of the number of the detected hh with ultrasonography (US), planar and SPECT sc were compared. The total number of detected lesions as the number of the right and left hepatic lobe (rhl and lhl) separately were compared. **Results:** In the 43 pts, ultrasonography detected 58 lesions suspicious for hemangioma: 44/58 (76%) in the rhl and 14/58 (24%) in the lhl. 8/44 lesions (18%) in the rhl were equal or less than 1 cm in diameter; 24/44 (55%) were lesions between 1-2 cm and 12/44 lesions (27%) were equal or over 3 cm. Planar sc detected 44 lesions for hemangioma; 34/44 (77%) were in the rhl, and 10/44 (23%) in the lhl. 4/34 lesions, (12%), in the rhl were less than 1 cm, 18/34 (53%) were between 1-2 cm and 12/34 (35%) were equal or over 3 cm in diameter. 3/10 lesions in the lhl (30%) were equal or less than 1 cm, from 1-2 cm diameter were 4/10 (40%) lesions and equal or over 3 cm were 3/10 (30%) detected lesions. The SPECT sc confirmed 51 lesions for hh - 40/51 (78%) in the rhl, and 12/51 (22%), lesions in the lhl. 6/40 lesions were less than 1 cm in diameter, 22/40 were between 1-2 cm and 12/40 lesions were equal or over 3 cm in diameter. 3/11 lesions in the lhl were less than 1 cm, 5/11 lesions were between 1-2 cm and 3/11 lesions were equal or over 3 cm in diameter. The results are presented in the table below:

43p (29-68yrs)		Right lobe		Left lobe	
f 32 (74%)					
m 11 (26%)					
US	58	44 (76%)		14 (24%)	
		≤1 cm	1-2 cm ≥ 3 cm	≤1 cm	1-2 cm ≥ 3 cm
	8 (18%)	24 (54%)	12 (28%)	6 (43%)	5 (36%) 3 (21%)
	34 (77%)			10 (23%)	
Planar scintigraphy	44	≤1 cm	1-2 cm ≥ 3 cm	≤1 cm	1-2 cm ≥ 3 cm
	4 (12%)	18 (53%)	12 (35%)	3 (30%)	4 (40%) 3 (30%)
	40 (78%)			11 (22%)	
		≤1 cm	1-2 cm ≥ 3 cm	≤1 cm	1-2 cm ≥ 3 cm
SPECT scintigraphy	51	6 (15%)	22 (55%) 12 (30%)	3 (27%)	5 (46%) 3 (27%)

Conclusion: Our findings confirmed the proven ability of SPECT scintigraphy for detection of hepatic hemangioma, compared to classic planar scintigraphy. The contribution of SPECT scintigraphy is specially of importance for small lesions in the right hepatic lobe which are 1-2 cm in diameter. SPECT scintigraphy is close in sensitivity to ultrasonography findings but its specificity is much more expressed in detection of hepatic hemangiomas of this size.

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Follow up of Primary Achalasia: The importance of esophageal transit scintigraphy

A. M. Alvarez, A. Serena, F. Loira, J. Barandela, L. Campos, J. M. Nogueiras, J. Pou; Hospital Meixoeiro, VIGO, SPAIN.

AIM: Achalasia is an infrequent primary motor disorder characterized by loss of the esophageal peristalsis with lack or incomplete relaxation of the lower esophageal sphincter. The esophageal manometry is the main diagnostic test of the disease, use in the follow up of these patients as well. Although in the last years new therapeutics techniques had been introduced, some of them fail over the time of follow up. The aim of the study was to evaluate the usefulness of esophageal transit scintigraphy in the follow up of patients treated of primary achalasia. **PATIENTS AND METHODS:** Review of esophageal transit scintigraphy records from 1999 - 2010. A total of 135 studies performed in 45 patients with primary achalasia treated sequentially with botulinum toxin and/or pneumatic dilatation and/or Heller esophagectomy. After acquiring the dynamic study, an evaluation of the esophageal transit time and the quantitative indices of radiopharmaceutical retention at 30 seconds, 2, 5 and 10 minutes were performed. Patients were divided in 2 groups, according to clinical response to the therapeutic procedures based on a semiquantitative scale of symptoms (dysphagia, regurgitation and chest pain) at the last follow up. Correlation with manometry was evaluated. **RESULTS:** Group 1: Patients with good final clinical response ($n = 36$). Group 2: Patients with poor final clinical response ($n = 9$). Comparison of the pressure of lower esophageal sphincter (Manometry) and the retention index (Esophageal transit scintigraphy) before and after a therapeutic modality in both groups evidenced a significance correlation between the clinical response and the effectiveness of the therapy, with higher association observed by gammagraphic study. By ROC curves, we establish the cutoff

point of improvement for esophageal transit scintigraphy considered as a minimum 35% decrease of retention radiotracer from baseline (CI 95% - 75% Sensitivity Specificity 71%). **CONCLUSION:** Esophageal transit scintigraphy is a minimally invasive test use to quantify the retention index of primary achalasia after therapy, with superior correlation between final clinical response and effectiveness of the treatment compared to manometry.

P56 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized Nuclear Medicine: Hematology

P619

Platelet kinetic study in patients with autoimmune thrombocytopenic purpura during corticosteroid treatment.

K. K. Nikolova, D. Vassileva; SBALHZ, Sofia, BULGARIA.

Aim: A platelet kinetic study is indicated in the evaluation of patients with autoimmune thrombocytopenic purpura (ATP). Splenectomy is a standart treatment for patients who do not respond to glucocorticoid therapy. The aim of this study was to estimate the effects of corticosteroids on the platelet kinetic as a prognostic factor of splenectomy. **Material and methods:** The study was conducted on seventy four patients with ATP. In 21 patients studies were performed during corticosteroid treatment and in 53 patients before or after therapy. Platelet blood count, life span, sequestration index, sequestration site and platelet production (bone marrow biopsy) was determined. Platelet kinetic studies in all patients were performed after i.v. injection with donor platelets. The platelets were obtained by differential centrifugation and were labelled "in vitro" with $3,7\text{MBq }^{111}\text{In-oxine}$. Platelet survival was defined from daily blood sampling. Platelet distribution „in vivo" was determined by spleen/heart ratio(S/H) and liver/heart (L/H) ratio. **Results:** There was small difference in platelets count and survival between the untreated and treated groups. The patients with untreated ATP had a mean platelet count of $57 \pm 29,2 \times 10^9 / l$ (normal $140-440 \times 10^9 / l$), a severely decreased platelet survival time-mean $1,60 \pm 1,0$ days (normal $8,10 \pm 0,32$) and increased sequestration indices. In the second group, (during corticosteroid treatment) the mean platelet count was $59 \pm 37,8 \times 10^9 / l$, mean platelet survival time- $2,2 \pm 1,7$ days and increased sequestration indices. **Conclusions:** Our results demonstrate that corticosteroid therapy slowly increase mean platelet survival time while splenic uptakes remained abnormally elevated. In conclusion the platelet kinetic studies, during corticosteroid treatment may be used to locate the site of platelet sequestration and to determine whether splenectomy will be of benefit in patients who do not respond to glucocorticoid therapy.

P620

Kinetics of ^{111}In oxine labeled platelets in patients with malignant lymphomas.

D. Vassileva, K. Nikolova; SBALHZ, Sofia, BULGARIA.

Thrombocytopenia occurs frequently in patients with malignant lymphomas. Determining the causes of thrombocytopenia in these patients is often difficult. **Aim:** The aim of this study was to assess the clinical impact of the platelet kinetic studies for determination the mechanisms of the low thrombocyte counts in the management and treatment the thrombopenia in patients with malignant lymphoma. **Methods:** Forty five patients with malignant lymphoma associated with thrombopenia (25 with Hodgkin's disease and 20 with non-Hodgkin's lymphoma) were investigated. The platelets were labeled with $3,7 \text{ MBq }^{111}\text{In oxine}$. Platelet survival was defined in daily blood sampling. Platelet distribution in vivo was determined by spleen/heart and liver/heart ratio. **Results:** According to our data the patients are divided into 3 groups. The results in group A established the platelet survival time and the sequestration indices near to the normal rate. Many chemotherapeutic agents used to treat malignant lymphoma have a myelosuppressive effect and depress megakaryocyte production. The data in patients (group B) showed a severe decreased platelet survival time mean $1,60 \pm 0,26$ days (normal $8,10 \pm 0,32$) and increased sequestration indices. Secondary immune thrombocytopenia can occur in association with lymphoma. In patients (group C) platelet survival time was negligibly decreased, mean $6,2 \pm 0,62$ days, the spleen sequestration index was increased. The rate of platelet associated antibodies was normal. Patients with lymphoma often have splenomegaly and hypersplenism. **Conclusions:** Thrombopenia is a common feature in patients with malignant lymphoma. Our results show, that it can be caused by platelet underproduction, increased platelet destruction, or disturbed platelet distribution (hypersplenisms). The determining of the mechanisms of the thrombopenia in patients with malignant lymphoma determine the choice of the most rational therapy (medication or splenectomy).

P621

HiSPECT allows recognition of specific anatomical areas affected in canine elbow pathology

K. Peremans, S. Vermeire, I. Gielen, E. De Bakker, A. Dobbeleir, T. Waelbers, B. Van Ryssen, K. Dik, H. van Bree; Faculty of Veterinary Medicine, UG, Mellebeke, BELGIUM.

Canine orthopedic problems in the forelimb are frequently originating from the elbow. Planar bone scintigraphy is included in the diagnostic frame work when clinical/radiographic examination is inconclusive or non-localizing. However, determination of the exact localization of pathology within the elbow is usually not possible due to resolution limits of the conventional gamma camera systems. The HiSPECT system consists of multipinhole collimators for conventional triple head gamma camera's. This system allows adjustment of the space between the camera heads and thus investigation of larger structures. The aim of the study was to investigate the value of HiSPECT in the evaluation of elbow pathology in the dog. **Material and Methods** 15 dogs were included (30 elbows) with suspected elbow disease. Radiographic examination was negative ($N = 2$) or inconclusive ($N = 13$). HDP (mean 22 MBq/kg) was injected 2-3 hours prior to acquisition. Micro-SPECT was performed with a conventional triple head gamma

camera (Triad, Trionix USA), adapted with 3 multi-pinhole collimators (6 holes, 3 mm \varnothing , resolution 2.4mm) (Bioscan, USA). Data were acquired for 20 minutes in step-and-shoot mode (10 steps, 36° angular step, 120 sec per step, matrix 256 x 256). Images were reconstructed using a dedicated ordered subset-expectation maximisation (OSEM) algorithm (Scivis, Göttingen, Germany). CT/MRI and/or arthroscopy were performed to confirm pathology. Results On the HISPECT images, pathology could be confined to specific anatomical regions. Twelve elbows showed high focal uptake in typical predilection sites for pathology: the medial humeral epicondyle (flexor tendon insertion)(N=4), the medial coronoid process of the ulna (fragmentation of the coronoid process)(N=7) and the anconeal process of the ulna (N=1). In 4 elbows focal uptake was noted in the medial coronoid region as well as in the medial humeral epicondyle identified on CT/MRI as fragmented coronoid processes and insertion desmitis of flexor tendons. In 14 elbow, focal uptake in the aforementioned predilection sites (medial humeral epicondyle: N = 9; medial coronoid process: N = 5) was accompanied by several areas of mild increased uptake in the articular region of the humerus and radius representing articular changes (cartilage and subchondral erosion, and synovitis) on arthroscopy. Conclusion With the HISPECT system increased uptake was discernible in specific elbow areas correlating well with pathology found on CT/MRI and/or arthroscopy. This modality may allow a more accurate choice of subsequent targeted structural imaging modalities and more specific therapeutic interventions in cases with questionable clinical and radiographic findings.

P622

Imaging and Biodistribution of Tc-99m PEG-Liposomes for Infection Imaging in Horses

C. Underwood¹, A. W. Van Eps¹, G. Storm², L. Van Bloois², M. W. Ross¹, W. J. G. Oyen³, O. C. Boerman³, T. P. Schaer¹, P. Laverman³, ¹University of Pennsylvania, Kennett Square, PA, UNITED STATES, ²Utrecht University, Utrecht, NETHERLANDS, ³Radboud University Nijmegen Medical Centre, Nijmegen, NETHERLANDS.

Liposomes are phospholipid nanoparticles that extravasate at sites of increased vascular permeability and are used for targeted drug delivery and diagnostic imaging. This study is the first to describe the i.v. administration of Tc-99m labeled polyethylene glycol (PEG)-coated liposomes in normal horses with a final aim to use them for infection imaging and targeted drug delivery. Here we present imaging and biodistribution data. In addition, in vitro and in vivo complement activation data are presented. Liposomes containing glutathione were prepared via the film hydration method and labeled using Tc-99m-HMPAO. An assay was developed to establish the 50% serum hemolytic complement activity (CH₅₀) in horses, as complement-mediated reactions are a common adverse effect in other species such as rats and humans. Ten horses were administered Tc-99m PEG-liposomes intravenously. Clinical parameters, hematology, plasma biochemistry and serum complement activity were monitored serially. Imaging was performed at 1, 12, and 21 h p.i.. Six horses were euthanized at 23 h and tissues of interest were dissected and uptake was calculated as %ID/kg. Complement assays required the addition of C3 depleted human serum to the standard hemolytic assay to obtain a CH₅₀ value. In contrast to previous findings in humans, no significant complement activation was detected. No significant clinical changes occurred following liposome administration. Scintigraphic studies revealed a prolonged vascular phase that lasted to 21 h, with increased radiopharmaceutical uptake in the liver, lungs, spleen and kidney. There was a repeatable pattern of organ distribution similar to that seen in other species. Evaluation of tissue samples revealed greatest Tc-99m activity within the lung, kidney, liver and spleen. There were minimal adverse effects associated with intravenous liposome administration in normal horses. This study establishes normal scintigraphic findings after administration of Tc-99m-PEG liposomes. Comparative studies with Tc-99m labeled leukocytes in horses with infections are ongoing. PEG-liposomes have potential for diagnostic identification and targeted drug delivery in the treatment of refractory infections and neoplasia in horses.

P623

Seasonal temperature variations and blood volume analysis

E. Moralidis¹, G. Arsovs², E. Papanastasiou¹, I. Hiliadis¹, G. Gerasimou¹, A. Gotzamani-Psarrakou¹, ¹AHEPA Hospital, Thessaloniki, GREECE, ²Hippokraton Hospital, Thessaloniki, GREECE.

Aim. It is known that technical errors and biological variations may influence blood volume analysis. This study aimed to assess the effect of environmental temperature in the determination of red cells volume (RCV) with ⁵¹Cr and plasma volume (PV) with ¹²⁵I human serum albumin (HSA). **Method.** Ninety-nine patients (80 referred for erythrocytosis) and 12 healthy volunteers were enrolled (aged 52±16 years, 77 male). Based on the local Mediterranean climate, 52 participants examined from May to October (mean period temperature 22°C, range of average month temperature 16-27°C) formed a Warm Group and 59 subjects examined from November to April (mean period temperature 9°C, range of average month temperature 5-14°C) were allocated into a Cold Group. Subjects were submitted to both RCV and PV measurements recurrently in the morning and in the fasting state, according to the techniques proposed by the International Committee for Standardization in Hematology. The venous hematocrit (Ht_v) was determined, the body hematocrit (Ht_b) was assessed from fractional blood volumes and the ratio of Ht_b to Ht_v (f ratio) was also calculated. **Results.** Ht_v ranged from 0.36-0.65 in all study participants. There was no significant difference between the Warm Group and the Cold Group in age (50±16 versus 54±15 yrs, respectively), weight (78±13 versus 80±13 kg, respectively), the gender (male 64% versus 73%, respectively) and the reason for testing (presumed erythrocytosis 65% versus 78%, healthy volunteers 15% versus 7%, chronic kidney disease 14% versus 12%, other 6% versus 3%, respectively). The blood measurements (Warm Group versus the Cold Group, respectively) for RCV were 33±9 versus 33±9 ml/kg (p=0.787), for PV 39±11 versus 35±10 ml/kg (p=0.042), for Ht_v 0.50±0.05 versus 0.53±0.06 (p=0.034), for Ht_b 0.46±0.05 versus 0.49±0.06 (p=0.002) and for the f ratio 0.91±0.04 versus 0.94±0.06 (p=0.005). Similar tendencies were found when men and women were analyzed separately. **Conclusion.** Blood volume analysis may be affected by variations of the environmental temperature. Although RCV is not influenced, it seems that in the cold months PV diminishes slightly, accompanied by an increase of Ht_v and Ht_b. This may be the result of increased sympathetic tone and vessel contraction in lower temperatures, causing plasma shift from the intravascular into the interstitial space. Moreover, the decreased f ratio in hot weather probably reflects dilation and augmented volume capacity of the superficial veins.

P624

Diagnosis and Follow-up of Pulmonary Embolism in 15-25 Year-old Females in Relation to Hormonal Contraception Use

D. Chroustova¹, M. Sindelarova¹, P. Jansa², L. Veprekova³, J. Kubiny¹, J. Trnka⁴, ¹Department of Nuclear Medicine, General Teaching Hospital and First Faculty of Medicine, Charles University, Prague, CZECH REPUBLIC, ²Department of Cardiovascular Medicine, General Teaching Hospital and First Faculty of Medicine, Charles University, Prague, CZECH REPUBLIC, ³Thrombotic Centre, General Teaching Hospital, Prague, CZECH REPUBLIC, ⁴Department of Medical Physics, General Teaching Hospital and First Faculty of Medicine, Charles University, Prague, CZECH REPUBLIC.

Aim: An analysis of medical records of young females who were examined in our department during a five-year period (2005-2009) on suspicion of pulmonary embolism (PE) in relation to hormonal contraception (HC). **Material and methods:** The patient sample included 86 young females aged 15-25 (average 21) years who underwent a perfusion/ventilation scintigraphy (P/V scan). Seventeen of them were examined repeatedly. Altogether, 114 scintigraphic examinations were performed. Lung perfusion scintigraphy was performed using a planar gammacamera (Mediso MB 9200) in 4 projections following 100 MBq ^{99m}Tc-MAA i.v. application with 81mKr ventilation scintigraphy concurrently. **Results:** 1) Among 57/86 (66%) patients, who were using HC, 24 (42%) had scintigraphic signs of PE. 2) 11/57 (19%) of them had clinical signs thrombosis of deep venous system of lower limbs that were confirmed by sonography. Leiden mutation was found in 9/24 (37%) patients with PE. 4) Among 29/86 (34%) females not using HC, PE was detected in only 3 patients (10%). 5) 10/17(59%) females, who were examined repeatedly, had permanent postembolic residual changes of lung perfusion. **Conclusion:** In our group of patients, who underwent a P/V scan, dominated females using HC, 42% of whom were diagnosed with PE on scintigraphy, compared to 10% of those not using HC with PE. Among the patients with PE were 10/24 (42%) young females with persistent postembolic changes. The risk of venous thromboembolism related to the use of HC is well known. Our study indicates that it needs to be considered as a cause of PE even among very young females. In our experience, prevention of these life-threatening states in patients with family history of venous thromboembolism consists of timely examination of their thrombotic profile and selection of appropriate contraception.

P625

The value of gated cardiac blood pool SPECT and lung perfusion SPECT in examination of patients with pulmonary embolism

K. W. Zavadovskiy, A. N. Pankova, Y. B. Lishmanov; Institute of Cardiology, Tomsk, RUSSIAN FEDERATION.

Aim. To reveal the most informative indicators lung perfusion scans and gated blood pool SPET in not massive pulmonary embolism. **Materials and methods:** 72 patients were examined in the course of investigation. Among them - 15 patients (average age 59±9) suffering from coronary heart disease (NYHA I-III); 57 patients (average age 62±11) with suspicion of pulmonary embolism (PE). Radionuclide evaluation included realization of quantitative blood pool single photon emission computer tomography (QBS) and lung perfusion scintigraphy (LPS). There was defined the following indices: ejection fraction (EF), right ventricle end systolic and diastolic volume (ESV and EDV), peak ejection and filling rates (PER and PFR), mean filling rate for first third of cardiac cycle (MFR/3). According to perfusion lung scintigraphy and QBS there was defined U/L index reflecting correlation of impulse count of upper and lower parts of the lungs. **Results:** values of ejection fraction of right ventricle were revealed to be significantly low in the group of patients with PE. EDV and ESV values between the groups did not differentiate significantly. It was revealed that patients with PE had significantly lower values of RV stroke volume. Main differences between the groups were revealed according to diastolic index. Pulmonary blood filling in patient without PE equally increased from base of lungs to apical parts. In patients with signs of PE there were observed signs of pulmonary blood flow redistribution. In the areas of the lungs corresponding with pool of embolized pulmonary artery the blood flow was authentically low in comparison with conventionally intact area. We do not find any correlation between extent of PE and right ventricle dysfunction indices. In patients with PE extent less than 50% the normal right ventricle can be interpreted as the sign of acute PE. On the other hand, right ventricle dysfunction is typical for chronic tromboembolic pulmonary hypertension. **Conclusion:** Development of pulmonary embolism is accompanied by significant lowering of diastolic RV function. QBS allows to define pulmonary blood flow and semiquantitatively estimate pulmonary embolism intensity. Right ventricle dysfunction in case of pulmonary embolism extent less than 50% is typical for chronic tromboembolic pulmonary hypertension.

P626

Value of Labeled RBC Scan in the Non-invasive Diagnostics of Endometriosis

G. Koca¹, F. Demirel², K. Demirel¹, M. Korkmaz¹, B. Gokmen², ¹Health of Ministry, Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara, TURKEY, ²Health of Ministry, Ankara Training and Research Hospital, Department of Obstetrics and Gynecology, Ankara, TURKEY.

AIM: Endometriosis is a hormone-dependent clinically benign disease associated with pelvic pain and infertility. The gold standard for diagnosis of endometriosis and evaluation of the implants are laparoscopy and histopathology. Our aim was to show the activated implants with labeled red cell scintigraphy in patients with recurrent endometriosis and compare the results with pelvic MRI results. **MATERIAL METHOD:** Patients who had operated with diagnostic and / or therapeutic, laparoscopy or laparotomy and diagnosed histopathologically as endometriosis, were included to our study. Thirty patients, who were diagnosed as recurrence by clinical and laboratory terms and 10 healthy volunteers (control group) patients were included in the study. Between the second and fifth days of menstruation when the endometriotic lesions were highly activated, radionuclide imaging was performed by red blood cell scintigraphy in both early&late

phases and compared with pelvic MRI findings. The results were statistically assessed. **RESULTS:** The patients mean age was 33.33 ± 8.05 years. Compared to the control group we found a total of pathological accumulation of radioactivity with marked red blood cell scintigraphy in 27 patients out of 30 (90%). The pathological accumulation observed in 26/30 (86.7%) patients, there was definite increased focal accumulation in scintigraphy and in one patient, however was moderate focal accumulation. The location of the increased accumulation was in ovarian region in 19 patients, in extra-ovarian region in 2 patients and in 6 patients there were increased accumulation in both ovarian in extra-ovarian regions. Extra-ovarian regions were peritoneal cavity in 3 patients, uterus in 3 patients, rectum in 1 patient, pouch of Douglas in 1 patient. MRI findings were in ovarian region in 18/30 patients (60%), in extra-ovarian region in 1 patient (3.3%) and in 4 patients (13.3%), it was both in ovarian and extra-ovarian regions. In 21/27 patients (77.8%) there was increased radioactivity accumulation in early phase of radionuclide images and in 22/27 patients (81.5%) there was increased radioactivity accumulation in late phase of radionuclide images where there was findings of endometriosis in MRI. Additionally scintigraphy detected four patients with endometriosis that MRI couldn't. **CONCLUSION:** Imaging of endometriosis regions with labeled RBC scan can be used as an alternative diagnostic procedure for the patients with recurrent endometriosis.

P627

Intradermal lymphoscintigraphy at rest and after a quick exercise in the functional assessment of the lymph drainage in patients with secondary lymphoedema.

G. Tartaglione¹, M. Pagan¹, A. Scoppola², C. Capalbo², V. Picone², C. Z. Di Rocco², M. Morelli², F. De Galitis², R. Bartoletti³, P. Marchetti⁴, ¹Nuclear Medicine, Cristo Re Hospital, Rome, ITALY, ²Oncology, IDI-IRCCS, Rome, ITALY, ³Rehabilitation, IDI-IRCCS, Rome, ITALY, ⁴Oncology, University Sant'Andrea Hospital, Rome, ITALY.

Aim of this study was to evaluate the Intra Dermal Injection (IDI) Lymphoscintigraphy at rest and after a quick muscular exercising or walking, on the functional assessment of lymph drainage in secondary lymphoedema patients **Methods:** We selected 40 patients (30 f, 10 m) with secondary lymphoedema after lymph node dissection for melanoma or breast cancer. A dose of ^{99m}Tc-albumin-nanocolloid, 50 MBq, 0.3-0.4 mL, was given IDI at the top in the first inter-digital space of hands or feet. Two planar static scans were taken immediately afterwards (LEAP collimator, acquisition matrix 128x128, anterior and posterior views, pre-set time 5 minutes). If lymph drainage were slow or absent, the patients would be asked to walk or exercise for 2 minutes. A post-exercise scan was then performed to monitor and record the tracer pathway and the Tracer Appearance Time (TAT) in the main lymph node basin. **Results:** In normal limbs the lymph pathway drainage was along the main vein (TAT <10 mins). In limbs with delayed lymph drainage an isotonic muscular exercise for 2 minutes counteracted the increased gradient pressure of the lymphatic system accelerating lymph drainage. The post-exercise scans revealed that: 1) 7 limbs had lymph stagnation points; 2) 13 limbs presented a superficial collateral lymph drainage pathway; 3) 12 limbs showed a lymph drainage towards the deeper subfascial lymphatic compartment, confirmed by an unusual uptake of the popliteal or elbow lymph nodes; 4) 12 limbs had a "dermal backflow"; 5) 3 limbs had a lymph drainage failure. **Conclusions:** A quick isotonic exercise (for 2 minutes) accelerated tracer drainage, revealing several compensatory mechanisms of lymphoedema. The effects of a post-exercise routine on TAT and the qualitative evaluation of IDI lymphoscintigraphic patterns could result in a more accurate and time saving functional assessment of secondary lymphoedema patients.

P628

Saving the zone of stasis in burns with cerium nitrate bathing: An experimental study with Tc-99m methoxyisobutylisonitrile (MIBI) imaging

M. Eski¹, F. Ozer¹, C. Firat¹, N. Arslan², T. Senturk¹, S. Isik¹, M. A. Ozguven²; ¹Gulhane Military Medical Academy and Medical Faculty, Department of Plastic Surgery, ANKARA, TURKEY, ²Gulhane Military Medical Academy and Medical Faculty, Department of Nuclear Medicine, ANKARA, TURKEY.

AIM: Saving the zone of stasis is an important issue not only for experiment but also clinical management of burn. Although many molecules and techniques have been studied; none of them became practically popular. Cerium nitrate bathing is one of the newest techniques that may prevent the inflammation in the zone of stasis. An experimental study was designed to show the efficacy of cerium nitrate bathing for saving the zone of stasis by using Tc-99m-methoxyisobutylisonitrile (MIBI) imaging. **MATERIALS&METHODS:** In this study, fifty-four Sprague-Dawley rats were divided in two groups randomly. We made a standard full-thickness burn with using 'Burn Comb Model'. In the Group1 (control) 0.09% saline and in the Group 2 (experiment) 0.04 molar cerium nitrate were applied on the entire back skin of the rats topically at the first thirty minutes. At the 3rd and 7th days, planar scintigraphic images of the dorsal skin were obtained at 30 minutes after injecting 111 MBq of Tc-99m MIBI via the tail vessel under general anesthesia. The average counts in the regions of interests which were drawn in the burned areas and the interspaces (stasis zone) were determined to show the extent of viable tissue. At the 21th day, the viable area in the dorsal skin was evaluated macroscopically and histologically. **CONCLUSION:** Tc-99m MIBI uptake reflecting the saved stasis zone was statistically different between the Group 1 and 2. The results indicated that cerium nitrate bathing is an effective method for saving the zone of stasis and Tc-99m MIBI imaging is a simple and effective method to reflect the viable tissue.

P629

Nonpalpable breast lesions: Our experience radioguided occult lesion localisation

H. A. Ayan Eke, O. M. Emer, R. Yildiz, E. Ozturk, T. Tufan, M. A. Ozguven; Gülhane Military Medical Academy, Ankara, TURKEY.

Aim: Our aim was evaluating radioguided localisation of nonpalpable breast lesions in routine clinical use. **Patients and Method:** 171 patients with 201 nonpalpable breast lesions with radiologic suspicious findings who were undergone a biopsy by radioguided occult lesion localisation technique (ROLL) were included to the study and evaluated retrospectively. All lesions were visualised by ultrasound or mammography and marked intralesionally via injection of 0.25 mCi Tc-99m macroaggregate albumin on the day of surgery. In case of mammographic suspicious microcalcification areas mammography guided injection was done with adding a small amount of radiocontrast and a control mammogram was taken a few minutes later, to verify the correct localization of the lesions. Intraoperative detection was performed with a handheld gamma probe. The area of maximum radioactivity was excised according to the radiological size of the lesion. Frozen-section histological examination was performed immediately to determine whether the lesion was malignant or not. In case of malign histopathologic findings in frozen section further surgical procedures were continued. Also in 14 cases with indetermined findings in ultrasound or mammography patients undergone a breast MRI. **Results:** Mean age was 47.5 years (range 16-83 years). Tumor marking completed with sonographic guidance in 119 (70%) and in 52 (30%) cases with mammography. Localization of the lesions was successful in all cases. 20 patients had a cancer diagnosis (a patient with colloidal carcinoma and two patients tubular carcinoma). Seventeen patients had undergone preventive breast surgery, three had mastectomy whereas only one patient had undergone axillary dissection. Clear margins were achieved in all cases. Besides 6 patients were diagnosed as atypical ductal-lobular hyperplasia, 2 with intraductal papilloma and 3 patients were diagnosed as intermediate-advanced ductal epithelial hyperplasia. Most frequent benign diagnosis were fibrocystic changes and sclerosing adenosis. Patient preparation and radionuclide lesion localization and excision last for 8-90 minutes. **Discussion:** The frequency of non palpable lesions has increased due to the widespread use of mammography, and ultrasonography. The main problem with non-palpable lesions is that of precise preoperative localization to make easy complete excision with free margins. Radioguided occult lesion localization is a preferable method for our institute when compared to guide-wire localization. It provides better centering of the lesion and it is time and cost effective. ROLL leads less patient discomfort and pain, it has better cosmetic results due to relative low volume of excised tissue. So ROLL is a practical and reliable localization technique for excision of suspicious small lesions.

P630

An Evaluation of Lung Toxicity Formed by Bleomycin and Amiodarone through Tc-99m HMPAO Lung Scintigraphy in Rats

F. Gumuser, K. Vural, T. Varol, I. Tuglu, G. Topal, Y. Parlak, E. Sayit; Celal Bayar University, Manisa, TURKEY.

Objective: The purpose of the study is to determine the lung toxicity formed by amiodarone (AD) and bleomycin (BLM) in rats, by means of Tc-99m HMPAO lung scintigraphy. **Methods:** Thirty albino rats were randomly divided into five groups. After AD or BLM was dissolved with serum physiologic (SF), a 0.5 ml. solution was applied to the right bronchus by a catheter. Group 1 (n=5 rats) received a single dose of AD, group 2 (n=5) received two doses of AD, group 3 (n=9) received BLM, group 4 (n=3) received hydrochloric acid (HCl), and group 5 (n=8) received SF. Rats in group 1, 2, 3 and 5 were given 1mCi Tc-99m HMPAO from the tail vein on the 7th, 14th, 21st and 28th days, whereas in group 4 on 4th and 24th hours. Static images of 10 minutes duration were obtained on 30th and 60th minutes by a double headed gamma camera (Infinia, GE, Tirat Hacermel, Israel) on 256x256 matrix. Regular regions of interests were drawn over the the right lung (RL), left lung (LL) and the liver (Li) and Lung/Liver (L/Li) ratios were calculated. After the scintigraphic imaging procedures were completed, rats were sacrificed. Lung tissues were evaluated on a scale of (+) to (+++++) for edema, alveolar structural integrity and irritation of inflammatory cells. **Results:** Group 2 and 3 showed a statistically significant difference in RL/Li and LL/Li ratios (p<0.05). There was no significant difference in RL/Li and LL/Li ratios in group 5 (p>0.05). In histopathological evaluation, minimal damage or artifacts were observed in Group 5. In Group 4, almost all pathological findings were present in the right lungs. Statistically significant (p<0.01) histological differences were found when Groups 1 and 5 were compared. Significantly (p<0.001) more pathological effects were noted when Groups 2 and 3 were compared to both Groups 5 and 1. Injury was more prominent in the lung tissue of the control rates that were given HCl. Increased L/Li ratios and histopathological findings were congruent. **Conclusion:** It was concluded that Tc-99m HMPAO lung scintigraphy is a non-invasive and easy method for diagnosing drug induced lung toxicity. For patients using AD and BLM, Tc-99m HMPAO can be used in the diagnosis and follow up of the lung toxicity.

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Evaluation of Lung Perfused Blood Volume (PBV) image of DECT compared with Tc-99m MAA SPECT in CPTe patients

T. Shinkai¹, T. Imai², S. Kitano¹, S. Miura¹, N. Shirone³, K. Kichikawa¹, M. Hasegawa¹; ¹Nara Medical University, Kashihara, Nara, JAPAN, ²Saiseikai Nara Hospital, Nara, Nara, JAPAN, ³Takai Hospital, Tenri, Nara, JAPAN.

Dual energy CT (DECT) provides us precise information about pulmonary perfusion, taking patient's dose reduction into consideration. Lung Perfused Blood Volume (PBV) is a post-processing software, especially useful for evaluating pulmonary thromboembolism (PTE). **Aim** The purpose is to compare Lung PBV images with Tc-99m MAA SPECT images in chronic PTE (CPTe) patients. **Materials & methods** Twelve patients with CPTe were analyzed. The dual-source CT (Definition, SIEMENS) scan was performed at 80/140kV dual energy mode from caudal to cranial, contrast medium (CM) injection was administered at rate of 4ml/s. Lung PBV image was obtained on the workstation. Tc-99m MAA of 185MBq was administered in supine position. SPECT was performed on a 3-headed gamma camera (MULTISPECT3, SIEMENS) in two conditions (free breath and deep inspiration breath hold). Difference between the Lung PBV and MAA SPECT for each lesion was investigated by using DICOM viewer (FUSIONVIEWER3.0, Nihon Mediphsics). **Results** The resolution of Lung PBV image was superior to that of SPECT images. There were artifacts due to the CM, especially in the middle lobe and the lingual portion of the left upper lobe. However, there is no problem to distinguish the artifacts from real perfusion defect. In 6 of 12 patients, peripheral areas of lung were invisible due to limited FOV. In 8 patients, parts of perfusion defect of MAA SPECT imaging were not identified by Lung PBV imaging, regardless of artifacts or FOV limitations. **Conclusion** In patients with CPTe, the perfusion of affected segment

was frequently overestimated by Lung PBV image. Collateral blood flow through bronchial artery and intercostal artery etc. is suggested to be responsible for this dissociation.

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Relation between patient age and SUV-HU values in genitourinary structures in F18-FDG PET/CT

B. Cavusoglu, H. Durak; Dokuz Eylul University The Institute of Health Sciences, Inciraltı/Izmir, TURKEY.

Purpose: In this study, the relation between patient age and Hounsfield Unit (HU) and SUV values measured in the areas of interest drawn to prostate, seminal vesicles and testicles in 18F-fluorodeoxyglucose (F-18 FDG) Positron Emission Tomography/ Computed Tomography (PET/CT) images was investigated. **Method:** Mean and maximum SUV and HU values were recorded from the areas of interest (min 12 mm in diameter) which showed FDG uptake in prostate, seminal vesicles and testicles from F-18 FDG PET-CT images of 21 male patients under 40 years without genitourinary cancer. The effect of patient age to SUV and HU values was examined with Pearson correlation test using SPSS program. **Results:** Mean patient age, mean SUV_{max} and SUV_{mean}, mean HU_{max} and HU_{mean} values obtained from the areas of interest are shown in the Table.

	Patient Age Mean/Std. Dev.		SUV _{max} Mean/Std. Dev.		SUV _{mean} Mean/Std. Dev.		HU _{max} Mean./Std. Dev.		HU _{mean} Mean./Std. Dev.	
Prostate	26.0	7.0	2.8	0.7	2.0	0.5	142.7	75.8	43.2	15.0
Seminal vesicles	26.4	6.8	4.0	9.8	1.7	2.0	82.0	32.9	13.5	11.3
Testicles	25.1	8.5	3.2	0.9	2.6	0.9	54.4	13.9	19.6	13.8

There was a negative insignificant correlation between patient age and SUV and HU values for prostate. For seminal vesicles, correlation between patient age and SUV values and HU_{max} were positive but insignificant, while correlation with HU_{mean} was significant ($r = 0.459$, $p = 0.00$). Correlation between patient age and SUV_{max} and SUV_{mean} values were significant for testicles ($r = 0.506$, $p = 0.002$ and $r = 0.467$, $p = 0.005$, respectively) but the correlation between patient age and HU_{max} ve HU_{mean} values was not significant. **Conclusion:** F-18 FDG uptake in testicles in males increases with age until 40 suggesting an increase in metabolic rate. The significant correlation between age and mean HU values is probably caused by thickening of the tissue without an increase in glucose metabolism in seminal vesicles. In prostate, the effect of patient age to SUV and HU values was not observed until the age 40.

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99mTc-HMDP to assess pulp revascularization in transplanted teeth: an in vivo experimental model

M. Marques-Ferreira¹, A. M. Abrantes², E. V. Carrilho¹, M. F. Botelho³,
¹Department of Dentistry, Faculty of Medicine, University of Coimbra, Coimbra, PORTUGAL, Coimbra, PORTUGAL, ²Institute of Biophysics and Biomathematics, IBILI, CIMAGO -Faculty of Medicine; ICNAS, University of Coimbra, Coimbra, Portugal, Coimbra, PORTUGAL, ³Institute of Biophysics and Biomathematics, IBILI, CIMAGO -Faculty of Medicine; ICNAS, University of Coimbra, Coimbra, Portugal, Coimbra, PORTUGAL.

Abstract: Aim: The purpose of this study is to learn more about the pulpar changes associated with autogenous single-rooted immature teeth transplantation in dogs, using one or two-stage surgical techniques. **Methods:** The study group consisted of 3 Beagles, 5 months old, in which twelve incisors and twelve premolars were transplanted to mechanically prepare recipient sockets. One group, (Group-A) were transplanted using a one-stage method in that recipient beds were prepared immediately before transplantation. The second groups of teeth, (Group-B) were transplanted using a two-stage method in which the recipient beds were prepared and left to heal for a period of 7 days before transplantation. Clinical examinations were done every week and the animals were euthanized 9 weeks later. Before euthanizing the animals were injected with 555-740 MBq of 99mTc-hydroxymethylene diphosphonate (99mTc-HMDP) and performed a scintigraphic acquisition 3 hours later. After euthanized, the teeth were extracted and radiopharmaceutical uptake was calculated using a DPC gamma counter. The absorption of the radiopharmaceutical was evaluated and analyzed using the Mann-Whitney test ($p < 0.05$). **Results:** This study documented a favorable outcome of revascularization in immature permanent transplanted teeth, using the 99mTc-HMDP. The results showed no statistically significant difference found in the absorption of the 99mTc-HMDP, between the treatment groups ($p = 0.464$) and between them and the control group (Group-A vs. control $p = 0.713$ and Group-B vs. control $p = 0.157$). **Conclusions:** This study demonstrated that there was no difference between the two surgical techniques in terms of the pulp revascularization in transplanted teeth. Besides that it is also possible to conclude that 99mTc-HMDP is a reliable method to assess the pulp revascularization.

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Use of ventilation/perfusion scintigraphy to detect patients with potentially treatable chronic thromboembolic pulmonary hypertension

M. Grmek, J. Fettich, B. Salobir, M. Harlander, J. Toplisek; University Medical Centre, Ljubljana, SLOVENIA.

Introduction: Ventilation/perfusion (V/P) scintigraphy can detect patients with potentially treatable chronic thromboembolic pulmonary hypertension. Therefore it is not surprising that "Guidelines for the diagnosis and treatment of pulmonary hypertension" (prepared by European society of cardiology and European respiratory society) established V/P scintigraphy as a very important investigation in diagnostic algorithm in patients with pulmonary hypertension. **Aim:** The first aim of the study was to find out what were referral diagnoses at the initial V/P scintigraphy in patients with chronic thromboembolic pulmonary hypertension (CTEPH). The second aim of the study was to find out what were scintigraphic findings in patients with CTEPH

before and after pulmonary endarterectomy. **Material and methods:** Patients in whom treatment of CTEPH was started on Clinical department for pulmonary diseases and allergy in University medical centre Ljubljana in years 2008 and 2009 were included in the study. V/P scintigraphy following EANM guidelines for ventilation/perfusion scintigraphy was done more than once in all patients included in the study. 99mTc - Technegas was used for ventilation scintigraphy and 99mTc - MAA for perfusion scintigraphy. Planar scans performed in anterior, posterior and both posterior oblique projection were done and used for interpretation. For V/P scans interpretation approach proposed in EANM guidelines was used. Results of V/P scintigraphy were compared with the efficiency of pulmonary endarterectomy. Endarterectomy had been done at University Medical Center in Austria in excellent cooperation with team of professor Irene Lang and professor Walter Klepetko from Department of Cardiology and Cardiothoracic Surgery. **Results:** In the two-year period 14 patients with CTEPH were treated in our hospital. The referral diagnoses at the initial V/P scintigraphy were: CTEPH - 8x, pulmonary hypertension - 2x, pulmonary embolism - 4x. Until now pulmonary endarterectomy was performed in 7 patients in all of them with success. The right ventricle systolic pressure fell in average for 31 ± 16 (min. 15, max. 62) mm Hg. Before endarterectomy treated patients had multiple segmental and subsegmental V/P mismatch defects. After surgery lung perfusion significantly improved but also some new defects were detected in all cases. **Conclusion:** Referral diagnoses at the initial V/P scintigraphy in patients with confirmed chronic thromboembolic pulmonary hypertension were: chronic thromboembolic pulmonary hypertension, pulmonary embolism and pulmonary hypertension. V/P scintigraphy is an important diagnostic tool in patients with chronic thromboembolic pulmonary hypertension. It can be used also for follow up after pulmonary endarterectomy.

P635

Is lung protection potentially better using polyurethane endotracheal tubes than polyvinyl ones?

P. Bulpa, S. Bouhon, F. Schryvers, J. Jamart, P. Evrard, I. Michaux, A. Dive, T. Vander Borgh, B. Krug; UCL Mont-Godinne, YVOIR, BELGIUM.

Introduction: Mechanically ventilated patients (MVpts) are prone to develop ventilator associated pneumonia. One of the major risk factors is micro-aspirations of supraglottic secretions around the endotracheal tube cuff (usually in polyvinyl [PV]). A novel polyurethane (PUE) cuff was designed to minimize these leakages. We, therefore, compared the sealing capacities of both tubes in MVpts. **Materials and methods:** Among ICU pts who required intubation, 29 (mean age \pm SD: 68 ± 13 , 21 males) received randomly either PV (HI-LO Evac, Mallinckrodt) or PUE (SEALGUARD Evac, Mallinckrodt) endotracheal tube (size 9 for men and up to 8.5 for women). Only the physician who proceeded to intubation knew the endotracheal tube type. Exclusion criteria includes: emergency intubation, hemodynamical instability, severe respiratory failure or tracheal/laryngeal disease. After intubation, cuff pressure was controlled to be 30 cmH₂O and ventilator parameters, set by the intensivist in charge but with a plateau pressure < 30 cmH₂O, were not modified during the study. Patients were placed on semi-recumbent position (45°), sedated if needed, and no food was allowed through gastric tube. To check for leaks, 74 MBq ^{99m}Tc-DTPA diluted in 5ml 0.9% NaCl were injected through the aspiration channel of the tube, just above the cuff. Sealing capacities were assessed steadily up to 12 h post administration by counting the tracheal aspirates and by imaging the patient using a scintillation camera. Data were read by the nuclear medicine physicians blinded of the endotracheal tube type. The study was approved by the hospital ethics committee and an informed consent was obtained from next of kin. **Results:** Sixteen PUE and 13 PV tubes were introduced into the trachea. Time intervals (mean \pm SD) between ICU admission and beginning of the study or tube insertion and study start were 8.3 ± 9.6 and 3.2 ± 2.8 days, respectively. Ventilator parameters were the following: volume control or pressure support but one on T tube, FiO_2 0.43 ± 0.14 , $Peep$ 6 ± 2 cmH₂O. Leakages were observed in 11/29 patients (38%) corresponding to 5/16 PUE and 6/13 PV tubes (not statistically significant). Leakages were more present in female (7/8) than in male patients (4/17) [$p < 0.001$]. There was a trend that passage was less frequent using a 9 tube size than an 8.5 ($p = 0.062$). **Conclusions:** Our study could not demonstrate *in vivo* a better protection against lung micro-aspirations using the new endotracheal tube with PUE cuff compared to the conventional PV one. Further studies are warranted to study gender specificity as well as influence of endotracheal tube size.

P57 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized Nuclear Medicine: Pediatrics

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Tc99 DMSA scintigraphy in children with Dent 2 disease

M. Angjeleska¹, A. Bogdanovska¹, S. Miceva Ristevska¹, V. Tasik²;
¹Institute of pathophysiology&nuclear medicine, Skopje, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF, ²Department of Pediatric Nephrology University Children's Hospital, Skopje, MACEDONIA, THE FORMER YUGOSLAV REPUBLIC OF.

Background: Dent 2 disease is proximal tubulopathy characterized with low molecular proteinuria (LMWP), hypercalciuria, hematuria, nephrocalcinosis, nephrolithiasis and in some cases progression to renal failure. The aim of this study was to describe the abnormalities on Tc-99mDMSA scintigraphy in children with Dent 2 disease. **Methods:** The diagnosis of Dent 2 disease was established on the basis of presence of LMWP, hypercalciuria and mutation in the *OCRL1* gene. Cortical scintigraphy with Tc-99mDMSA was performed in standard manner, the images were interpreted after 15 minutes, 2 hours, and after 24 hours. **Results:** There were three male children who presented with LMWP hypercalciuria and intermittent microhematuria. None of them had mutation in *CLCN5* gene. All three had mutation in *OCRL1* gene. None had clinical features of Lowe syndrome and all 3 children had elevated muscle enzymes. The Tc-99 DMSA scan was abnormal and revealed poor visualization of the kidneys after 15 minutes, 2 hours and 24 hours. There was high bladder content of the radionuclide suggesting vivid tubular excretion of the radionuclide. **Conclusion:** Abnormal DMSA scan along with elevated muscle enzymes may be useful screening tool for Dent 2 disease. **Key words:** DMSA, Dent 2 disease

P637**Radionuclide esophageal transit study in children with asthma.**

V. Dedek; Faculty hospital, Ostrava-Poruba, CZECH REPUBLIC.

Background: In the Czech Republic, the prevalence of bronchial asthma in children is up to 15%. Gastroesophageal reflux disease (GERD) and asthma occur together frequently. It is reported, that 26- 63 % of infantile asthmatics have abnormal pH-metry. Additionally, 25 % of them have „silent reflux“, i.e. without reflux symptoms. Generally, GERD is often caused by ineffective esophageal motility and incompetence of lower esophageal sphincter (LES), which may be demonstrated by radionuclide esophageal transit study (RETS). **Aim:** Estimation of the occurrence RETS pathological findings in two groups. First group includes children with asthma and second one consists of controls without this diagnosis. **Material:** Group A (Asthma) enrolled 41 children with asthma (20 boys, 21 girls, aged 3- 17) with reflux symptoms and/or worse medically controlled asthmatic complaints. Group C (Controls) enrolled 31 children (15 boys, 16 girls, aged 4- 17) without asthma. **Method:** RETS was performed by single swallowing bolus of 5 ml water labeled 20- 50 MBq ^{99m}Tc -sulfur colloid. Two sets of images were acquired. First step: high speed framing (120 ms per frame) during 30 s. Second step: slower framing (15 s per frame) during 30 minutes. Between steps pts were given orally 100- 300 ml of water to fill stomach. We observed esophageal transit (mean transit time- MTT), antiperistalsis, retention radioactivity in esophagus and finally signs of gastroesophageal reflux (GER). Upon request of pediatrician we performed chest scintigraphy next day to demonstrate a signs of aspiration. It was at 25 children (18 asthmatics and 7 controls). **Results:** Group A had MTT between 4.4- 20.4 s (avg. 7.5 s, SD 1.4 s), 13 children had antiperistalsis and 6 of them GER. Group C had MTT between 4.6- 11.8 s (avg. 7.6 s, SD 1.5 s), antiperistalsis and signs of GER were seen at 2 children. No one of both groups (72 children) had retention radioactivity in esophagus after swallowing and all of 25 chest scintigraphy were negative. We have observed the difference in age, gender, MTT and signs of GER were not statistically significant between groups (Mann-Whitney test). Occurrence of antiperistalsis was more frequent in group of asthmatics (statistically significant $p=0.05$). **Conclusion:** RETS is noninvasive, physiological test with low radiation burden. Signs of esophageal dysmotility (antiperistalsis) and GER especially in children with asthma may lead to other testing (eg. pH-metry) and antireflux or prokinetic therapy may improve their symptoms and reduce the need of antiasthmatic medication.

P638**Renal cortical scintigraphy in children with the first episode of acute pyelonephritis**E. Jaksic¹, R. Bogdanovic², L. Bojic¹, M. Blagic¹, S. Beatovic¹, V. Artiko¹, D. Sobic-Saranovic¹, S. Pavlovic¹, N. Petrovic¹, V. Obradovic¹; ¹Institute of Nuclear Medicine Clinical Center of Serbia, Belgrade, SERBIA, ²Institute of Mother and Child Health Care of Serbia, Belgrade, SERBIA.

Aim: Diagnosis of acute pyelonephritis (APN) in children is usually based on clinical and biological data. The aim of this study was to assess the role of initial cortical scintigraphy in detection of early renal parenchymal damage in children highly suspected on APN, comparing scintigraphic findings with selected clinical/laboratory factors and ultrasonography. **Material and Methods:** A prospective study was conducted in 34 infants and young children (18 boys, 16 girls), aged 1.5 to 36 months (mean 9.8 ± 8.7 months), hospitalized with the first episode of clinically suspected APN. Within the first 5 days after admission Tc-99m DMSA renal scintigraphy, ultrasonography (US), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell count (WBC) and urine analyses were performed. Tc-99m DMSA scintigraphy was obtained 2-3 h after intravenous injection of 0.74 MBq/kg body weight (minimum 15 MBq) in three standard projections. The criteria indicative of early parenchymal damage were divided into three types of abnormalities of increasing severity. **Results:** The DMSA scan showed changes consistent with APN in 27/34 patients (79.4%), mean age of 10.9 month, 44% males and 56% females. Out of 9 febrile children with negative urine culture and supportive evidence of UTI, scintigraphy showed parenchymal involvement in 8 children, 23.5% (8/34) in the whole group and 29.6% (8/27) in scintigraphically documented APN, mild/moderate in 4 and severe in 4 patients. There were not any statistically significant correlations between the frequency or size of initial scintigraphic abnormalities and age, sex, body temperature, CRP levels, or ESR. US showed changes consistent with APN in 7/27 (25.9%) patients with positive cortical scan ($p<0.05$). **Conclusion:** Initial DMSA renal scintigraphy is a sensitive method for early diagnosis of APN in young children, useful in detection of the severity of kidney injury even in patients with negative urine culture. Clinical, biological and ultrasound parameters do not identify children with renal damage. Normal DMSA study, excluding parenchymal involvement and late sequelae, could minimize the use of scintigraphy in the follow up and reduce the redundancy of cystography. We recommend DMSA scan to be added to the initial work-up of children with APN.

P639**Thyroid Cancer in Pediatric Age Group: An Institutional Experience**P. O. Kiratli¹, E. Ceylan Gunay², M. Buyukpamukcu¹; ¹Hacettepe University, Ankara, TURKEY, ²Mersin University, Mersin, TURKEY.

Thyroid cancer is a rare malignancy of childhood with an incidence of 0.7%. This study was aimed to review the course of patients treated for differentiated thyroid cancer (TC), with a special interest of evaluating different parameters as age, gender, clinical presentation, tumour characteristics, method of treatment to the risk of recurrence as well as to the outcome of treatment. Analysis of 53 children (37 girls, 16 boys) with TC were included to the study. Median age was 13y (5 to 19). Histopathologic examination revealed 47 papillary, 4 follicular, 1 mixt and 1 medullary thyroid carcinoma. Near-total/total thyroidectomy was performed on 18, total thyroidectomy with lymph node dissection on 28, where both radioactive iodine (RAI) was given all except 3 patients. The dose ranged from 50 to 200 mCi, where 32 received single and 16 multiple doses. At the time of diagnosis 17 had local disease and 36 had regional lymph node metastases where 13 of them had distant metastases (12 lung and 1 bone metastases). Metastasis was common in girls (66%) and in younger (67%) patients. The mean follow-up after surgery was 59 months (range 3 to 296). Overall survival rate was 98%, only 1 child deceased at

65 months. Recurrence was seen in 11 patients with a median of 12 months. The majority of them were female patients (88%), and under 15 years of age (%72) Almost all the patients with recurrence had extensive disease at initial diagnosis. No significant relation of metastases was observed with tumour histology ($p<0.27$), but multifocality of the tumour seems to be important for metastases ($p<0.04$). Although the number of patients is relatively small in this study, it has a fairly long follow-up period. Besides it confirms good overall prognosis of TC in children. However relapses of the disease and cause specific deaths are possible even after 2-3 decades from the time of initial diagnosis. This fact should force the clinicians the need for intensive follow-up during the first years, which should be maintained throughout the patients' life in order to detect and effectively treat late relapse.

P640**Prevalence of Helicobacter Pylori Infection in Early School and Pre-school Children with C14 Urea Breath Test**

G. Koca, K. Demirel, H. I. Atilgan, A. Baskin, S. Ozyurt, M. Korkmaz; Health of Ministry, Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara, TURKEY.

AIM: In the etiology of chronic active gastritis and peptic ulcer disease Helicobacter pylori (Hp), has one of the important roles. Hp prevalence in our country is about 85 %, but not enough data is available for early childhood group. In our study, we determined to find out the incidence of HP infection in pre-school children and compare the prevalence with early school age children. **MATERIAL METHOD:** Hundred-and seventy-four children, 77 boys, 97 girls, were included to our study. Mean age of the children was 6.02 ± 1.56 years (min: 3 max: 8 years). A standard questionnaire was prepared and it was completed by the children's parents and the assessments were taken into account according to these questionnaires. C14 urea breath test was performed after at least 6 hours of fasting. The children under medication were not eligible to have the test. For the statistical analysis, the children were grouped into 2 groups according to their ages, group 1: 6 years and older and group 2: 7 and 8 years old. **RESULTS:** Helicobacter pylori was positive in 66 cases out of 174 (37.9%). In pre-school age group, 35 cases were positive out of 94 (37.2%) children were found to be positive for HP. In early school age group 31 children out of 80 (38.8%) children had positive urea breath test. In 29 boys out of 77 boys (37.7%) the test was positive, while 37girls in out of 97 (38.1%) girls were positive for Helicobacter. There was no statistical difference between age groups and gender for C14 urea breath test positivity ($p> 0.05$). The number of rooms in the children's apartment was 2.74 ± 0.70 (min: 2, max: 4). There was no statistical difference between the urea breath test positivity and the number of rooms in the children's apartment in terms of age groups. Residential heating method was stove in 90/174 (51.7%), natural gas-boiler in 71/174 (40.8%) and central heating system in 13/174 (7.5%) children's apartment. HP positivity was 37/90 (41.1%) in the children's apartment heated with a stove, 26/71 (36.6%) in the children's apartment heated with natural gas-boiler and 3 / 13 (23%) in the children's apartment heated with central heating system. There was no statistical difference between the groups ($p> 0.05$). **CONCLUSION:** Urea breath test was positive in 37.9% of pre-school age children and 37.2% positive in early school age children.

P641**Tc-99m MAG3 Scintigraphy Findings in Infants with Antenatally Diagnosed Hidronephrosis**

H. I. Atilgan, G. Koca, K. Demirel, A. Baskin, M. Korkmaz; Health of Ministry, Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara, TURKEY.

AIM: Our aim was to evaluate renal function of the infants with antenatal hidronephrosis by Tc-99m MAG3 scintigraphy. **MATERIAL METHOD:** Twenty-one patients (15 male, 6 female) who had been diagnosed by USG as unilateral antenatal hidronephrosis with a mean age 4.52 ± 3.19 months (age range 1-12 months) were included to our study. All the patients performed Tc-99m MAG3 scintigraphy. Each kidneys' relative uptake ratios, time to peak (TTP: reached maximum activity time) values, T $\frac{1}{2}$ (renal activity half-time) and diuretics T $\frac{1}{2}$ (after injection of diuretic renal activity of half-time) values, as well as renogram curve patterns were evaluated by Tc-99m MAG3 scintigraphy. According to the renogram patterns patients were divided into 4 groups. Renogram curve patterns with no obstruction, indeterminate curve pattern, obstruction curve pattern, prolonged parenchymal retention pattern was determined as 1,2,3 and 4 respectively. Relative uptake ratios of the hidronephrotic kidneys over 55% were indicated as supranormal regarding to their renal function. **RESULTS:** Of the 21 hidronephrotic kidneys, there were 3 cases with ureteropelvic stenosis. There was no obstruction in 11 cases recorded as renogram curve pattern 1. Six cases had an indeterminate renogram curve pattern, and in only one case there was prolonged parenchymal retention, curve pattern 4. renogram curve pattern was 1 in 2 nonhidronephrotic kidneys and in one case there was indeterminate curve pattern. Hidronephrotic kidneys had lower uptake ratios than their symmetry (46% to 54%). Two hidronephrotic kidneys had relative uptake ratios over 55% (supranormal function) which were 66.7% and 60.8%. There was no obstruction in these two cases. Mean TTP values of hidronephrotic and non hidronephrotic kidneys were as follows respectively 16.48±9.94 min and 11.91 ± 6:42 min. Average T $\frac{1}{2}$ and T $\frac{1}{2}$ diuretics values in hidronephrotic and nonhidronephrotic kidneys were as follows respectively 42.89 ± 75.38 min, 24.36 ± 33.04 min; 10.36±7.23 min and 7.72±6.50min. Hidronephrotic kidneys' TTP, T $\frac{1}{2}$, T $\frac{1}{2}$ diuretic values were higher than nonhidronephrotic kidneys. TTP and T $\frac{1}{2}$ diuretic values of hidronephrotic kidneys showed significant difference between nonhidronephrotic kidneys ($p < 0.05$). **CONCLUSION:** Antenatally detected hidronephrotic kidneys had longer TTP and diuretic T $\frac{1}{2}$ values and lower uptake ratios than nonhidronephrotic kidneys and 2 hidronephrotic cases showed supranormal function.

P642**Evaluation of adrenal hyperplasia and physiological uptake in adrenal gland at I-123 and I-131 labelled MIBG scintigraphy in operated and non-operated child patients with the diagnosis**

of either adrenal neuroblastoma or extra-adrenal neuroblastoma

N. Kadioglu¹, I. Adalet¹, Y. Sanli¹, D. Balkose¹, E. Yekeler², H. Emiroglu³,
¹Istanbul University Istanbul Medical Faculty Nuclear Medicine Department, Istanbul, TURKEY, ²Istanbul University Istanbul Medical Faculty Radiology Department, Istanbul, TURKEY, ³Istanbul University Institute of Oncology, Istanbul, TURKEY.

Introduction: After adrenal surgery for neuroblastoma, hyperplasia may develop in the contralateral other side adrenal gland, and this uptake can be interpreted as false-positive. **Purpose:** In this study, we aimed to investigate hyperplasia in the contralateral adrenal gland in those undergoing operation for adrenal gland out of the child patients with neuroblastoma and ganglioneuroblastoma having I-123 and I-131 MIBG scintigraphy, and to examine bilateral physiologic involvement in those with contralateral adrenal and extra-adrenal mass in the contralateral adrenal gland out of non-operated patients with neuroblastoma. **Materials and Methods:** 51 MIBG scans of 33 patients (18 males, 15 females; age range 7 months - 17 years) were included in this study. Prior to scintigraphy all patients were supplied with potassium perchlorate p.o. (600 mg/m²) for sufficient duration. Images were recorded as follows: for I-131 MIBG scan by 24h and by 48 hour by means of HEGP collimators as the whole body and static, after intravenous administration of 0.5-1.0 mCi /1.7 m² body surface area (~7 µCi/kg to 15 µCi/kg); for I-123 LEHR collimators by 4h and by 24hours as the whole body, static, and SPECT, after intravenous administration of 10 mCi/1.7 m² body surface area (~150 µCi/kg, maximum 10 mCi). Scintigraphic findings were compared with those of CT, and USG. **Findings:** A total of 21 MIBG studies were performed in 12 patients undergoing unilateral adrenalectomy. Uptake suggesting hyperplasia was observed in the contralateral adrenal glands in 10 MIBG studies of six of these 12 patients. Hyperplasia was radiologically confirmed in 5 of the six patients. The adrenal gland of one patient was evaluated as normal. No uptake was observed in 4 MIBG scans of the contralateral adrenal glands of the 4 patients with adrenal masses who were not operated. The physiologic MIBG uptakes were observed in 5 MIBG scan of the bilateral adrenal glands when 26 MIBG scans of 17 patients with extra-adrenal masses were assessed. **Conclusion:** In patients following unilateral adrenalectomy for neuroblastoma the MIBG scans of contralateral adrenal glands show uptake suggestive of hyperplasia. To eliminate false-positive findings, correlation with radiologic methods is preferred.

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Diagnosis of Acute Osteomyelitis in Children: Bone Scintigraphy vs. MRI

I. Slim¹, I. Yeddes¹, I. Ei Bez¹, W. Ei Ajmi¹, B. Letaief¹, A. Mhiri¹, M. Ben Ghachem², F. Ben Slimene¹; ¹Nuclear Medicine Department, Salah Azaiez Institute, Tunis, TUNISIA, ²Department of Paediatric Orthopaedics, Tunis Children's Hospital, Tunis, TUNISIA.

Introduction: Acute hematogenous osteomyelitis (AHO) is a common pediatric problem. Early diagnosis and treatment helps prevent complications. Unfortunately, diagnosis can be difficult. The aim of this study was to evaluate and compare diagnostic accuracy of plain x ray, bone scintigraphy and magnetic resonance imaging (MRI) in pediatric AHO. **MATERIALS AND METHODS:** During the period of 2006-2008, 1-16 year old patients with suspected AHO (with non violated bone) admitted to the Department of Orthopedic Surgery, Children's Hospital of Tunis, were included in this prospective study. Three-phase bone scintigraphy using Tc99m-HMDP was performed, in our department, within 48h of hospitalization. Plain x-ray, and MRI were also performed. The diagnosis made by the referring physicians after their evaluation of clinical, laboratory, and imaging findings was used as the final diagnosis. **RESULTS:** During the study period, 41 children were included. AHO was diagnosed in 22 (14 boys and 8 girls with a mean age of 7.85 years). All patients underwent conventional radiography and bone scintigraphy. MRI was performed in 20 children at a mean period of 1 day after the bone scan. The sensitivity of Plain x-ray for diagnosing AHO was 9.1%. The Sensitivity, specificity and negative predictive value of bone scintigraphy (focally increased uptake in all three phases) were 86%, 100% and 86%, respectively. When the diagnosis of osteomyelitis was also retained if a diffuse and intense bone uptake on the delayed images was associated with focal hyperemia in the early two phases, the sensitivity of bone scintigraphy increase to 95% without false positive scans. The sensitivity of MRI for diagnosing AHO was 89% (16/18). There were no significant differences in sensitivity between MRI and bone scintigraphy. The results of skeletal scintigraphy and MRI were concordant for 90% of the patients. **CONCLUSION:** According to our study, three-phase bone scintigraphy should be the first test to perform when AHO is suspected after negative radiography results. MRI will be useful in selected patients.

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Gated myocardial perfusion scintigraphy in children with sickle cell anemia: clinical relevance and correlation with echocardiography

E. Ceylan Gunay¹, O. Hallioglu², S. Unal², A. Erdogan¹, S. Balci², D. Citirik²;
¹Mersin University Faculty of Medicine Department of Nuclear Medicine, Mersin, TURKEY, ²Mersin University Faculty of Medicine Department of Pediatrics, Mersin, TURKEY.

Aim: Cardiac involvement in children with Sickle cell anemia is one of the serious complications of the disease. Although myocardial ischemia is not a major complication, early recognition of cardiac involvement is important to prevent potential serious damages. The aim of this prospective study was to assess myocardial perfusion and left ventricular function with Tc^{99m}-MIBI Gated myocardial perfusion SPECT, and compare the results with echocardiographic measurements and clinical data of children with sickle cell disease. **Material-Methods:** We prospectively evaluated 43 children (15 female, 28 male) with the diagnosis of sickle cell disease, aged between 4-18 years old (median age:11) between February 2007-April 2009. The exclusion criteria were sickle-cell crisis within the 3 month previous to entry in the study, thalassemia or presence of other cardiac problems or chronic disease. Tc^{99m}-MIBI gated myocardial perfusion SPECT was performed after pharmacological stress testing by using dipyridamol. The rest study was omitted if stress myocardial perfusion was interpreted as normal. The reconstructed images

were evaluated visually as well as semiquantitatively by the software programs (QPS and QGS). Besides myocardial perfusion data, left ventricular (LV) wall motion and thickening has also been evaluated. LV end-diastolic volume (EDV), end-systolic volume (ESV), ejection fraction (EF) parameters were calculated. LV function was also evaluated by M-mode echocardiography; LV end-diastolic diameter (LVDD), end-systolic diameter (LVESD) and EF were recorded. Results of radionuclide studies were compared with echocardiographic and clinical data. **Results:** None of the patients showed stress perfusion impairment in myocardial perfusion scintigraphy. However, LV dilatation in 12 patients, septal hypokinesia in 3 patients, and anterolateral hypokinesia in 1 patient has been observed. Echocardiographic LV enlargement was present in 15 patients. LV dilatation detected by both methods were correlated with each other (p = 0.010). Although correlation between EF values calculated by QGS and M mode were not statistically significant, EDV and ESV values were correlated to LVDD and LVESD values, respectively (p<0.05). There was also significant relationship between LV dilatation and frequent blood transfusions (>5/years) and acute chest syndrome (p<0.05). **Conclusions:** Gated myocardial perfusion SPECT seems to be a useful tool in follow-up of patients with sickle cell disease. Particularly, LV dilatation should be considered as a significant parameter other than EF or perfusion data.

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Pediatric diagnostic procedures in Brazil: the need of optimization of radiopharmaceuticals activities

S. M. V. D. Oliveira, F. S. Santos; Institute of Radiation Protection and Dosimetry, Rio de Janeiro, BRAZIL.

In Brazil, the incidence of pediatric cancer is about 3% of the total. For 2010, they are expected ten thousand new cases of cancer in children and teen-agers behind 18 years. Recent studies recommended new criteria to determine radiopharmaceuticals activities per diagnostic procedures for children and teenagers because the reduction of maximum activities minimizes the probability of detriment of radiation. In Brazil, an investigation evaluated radiopharmaceuticals activities in sixteen institutions. Homogeneity of independent samples was evaluated by T test for and Pearson correlation for "activity" as independent variable and the others as dependent with SPSS v10.0. The cohort was formed by 2,411 children (1,286 male and 992 female). Individual weight was registered in 257 patients and patient corporal mass ranged between 8.0 kg and 75.0 kg, varying between 8.0 kg and 22.0 kg (n=46) for one year, 13.5 kg and 24.0 kg (n=74) for 5 years, 26.5 kg and 55.7 kg (n=69) for 10 years and 29.3 kg and 75.0 kg (n=40) for 15 years. The most frequent procedures were: bone scintigraphy with ^{99m}Tc MDP (37%); renal studies with ^{99m}Tc DMSA and ^{99m}Tc DTPA (18%), ⁶⁷Ga citrate scintigraphy (12%) and lung perfusion with ^{99m}Tc MAA (9%). The minimum activities used were compared with those recommended according Pediatric Dosage Card (PDC) methodology, taking into account the individual corporal masses. Nevertheless, the lack on registry of patient corporal mass constitutes a strong difficulty to implement the PDC in Brazil. The ranges of minimum activities are substantially more variable than those for maximum activity or activity per corporal mass, since these other parameters are based on values prescribed for adults and minimum activities are defined only for pediatric nuclear medicine. Considering the high activities used, the absorbed doses in bone surfaces of children due to ⁶⁷Ga citrate and ^{99m}Tc MDP should be evaluated. It was observed that the activities were not standardized and were higher for children with younger ages. Thus, the effective doses may be optimized accordingly. Despite the fact that radiation risks for children and teenagers should be estimated and it is necessary to establish standard criteria for radiopharmaceuticals activities, there were difficulties to improve this research. The PDC implementation, for instance, needs the collaboration of the nuclear medicine and pediatric professional staff in order to plan optimized protocols for pediatric patients.

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The role of dynamic renal scintigraphy and indirect radionuclide cystography with mercaptoacetyltriglycine in detection of vesicoureteral reflux and evaluation of renal parenchymal lesions

Z. Erdogan¹, U. Abdulrezzak¹, M. Kula¹, H. Poyrazoglu², A. Yikilmaz³, A. Tutus¹; ¹Erciyes University, School of Medicine, Department of Nuclear Medicine, Kayseri, TURKEY, ²Erciyes University, School of Medicine, Department of Pediatrics, Kayseri, TURKEY, ³Erciyes University, School of Medicine, Department of Radiology, Kayseri, TURKEY.

Objective: Timely detection of VUR and reflux nephropathy (RN) is considered to be a crucial step, since RN is an important cause of hypertension and renal failure. The aim of this study was compare of indirect radionuclide cystourethrography (IRC) performed with mercaptoacetyltriglycine (MAG3) and fluoroscopic cystourethrography (FC) for the diagnosis of VUR. In addition, we also aimed to oppose the parenchymal phase of MAG3 renal scintigraphy and DMSA scintigraphy for detection of renal parenchymal defects and in the estimation of DRF with standard criterions. **Materials and methods:** Total 141 renal units of 71 children were studied sequentially using IRC and FC. Additionally, we evaluated total 135 renal units of 68 patients who had MAG3 and DMSA scintigraphy. A 9-point semiquantitative analysis of each kidney was performed. Each kidney was divided in thirds graded from 0 (normal uptake) to 3 (no uptake). The scintigrams were also graded according to the severity of the abnormality using a modified system of Goldraich. Grade 0: Normal or nearly normal (score 0-1); Grade 1: no more than two focal/relative decreased activity sides and/or single renal scar (score 2-3); Grade 2: two or more renal scars but remnant areas of normal renal parenchyma and normal sized kidney (score 4-5); Grade 3: reduction in uptake of DMSA/MAG3 throughout the whole kidney with or without multiple renal scars (score 6-7) and Grade 4: shrunken kidney or margins of kidney were indistinct (score 8-9). **Results:** VUR was diagnosed by FC in 48 renal units (34%) in 36 patients (50.7%). Both studies showed VUR in 39 renal units. When FC considered the reference method, sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of IRC were calculated as 81.2%, 76.3%, 78%, 63.9% and 88.7%, respectively. There was no significant difference between the two methods in detection of VUR (p > 0.05). In the estimation of DRF, there was a high correlation between two methods (r= 0.986). The sensitivity, specificity, accuracy, PPV and NPV of the Tc-99m MAG3 cortical images for detecting renal lesions were calculated as 92.6%, 96.8%, 95.5%, 92.6% and 96.8%, respectively. There was a high correlation between two scintigraphic studies for detecting renal parenchymal scars (kappa = 0.895). **Conclusion:** Being single imaging modality with lowering the radiation exposure, dynamic renal

scan with IRC by MAG3 scintigraphy can provide simultaneous information of kidney's perfusion, concentration, drainage, parenchymal and split functions and evaluation of VUR.

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Testicular viability and fertility follow-up study in torsion correction surgery adolescent patients

M. Vljakovic¹, M. Rajic¹, M. Stevic¹, A. Slavkovic¹, V. Zivkovic¹, M. Matovic², V. Artiko³; ¹Clinical center Nis, Nis, SERBIA, ²Clinical center Kragujevac, Kragujevac, SERBIA, ³Clinical center of Serbia, Belgrade, SERBIA.

Aim of the study: The aim of this study was to investigate both testicular viability by means of scrotal scintigraphy, and endocrine function by hormonal analysis in children and adolescents long time after the treatment of torsion either by orchiectomy or orchiopexy. **Material and methods:** Study enrolled 14 boys aged 6-27 years treated for testicular torsion, 6 of whom were treated with orchiectomy and 8 with surgical detorsion and orchiopexy. The late follow up was conducted 1-12 years (5.4±3.7 yr) following the treatment of testicular torsion to analyse testicular viability and fertility potential by means of colour-Doppler ultrasound (CDU) and radionuclide scrotal scintigraphy (RSS), which was performed on the same day. Before RSS, blood was taken from all patients for testosterone measurement and follicle-stimulating hormone (FSH) tests. Two-phase RSS was performed using small field of view gamma camera "Siemens" equipped with pinhole collimator. Angioscintigraphy was started after bolus injection of 99mTc-pertechnetate (370MBq), collecting two-second frames over 1 minute. Static scrotal scintigraphy was performed following angioscintigraphy by collecting five-minute images. **Results:** High correlation was found between the results of CDU and RSS on the treated side in 12 patients, observed as the absence of perfusion in 6, normal perfusion in 4 and reduced perfusion in 2 patients (R 0.920, p<0.001). In one child the absence of testicular blood flow on CDU was found, as well as reduced perfusion on RSS, and in another one, with reduced perfusion on CDU, a normal finding was detected on RSS. Reduced perfusion on the contralateral side in orchiopexy group was detected in 3 patients by means of RSS, and in two patients by means of CDU, while the contralateral testes obtained by both methods came back normal in orchiectomy group. Abnormal serum FSH values were detected in 3/8 (38%) patients after testicular preserving surgery and in 2/6 (33%) patients following orchiectomy. The testosterone levels were within normal values in 7/8 (87%) children after orchiopexy and in 4/6 (67%) children after orchiectomy. **Conclusion:** Our results demonstrated that radionuclide scrotal scintigraphy represents an accurate method for the assessment of testicular viability following torsion correction surgery. Long term follow-up results suggest that preserving surgery might be harmful not only for the affected testicle but even more to the contralateral testicle. However, according to FSH analyses fertility was found to be impaired in children after either orchiectomy or orchiopexy.

P58 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized Nuclear Medicine: Urology

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Comparative study of dynamic renal scintigraphy and conventional ultrasonography for the diagnosis of hydronephrosis as a complication of nephro- and urolithiasis

V. H. Hadzhiyska¹, T. Petrov², I. Kostadinova³, R. Krasteva⁴, V. Marianovski⁵, V. Stojnova⁶; ¹Clinic of nuclear medicine, University hospital, Sofia, BULGARIA, ²Clinic of Nuclear Medicine, Medical University, Sofia, BULGARIA, ³Clinic of nuclear medicine, University hospital, Sofia, BULGARIA, ⁴Clinic of Nephrology, Medical University, Sofia, BULGARIA, ⁵Sofia, BULGARIA, ⁶Clinic of urology, Pirogov Emergency Hospital, Sofia, BULGARIA, ⁷Computed Tomography Dept., University hospital "St.Ekaterina", Sofia, BULGARIA.

The aim of the study was to compare the possibilities of the dynamic renal scintigraphy (DRS) and the conventional ultrasonography (US) for the diagnosis of hydronephrosis as a complication of lithiasis. Forty-six patients (21 male, 26 female) aged between 13 and 85 years, with 92 kidneys, and suspected unilateral or bilateral hydronephrosis and proved lithiasis were studied. All of them first underwent US and then, during the two consecutive days, DRS with 99mTc-DTPA (255 MBq). A diuretic test with furosemide, administrated 15 min. after the radiopharmaceutical injection was performed in 24 (52%) of the patients with an accumulation renographic curve (in 48 kidneys). The final diagnosis was proved with surgery or with a clinical follow up of the patients. In 55 (60%) of the kidneys a pathological result was found in one or in both of the tests. We have estimated that the results of DRS and US were corresponding in 30/55 (72%) of the kidneys, but in 14 (26%) of them DRS gave more detail information concerning the degree and duration of the pathological changes through interpreting the renographic curve. In the rest of the kidneys 16/55 (28%) the results from DRS and US were not corresponding. The false positive or negative findings in DRS were respectively 10 (11%) and 0 (0%) (sensitivity - 100%, specificity - 84%, accuracy - 89%). The false positive or negative findings in US were respectively in 8 (9%) and in 13 (14%) of the kidneys (sensitivity - 66%, specificity - 85%, accuracy - 76%). The reasons for the false positive results in DRS were: diuretic intake during the days before examination or insufficient hydration. The false positive results in US were due to parapelvic cysts, extrarenal pelvis and the false negative results were due to - parapelvic cysts, intermittent obstruction, low urine volume, acute obstruction without dilatation. The diuretic test showed: nonobstructive nephropathy in 31 of the kidneys (64%), an obstructive nephropathy - in 12 (25%), and intermediate reaction - in 5 (11%) of the kidneys. We could conclude, that DRS is a more accurate method than US for the diagnosis of hydronephrosis as a complication of nephro- and urolithiasis, but their combine application give complex information concerning function, morphology of the kidneys and determine the therapeutic approach. **Key words:** Dynamic renal scintigraphy, Ultrasound, Hydronephrosis, Nephrolithiasis

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Scintigraphic assessment of kidney grafts with double renal arteries

E. A. Gencoglu¹, A. Cinar¹, T. Bahceci¹, G. Yaman¹, K. Kavak¹, A. Aktas¹, M. Haberal²; ¹Baskent University Medical Faculty, Department of Nuclear Medicine, Ankara, TURKEY, ²Baskent University Medical Faculty, Department of Surgery, Ankara, TURKEY.

Aim: The aims of this study were to assess the perfusion and function of kidney grafts with double renal arteries and to evaluate the effects of different vascular anastomotic techniques on the grafts in the early post-transplantation period using Tc-99m DTPA scintigraphy. **Materials and Methods:** Thirty living-related kidney transplant recipients were studied (18 men, 12 women of overall mean age 29.77 ± 13.81 years). In these cases, all kidney grafts had double renal arteries. In 15 recipients (Group I), double renal arteries of grafts were converted to a single arterial vessel and then a single iliac vascular anastomosis was performed. In the other 15 recipients (Group II), double renal arteries of grafts were implanted with double arterial anastomoses to the iliac artery. In all patients, Tc-99m DTPA renal scintigraphy was performed at 7 days after the transplantation. Anterior dynamic imaging was performed immediately after intravenous injection of 3.7 MBq/kg of Tc-99m DTPA using gamma camera. To test graft perfusion data were recorded every one second for one minute, to evaluate graft function, data were recorded every 30 seconds for 20 minutes. The images were evaluated visually and quantitatively. The upper and lower half of grafts were assessed separately because they were supplied by 2 different renal arteries. **Results:** In 13/15 recipients of Group I, perfusion, extraction and excretion of the upper and lower half of kidney grafts were completely normal. However, in 2/15 cases of this group, perfusion and function parameters were lower than the normal limits in both half of grafts. In 12/15 recipients of Group II, both of the upper and lower half of grafts had normal perfusion and function. However, in 3/15 patients of this group, perfusion, extraction and excretion were abnormal in both half of grafts. When the graft biopsy was performed, acute rejection was found in all grafts that showed abnormal scintigraphic findings in both Group I and Group II. It is concluded that scintigraphic findings and dysfunction rates of kidney grafts with double renal arteries with single vascular anastomosis are similar to those of grafts with double renal arteries with double vascular anastomoses in the early post-transplantation period. This study also showed that Tc-99m DTPA scintigraphy, which is a noninvasive, quantitative, sensitive and objective method, is useful to assess kidney grafts with multiple renal arteries.

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Predictive values of pre-operative 99mTc-MAG3 and 51Cr-EDTA-GFR in the surgical outcome of cystectomy and urinary diversion for bladder cancer

L. I. Sonoda, M. Halim, K. Balan; University of Cambridge, Cambridge, UNITED KINGDOM.

Purpose: The importance of monitoring renal function in patients undergoing cystectomy and urinary diversion has been well documented. The aim of this study was to examine the usefulness of pre-operative 99mTc-MAG3 and 51Cr-EDTA GFR for predicting renal function in patients following cystectomy and urinary diversion for cancer. **Methods and Materials:** A retrospective electronic data analysis of 57 patients who underwent cystectomy with ileal conduit urinary diversion for cancer during a 7-year-period was performed. Results of pre and post-operative MAG3, GFR, serum urea and creatinine were obtained and statistically analysed. The patients were divided into stable and deteriorating groups based on their renal function post-operatively for up to 4 years. **Results:** There was no statistically significant difference in renal function assessed by MAG3 and GFR between pre-operative and immediate-post-operative studies. Similarly, there was no significant difference in pre-operative MAG3 and GFR results between patients with stable and deteriorating renal function. A single pre-operative or immediate-post-operative MAG3 scan was unable to predict long-term renal function. **Conclusion:** Our results confirm the usefulness of 99mTc-MAG3 and 51Cr-EDTA-GFR examinations in monitoring renal function following cystectomy and urinary diversion for cancer. The findings however do not justify the need to do a pre-operative MAG3 or GFR since either seem unable to predict post-operative renal outcome.

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Radionuclide renoscintigraphy in evaluation of renal function in children before and after radiocontrast angiography

Z. V. Vesnina, V. I. Varvarenko, Y. B. Lishmanov; Institute of cardiology, Tomsk, RUSSIAN FEDERATION.

Aim. Using radionuclide renoscintigraphy to evaluate the extent and character of contrast-induced renal dysfunction in children undergoing contrast angiography. **Material and methods.** Radionuclide renoscintigraphy with 99mTc-DTPA was used to examine fifteen patients with congenital heart disease (average age 7,8 ± 0,8 years) before and 48 hours after angiography. Iobitridole (2,0 ± 0,2 ml/kg) was used as radiocontrast. Filtration and excretory renal functions, including glomerular filtration rate (GFR), blood clearance, parenchymal and collecting system clearance half-time were estimated. **Results.** After angiography the average values of both total GFR and separate GFR of left and right kidney were insignificantly changed. Meanwhile the decrease of GFR under the influence of contrast media was marked only in 5 patients (33%). At the same time we observed significant increase of radiopharmaceutical clearance half-time from renal collecting system and cortical delay index of both kidneys and left kidney renal parenchyma clearance half-time. **Conclusion.** We found that contrast-induced renal dysfunction, which occurred in children after angiography, was limited by moderate degree disturbance of excretory renal function.

P654

Comparison of accuracy and precision of two methods of GFR determination.

M. J. Surma; Medical University of Lodz, Lodz, POLAND.

Two-sample procedure for GFR determination, elaborated by Russell et al., is more commonly used. The method was modified in our Department - the modification depending on widening the time period ranges, in which the blood samples should be withdrawn: first from 45 to 60 min and the second from 150 min to 180 min post injection. The aim of study: To analyze the accuracy and precision of the simplified two-samples method and to compare its characteristics with analogous multisample procedure. Methods. To estimate accuracy and precision the repeated determinations of GFR were performed using the simulated results of ^{99m}Tc -DTPA plasma concentration, based on typical, theoretically true course of blood clearing process and true activity injected to the patient (Ap). This assumption allowed to calculate the true plasma concentrations at defined moments of blood sampling. To these obtained values the stochastic numbers, from Gaussian random generator, were added. Obtained sums gave the simulated results of plasma concentrations. Similarly, the activity injected in to a patient was calculated by adding the stochastic error value to the assumed true Ap. For each assumed value of clearing process and Ap the GFR determination was repeated 5000 times. Each obtained GFR allowed to compute average value and standard deviation of the results. The study was performed for GFR from 6ml/min to 180ml/min. Results. When the GFR was determined using multisample procedure the maximum difference between the true GFR and average determined GFR was less than 5ml/min for the whole range of studied GFR. Such value of the systematic error may be assessed as negligible, and the multisample method as accurate. Analogous difference obtained for a simplified two samples procedure is greater and it reached 7ml/min. These difference suggests, that the accuracy of simplified two-sample method is satisfactory. Precision of each studied method depends on absolute GFR value. Precision of the multisample method varies from 17% at $\text{GFR} \leq 12 \text{ ml/min}$ to 2% at $\text{GFR} > 90 \text{ ml/min}$. Precision of the simplified method is comparable and varies from 20% at $\text{GFR} < 15 \text{ ml/min}$ to 4% at 100 ml/min and to 3% at $\text{GFR} > 150 \text{ ml/min}$. Conclusion. The accuracy and precision of multisample GFR determination are fully satisfactory and should be proposed for follow-up examinations. Accuracy and precision of two-sample method are similarly satisfactory, and they can be recommended for follow up examinations but also as the method of choice to use in children.

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Determination of Kidney Function with ^{99m}Tc -DTPA-Renography on Dual Head Camera

C. J. Madsen¹, B. Zerahn¹, M. L. Møller², J. J. Jensen³; ¹Department of Clinical Physiology and Nuclear Medicine, Herlev Hospital, University of Copenhagen, DENMARK, ²Department of Clinical Physiology and Nuclear Medicine, Frederiksberg Hospital, University of Copenhagen, DENMARK, ³Department of Nuclear Medicine, Herning Hospital, DENMARK.

Introduction Difference in kidney depths causes incorrect estimation of absolute and relative kidney function in single head camera renography. Dual head renography eliminates this error, but may introduce a poorer signal to noise ratio when estimating glomerular filtration rate (GFR). This may be partly compensated by using counts from the left ventricle in anterior projection instead of the traditional posterior projection. This study compares single versus dual head camera estimation of GFR using ^{99m}Tc -diethylenetriaminepentaacetic acid (^{99m}Tc -DTPA). **Material & methods** Thirty-four patients were examined with 1) single head renography acquiring counts from heart and kidneys from posterior projection and simultaneously with 2) dual head renography acquiring counts from heart from anterior projection and kidneys from both anterior and posterior projection using geometric mean value. An approximation of single kidney GFR from both models was estimated (GFRcam1 and GFRcam2 respectively) and compared to GFR determined with plasma samples of ^{99m}Tc -DTPA (GFRps). Variance and coefficient of variation (CV) of the two methods was calculated and compared. **Results** The absolute variance of GFRcam1-GFRps and GFRcam2-GFRps increased with increasing GFR. There was no significant difference of variance of GFR estimated from the two camera models compared to GFRps (CV of GFRcam1-GFRps = 16.5 % and CV of GFR2-GFRps 14.7 %, $P = 0.48$). **Conclusion** The variance of GFR estimated from dual head camera renography does not differ from the traditional single head camera method. The dual head method can be used in all patients and the main benefit is probably achieved in patients with difference in kidney depth.

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The precision of Cockcroft-Gault formula for estimation of glomerular filtration rate in acute renal failure in comparison with double plasma sample method using Tc-99m DTPA

A. Emami-Ardekani¹, B. Fallahi¹, M. Amini², D. Beiki¹, A. Fard-Esfahani¹, M. Eftekhari¹, M. Saghari¹; ¹Research Institute for Nuclear Medicine, Tehran University of Medical Sciences, Tehran, IRAN, ISLAMIC REPUBLIC OF, ²Department of Nephrology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, IRAN, ISLAMIC REPUBLIC OF.

Aims: Diagnosis and follow-up of chronic renal disease are based on the glomerular filtration rate (GFR) which is currently estimated from the standardized formulas; however the precision of estimation based on plasma creatinine level via the routine methods such as Cockcroft formula for diagnosis, follow-up and management of patients with acute renal failure (ARF) especially for the vast majority of cases with acute tubular necrosis (ATN) is under question. The goal of this study was to compare the real GFR values measured on double plasma sample method (DPSM) with the estimated GFR based on Cockcroft-Gault formula in two separate groups of patients with ATN and acute glomerulonephritis (AGN). **Materials and Methods:** Twenty-one patients with ARF (11 cases with ATN and 10 with AGN) were included in the study. After measuring plasma creatinine level for each case, GFR was estimated based on Cockcroft-Gault formula. At the same time, 18 MBq Tc-99m DTPA was intravenously injected and real GFR was measured using double plasma sample method (DPSM). The values of measured GFR (via DPSM) and estimated GFR (via Cockcroft-Gault formula) were compared in each group. **Results:** 21 patients with ARF (mean age: 44.76±19.49; 21 - 95 yrs) were studied. 14 cases (66.7%) were female and 7 (33.3%) were male. There was no significant difference between, age ($p=0.341$), weight ($p=0.169$), sex ($p=0.183$) and plasma creatinine level ($p=0.459$) between 2 groups. In the group with ATN, a significant difference was noted between measured GFR ($31.9 \pm 15.04 \text{ ml/min}$) and estimated GFR ($16.57 \pm 12.45 \text{ ml/min}$; $p=0.010$). There was no linear relationship between two methods ($r=0.464$, $p=0.151$). Also, in another group with AGN, the measured GFR with DPSM ($34.07 \pm 15.05 \text{ ml/min}$) and estimated GFR with formula ($16.31 \pm 7.08 \text{ ml/min}$) were significantly different ($p=0.009$) and

the estimated values were not significantly correlated with the measured values ($r=0.349$, $p=0.260$). There was no significant difference between ΔGFR (calculated GFR based on DPSM minus estimated GFR based on Cockcroft formula) in ATN ($15.34 \pm 14.44 \text{ ml/min}$; median=15.8, min=-6.74, max=35.83) and AGN groups ($17.75 \pm 13.08 \text{ ml/min}$; median=18.93, min=-2, max=31.34; $p=0.637$). **Conclusion:** It appears that the function of the kidneys in the case of ARF may be underestimated when GFR is calculated via the routine Cockcroft-Gault formula. GFR should be measured using a reliable method such as DPSM in any case of ARF in which the precision of the Cockcroft-Gault formula is insufficient especially when a clinical decision-making for urgent haemodialysis is considered.

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Exploration strategy of primitive congenital megauretere

R. Sfar, M. Ben Fredj, K. Chatti, M. Guezguez, W. El Ajmi, M. Noura, K. Ben Ali, H. Essabbah; Sahloul Sousse Tunisia, SOUSSE, TUNISIA.

Aim: Antenatal diagnosis of megauretere (MU) keeps pediatricians and pediatric surgeons in front of the question of their management. Abusive treatments and treatment delay should be avoided. The purpose of this presentation is to study the performance of primitive MU scintigraphic explorations and to propose a strategy of explorations for the management of primitive MU in children. **Materials and methods:** It's a retrospective study including 25 children with primitive megauretere referred for renal scintigraphy to Sahloul hospital Tunisia between 2001 and 2006. For each case, we recorded epidemiologic and clinico-biologic data, imaging explorations and therapeutic protocols. **Results:** All patients had a biological and bacteriological assessment, echography and cystography. Twenty patients have had IVU. These investigations established the diagnosis of reflux primitive MU or not reflux. Dynamic renal scintigraphy was performed in 24 cases. It differentiated between obstructive and not obstructive primitive MU and evaluated renal function. Cortical scintigraphy had been done in 7 cases to evaluate relative renal function and to seek scar lesion. We found 33 MU divided in 14 not obstructive not refluxant MU, 5 not obstructive refluxant MU, 9 obstructive not refluxant MU and 5 obstructive refluxant MU. Sixteen patients underwent surgery. In the follow up by dynamic scintigraphy, isotopic cystography and echography, we detected complications after surgery especially vesico-ureteral reflux. Nine patients with non refluxant MU had a medical follow up. Two patients underwent surgery because of deterioration of renal function. **Conclusion:** Congenital primitive MU is a disease which may engage renal function prognosis. Echography, cystography and isotopic assessment are essential for diagnosis and follow up. IVU should not to be systematic. Functional prognosis is generally good. Cortical renal scintigraphy is necessary for the follow up of refluxant MU because of the risk of scar lesion occurrence.

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Renal Hemodynamic Response to Losartan Treatment is Partly Influenced by the Angiotensin II Type 1 Receptor Gene Polymorphism

B. Ajdinovic¹, T. Dragovic², Z. Magic³, Z. Andjelkovic²; ¹Institute of Nuclear Medicine, Military Medical Academy, Belgrade, SERBIA, ²Clinic of Endocrinology, MMA, Belgrade, SERBIA, ³Institute for Medical Research, MAA, Belgrade, SERBIA.

Introduction. The aim of our study was to examine, if the individual hemodynamic response to short-term losartan therapy, is depending on 1166 A/C polymorphism gene for its target receptor. **Method.** Thirty five patients with type 1 diabetes mellitus and persistent albuminuria, were genotyped for the 1166 A/C polymorphism gene for the angiotensin II type 1 receptor (AT1R). Participants were segregated into groups, according to combinations of A or C allele: AA(43%), AC(46%), CC(11%). Patients received losartan therapy for 12 weeks. At baseline and after the examination period glomerular filtration rate (GFR), filtration fraction (FF), effective renal plasma flow (ERPF), effective renal blood flow (ERBF) and total renal vascular resistances (RVR) were determined. **Results.** Losartan therapy significantly reduced filtration fraction from baseline by $0,018 \pm 0,024$ ($p=0,012$) only in the AC genotype. Significant increase in effective renal plasma flow was obtained only in the AC genotype (544 ± 88 vs $575 \pm 90 \text{ ml/min}$; $p=0,02$), while significant reduction in renal vascular resistance were found in the AA genotype (115 ± 25 vs $95 \pm 21 \text{ mmHg} \times 1^{-1} \times \text{min}^{-1}$; $p=0,001$) and in the AC genotype (118 ± 30 vs $101 \pm 28 \text{ mmHg} \times 1^{-1} \times \text{min}^{-1}$; $p=0,001$). Reduction of renal vascular resistance in the CC genotype was weak ($p=0,061$). Glomerular filtration rate remained unchanged in all genotype groups and independent of the 1166 A/C gene polymorphism. **Conclusion.** Our study shows that individual renal vascular response to losartan treatment in diabetic patients with nephropathy is partly influenced by AT1R gene polymorphism. Although based on a small number of participants, our results could provide rational basis for future longitudinal pharmacogenetic examinations.

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A comparison of the determination of glomerular filtration rate by 51-Cr-EDTA bicompartmental method, Bröchner-Mortensen method and predictive equations in kidney donors and transplanted patients

J. M. Calero, L. Sanz-Ceballos, A. Ramirez-Navarro, J. M. Llamas-Elvira; H. U. Virgen de las Nieves, Granada, SPAIN.

INTRODUCTION: Determination of glomerular filtration rate normalized (GFR_n) by radioisotopic methods is a reliable and accurate measure. The use of predictive equations is based on serum creatinine and other factors. The MDRD (Modification of Diet in Renal Disease) and Cockcroft-Gault equations are used in renal disease management. **OBJECTIVES:** To determine the correlation and test clinical agreement with the stages described by the *Kidney Disease Outcomes Quality Initiative*, the values of the standard GFR_n obtained with the ^{51}Cr -EDTA bicompartmental clearance method are compared against the values obtained with Bröchner Mortensen method, MDRD and Cockcroft-Gault equations. **MATERIAL AND METHODS:** 217 Patients: 190 patients with renal transplants and 27 kidney donors who GFR_n were determined by the ^{51}Cr -EDTA bicompartmental clearance (six samples) method and applying Bröchner Mortensen method, MDRD and Cockcroft-Gault equations. **Descriptive statistics of GFR_n 's values obtained by the different used methods were compared calculating the Pearson correlation coefficient (r) and**

Faculty, Department of Nuclear Medicine, Elazig, TURKEY, ³Training Hospital, Department of Nuclear Medicine, Elazig, TURKEY.

Aim: Renal scintigraphies have privilege in imaging methods because of its property of providing functional information. They are repeatable and high sensitivity methods for the follow-up of the patients and to determine alterations of renal functions. Differential renal function is a quantitative measurement of renal cortical uptake scintigraphically. Tc-99m DMSA which is used to image renal parenchyma, is the best radiopharmaceutical for the measurement of differential renal function. This measurement could also be done using radiopharmaceuticals which are for dynamic renal scintigraphy. In this study, we aim to compare Tc-99m DTPA and Tc-99m MAG-3 which are the agents of dynamic renal scintigraphy by means of the measurement of differential renal function based on Tc-99m DMSA. **Materials & Method:** We performed Tc-99m DTPA and Tc-99m DMSA scintigraphy to 57 patients (23 female, 34 male) and Tc-99m MAG-3 and Tc-99m DMSA scintigraphy to 30 patients (15 female, 15 male). The average age of the patients whose performed Tc-99m DTPA scanning and Tc-99m MAG-3 scanning were 18,8 (range: 3 month-60 age) and 15,7 (range: 3 month-59 age) respectively. Differential renal functions which were calculated with Tc-99m DTPA and Tc-99m MAG-3 were compared with Tc-99m DMSA by using correlation and regression analysis. **Results:** Tc-99m DTPA was found very concordant with Tc-99m DMSA ($p = 0,968$, $R^2 = 0,94$). Tc-99m MAG-3 and Tc-99m DMSA were found nearly exactly concordant with each other ($p = 0,989$, $R^2 = 0,98$). **Conclusion:** Although DMSA is accepted as the most reliable radiopharmaceutical for the determination of differential renal function, DTPA or MAG-3 dynamic renal scanning has reliable results as well. In addition to differential function, we learn about renal dynamics with the use of these two agents. MAG-3 may be preferable to DTPA because of its characteristic of showing the renal parenchyma better than DTPA.

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Role of renal scintigraphy in patients with duplex kidneys/systems :In management and monitoring

K. Manohar, R. Senthil, R. Kashyap, A. Bhattacharya, B. Singh, B. R. Mittal; PGIMER, Chandigarh, INDIA.

Introduction: Duplex kidneys are one of the rare urinary tract anomalies prone to complications like ureteropelvic obstruction, ureteroceles, vesicoureteral reflux and frequent urinary tract infections. Diagnosis of duplex systems is mainly by radiological techniques like urography. Scintigraphy is useful in accurate estimation of functional status of affected kidneys and for monitoring of these patients during follow up. **Aim:** Present study was carried to assess the role of renal scintigraphy in management of patients with duplex systems. **Materials and Methods:** Retrospective analysis of medical records of renal scintigraphy performed during the past 4 years was done. Out of 3530 cases, 27 (0.7%) patients were found to have duplex systems/kidneys. Scintigraphy was done as per predefined protocol using Tc99m-DTPA or Tc99m-Ec with measurement of T_{1/2}, relative functional (RF) of each moiety. Each patient also underwent Tc99m-dimercaptosuccinic acid renal cortical scan for evaluation of scars. Follow up scans were done in 15 patients. **Results:** Of the 27 patients, 4 had bilateral duplex systems/kidneys, 14 had left sided duplex kidney and 9 had right duplex kidney. Scintigraphically evidence of duplex system was not evident in 8/27 patients of whom 7 patients had only duplication of ureters on urography suggesting partial duplication. Hydronephrosis was the most common anomaly detected (23/27). Hydronephrosis was observed in 16 upper moieties and in 7 lower moieties. Analysis of T_{1/2} revealed obstruction in 7(25%) patients and equivocal drainage in 9 (33%) patients and unobstructed drainage in remaining 11 (42%). Four of the patients with obstructed drainage underwent surgery to improve drainage which on subsequent follow up scans showed improvement in drainage in all and function only in 2,7 (6 upper and one lower)non/poorly functioning moieties(with relative function less than 10%) were found on scintigraphy which were surgically excised later. To conclude renal scintigraphy had influence on management in 11/27(40%) patients. Of the 9 patients with equivocal drainage, 6 had follow up renogram which revealed improvement in drainage in 3 patients, worsening in one patient and remained the same in other two. Tc99m DMSA cortical scintigraphy revealed scars in 5/27 (19%). **Conclusion:** Our study concludes that there is high incidence of complications in patients with duplex systems. Renal scintigraphy has a pivotal role in estimating functional status and drainage of affected kidneys and influencing the management and also in monitoring these high risk patients.

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Repeatability of a glomerular filtration rate (GFR) measurement method based on a single vein route and simple plasma samples determinations

G. Arsos¹, I. Tsechelidis¹, G. Sakagiannis¹, A. Svoukas¹, A. Iakovidou¹, Z. Athanasiadou², F. Dogramatzi¹, E. Psarouli¹; ¹Dept of Nuclear Medicine, Aristotle Univ. Med. School, Hippokraton Hospital, Thessaloniki, GREECE, ²Dept. of Biochemistry, Hippokraton Hosp., Thessaloniki, GREECE.

Aim GFR measurement with 51Cr-EDTA plasma elimination techniques requires multiple timed blood sampling. Separate venous lines for tracer injection and blood sampling, as well as sample counting in duplicate are suggested in order to minimize gross and random errors respectively. We have previously shown that GFR can be accurately calculated using a single venous line and simple counting of plasma samples, across a wide range of renal function. This modification is more friendly to the patient and effort and time sparing compared to the standard technique. The aim of the present study was to assess the test-retest repeatability of this approach. **Methods.** Thirty patients (14 females, 4 children) were enrolled (4 renal and 6 liver transplant recipients, 2 children with neoplasia under potentially nephrotoxic chemotherapy, 4 candidate kidney donors, 1 kidney donor and 13 with chronic kidney disease) aged 49.1±21.7 (range 5-87) years. Their body weight was 72.9±18.1 (range 20-104) kg with body mass index [BW (kg) / height (m)²] 27.1±5.5 (range 15.1-37.2) kg/m². Their serum creatinine level was 1.69±1.21 (range 0.52-5.43), median 1.22 mg/dl. GFR was measured using the slope-intercept, single 51Cr-EDTA injection, two sample technique with Brochner-Mortensen correction. Patients were injected with 1.85-3.81MBq 51Cr-EDTA dose escalated to body size. One 1 ml plasma samples per time point at 120 and 240 min p.i. were obtained after blood sampling through the vein catheter used for injection. Each sample was counted for 30 min. For each patient, the whole counting set was repeated twice (C1 and C2) on the same day. Statistically significant differences between C1 and C2 were tested by paired t-test. Between-set association was examined by linear regression analysis and agreement was assessed by means of Bland-Altman analysis of differences. **Results.**

C1 and C2 GFR values were very similar (54.5±27.8 (11.2-112.8) vs 54.6±28.7 (12.7-116.5) ml/min/1.73 m², range in parentheses) and the correlation between them excellent ($r^2 = 0.996$, $p < 0.00001$). The differences (range -5.15 to 4.89) were homoscedastically dispersed around their mean (0.02±0.02) and the 95% limits of their confidence interval were -3.94 to 3.97 ml/min/1.73 m². **Conclusions.** The simplified single vein route, simple counting of samples modification of the classic single injection - two samples slope intercept method of GFR measurement is highly repeatable in a wide range of renal function, age and patient physique.

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Differential Renal Function With ^{99m}Tc-DTPA: What Background To Subtract?

C. Oliveira¹, J. Neto¹, C. Capelo¹, P. Oliveira¹, P. Ferreira¹, M. Silva¹, S. Querido¹, C. Barros², S. Oliveira¹; ¹Nuclear Medicine Department of Portuguese Institute of Oncology, IPOCFG, EPE, Coimbra, PORTUGAL, ²Medical Physics Department of Portuguese Institute of Oncology, IPOCFG, EPE, Coimbra, PORTUGAL.

Aim: When calculating the differential renal function (DRF), the background subtraction from an infrarenal region of interest (ROI) seems to overestimate the function of the most compromised kidney (evaluated by visual analysis) and modify normal appearance of renographic curves. Moreover, due to the larger area of liver relative to that of spleen, this protocol tends to overestimate the function of the right kidney. We aim to determine if the background subtraction using infrarenal ROI is insufficient when compared with the results obtained with a ROI traced around almost the whole kidney. **Material and methods:** Retrospective study of renal scintigraphies performed between January/2003 and December/2009, in 90 patients: 54 female and 36 male, aged 26-85 years, mean age 62±13,3 years. Patients were divided in two groups: A, for functional asymmetries above 20% (43 patients), and B, comprising the remaining 47 patients. Renal imaging consisted of dynamic scans (128x128 matrix) acquired during the first 25 minutes after intravenous injection of 259MBq of ^{99m}Tc-DTPA, using a Siemens® E-Cam DCR Dual Head with low-energy high-resolution collimators. Each scan was processed with infrarenal and perirenal background ROI subtraction, utilizing the same kidney ROIs. **Results:** The perirenal ROI changed the DRF in the 43 patients of group A, with absolute values ranging from 0,8% to 24,6% (mean: 7,7%). The reduction affected the kidney with lower function in 39 patients (91%). In group B, DRF was modified in the 47 patients, the absolute change varying from 0,2% to 20,8% (mean: 3,3%). The kidney with lower function was affected in 28 patients (60%). The reduction of DRF was observed in the right kidney in 28 patients of group A (65%) and 34 patients of group B (72%). The renographic curves showed a change in time to peak in 62% of kidneys in group A (mean: 6min) and 37% (mean: 1,1min) of group B and in time to half-peak in 47% of group A (mean: 5,5min) and 88% of group B (mean: 2,5min). **Conclusion:** We confirmed the influence of the background subtraction protocol in DRF and renographic curve, mainly for renal asymmetries above 20%. The qualitative analysis suggests the infrarenal ROI does not compensate for the influence of vascular activity of spleen or liver in kidneys with poor renal function, which is thus overestimated. This aspect is more evident when it concerns the right kidney. The perirenal ROI gives DRF values and renographic curves more concordant with imaging findings.

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Evaluation of renal function changes in the experimentally created abdominal compartment syndrome

E. Kaya¹, C. Balci², A. H. İbiş², G. Akbulut³, & Demirkan⁴; ¹Acibadem Hospital Nuclear Medicine, Kayseri, TURKEY, ²Afyon Kocatepe University, Medical Faculty, Anesthesiology and Reanimation, Afyon, TURKEY, ³Afyon Kocatepe University, Medical Faculty, General Surgery, Afyon, TURKEY, ⁴Afyon Kocatepe University, Faculty of Veterinary Medicine, Afyon, TURKEY.

Background Abdominal compartment syndrome (ACS) is formed as a result of increased intraabdominal pressure (IAP) and can lead to dysfunction of many organs. In addition to the intra-abdominal organs cardiovascular system, respiratory system and renal functions are affected. The aim of our study, increased intra-abdominal pressure that may be associated with renal dysfunction to determine the dynamic renal scintigraphy and renal function was evaluated. **Materials and Methods:** Six healthy male dogs were included to the study. Before general anesthesia the dogs had been monitored by premedication and entubated by 1 mg/kg propofol, 0.1 mg/kg rocuronium bromide. All transactions during the arterial pressure, heart rate, ECG and peripheral oxygen saturation monitoring was performed. An intra abdominal catheter was placed and saline was used to increase IAP. Basal dynamic renal scintigraphy studies of 1 mCi technetium diethylenetriamin pentaasetik acid (Tc 99m DTPA) were used. Then IAP was increased by 5 cm H₂O in every 10 minutes up to 50 cmH₂O and this value was kept constant. A second study with 10 mCi Tc 99m DTPA was performed about 4 hours after the first study under the increased IAP. Dynamic images were recorded from the posterior projection by the general-purpose collimator using a single detector gamma camera for 30 minutes. Peak activity time (TTP), differential renal function (DRF) and the half-time (T_{1/2}) values obtained from renal scintigraphy of basal and increased IAP were compared. **Results:** There was no difference between heart rate, blood pressure, oxygen saturation values. TTP, DRF and T_{1/2} mean values obtained from dynamic studies comparison results are shown in Table 1. **Conclusion:** Some renal functions like TTP and T_{1/2} values were effected in the acute phase of Intra-abdominal pressure increase. Evaluation of renal functions by Tc 99m DTPA scintigraphy is a non-invasive and easy method for ACS. But larger series are needed to work.

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GFR measured by ⁵¹Cr-EDTA in the evaluation of renal complications in juvenile diabetes mellitus.

J. Koutsikos, E. Arhontaki, T. Liotsou, A. Fothiadaki, H. Fotinaki, V. Sarandi, C. Kardara, C. Zerva, A. Leondi; Alexandra University Hospital, Athens, GREECE.

Introduction The most serious complication of juvenile (type 1) diabetes is the development of hypertension resulting from diabetic angiopathy. The observation of protein in 24 hr urine

samples is a good indication of microangiopathy which leads to hypertension. The aim of our study was the demonstration of damage to the glomerulus as shown by measurement of GFR by ^{51}Cr -EDTA and its correlation with the measurement of 24 hr urinary protein levels in patients with juvenile diabetes. **Patients and methods** Forty six patients with juvenile diabetes (6 men and 14 women, mean age 33.3 y.o.) were studied. 32 patients did not have proteinuria (group A) and 14/46 patients did have (group B). A protocol of GFR measurement by 100 μCi (3.7 MBq) of ^{51}Cr -EDTA injection, three blood samples at 2, 3 and 4 hrs p.i., was performed. Volume of distribution was obtained by extrapolation of the clearance curve to zero time. GFR was scaled to a body surface area of 1.73 m², and according to reference values for age and sex was characterized as reduced, increased and normal. All patients had 24 hour blood pressure monitor, 24 hr urine protein and biochemical measurements of renal function. **Results** Ten patients from group A (31.3 %) had a reduced GFR, 5/32 (15.6 %) had increased (hyperfiltration) and 17/32 (53.1 %) had a normal GFR. All had biochemical parameters within normal values. Hypertension was detected in 3/32 (9.4 %) patients. In group B, 10/14 patients (71.4%) had a reduced GFR, 1/14 (7.2%) had increased and 3/14 (21.4%) had normal GFR. In this group 11/14 patients (78.6 %) had hypertension; 8/11 had reduced (72.7 %), 1/11(9.1 %) increased and 2/11 (18.2 %) a normal GFR. **Conclusion** The prevalence of hypertension is well associated with proteinuria in patients with juvenile diabetes. However the absence of proteinuria does not exclude the possibility of existing glomerular damage given that a large percentage (46.9 %) of the patients showed a disturbance of glomerular function as demonstrated by GFR measurement. Based on the results of this study it is recommended that patients with juvenile diabetes should have occasional measurements of GFR to allow early detection of glomerular damage and permit timely protective therapeutic intervention which also delays progression.

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Conventional/Specialized Nuclear Medicine: Infection & Inflammation

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The Value of Scintigraphy by Radiolabeled Antigranulocyte Antibodies in the Detection of Orthopedic Infections

V. Artiko, D. Sobic-Saranovic, S. Pavlovic, E. Jaksic, N. Petrovic, L. Brajkovic, A. Lesic, C. Vucetic, V. Obradovic; Institute for Nuclear Medicine, Belgrade, SERBIA.

Aim: The aim of the study is detection and evaluation of the infective foci in orthopedic patients using ^{99m}Tc -antigranulocyte antibodies. **Patients and Methods:** Total of 70 patients with clinical suspicion on orthopedic infection was investigated. Static acquisition was performed 2h after i.v. injection of 740 MBq of ^{99m}Tc -antigranulocyte antibodies. In all the patients, whole body skeletal scintigraphy was performed, followed by spot views. When necessary, additional scintigrams were acquired after 24h. In all the patients with negative or equivocal findings of planar scintigraphy, SPECT was performed. Additional data were provided using clinical finding, radiography, computer tomography and magnetic resonance imaging, laboratory analyses, and surgical or microbiological confirmation of infection. **Results:** There were 36 TP findings (8 with septic arthritis, 10 with osteomyelitis of femur, after fracture and osteosynthesis, 8 with flegmona of crural region and the foot caused by diabetes, and 10 with infection of the hip prosthesis), 24 TN (10 with osteoporosis, 10 with hip luxation and 4 with femoral fracture without infection), 6 FP (2 with femoral osteomyelitis without infection and 4 after loosening of hip prosthesis without infection), while 4 FN (2 due to TBC vertebral osteomyelitis, and the other two with resistance to antibiotic therapy). The smallest lesion found was 18 x 22 mm. Scintigraphy after 24h reduced the number of FP findings from 9 to 6 and increased the number of TP from 24 to 36. Sensitivity was 91%, specificity 81%, positive predictive value 87%, negative predictive value 85% and accuracy 87%. In 18 patients infection was caused by *Staphylococcus aureus*, in 6 with *Staphylococcus alpha haemolyticus* while in 6 infection was mixed (*Staphylococcus aureus* with *Pseudomonas* and *Staphylococcus aureus* with *Acino* bacter). In two patients with FN findings, infection was caused by *Micobacterium tuberculosis*, and in the other two it was resistant to antibiotic therapy. **Conclusion:** According to our results, scintigraphy with radiolabeled antigranulocyte antibodies is a useful method for detection and assessment of exact localization of orthopedic infections.

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Kidney infection in autosomal dominant polycystic kidney disease

M. Mitjavila, R. de la Cruz, M. Baeva, S. Pérez Rodrigo; Hospital Universitario Fundación Alcorcón, Madrid, SPAIN.

Approximately 30 to 50 percent of patients with autosomal dominant polycystic kidney disease (ADPKD) will have a kidney infection during their lifetime. The clinical manifestations of kidney infection in ADPKD include fever and flank pain. These infections may be due either to acute pyelonephritis or an infected cyst, and distinguishing between them is often difficult and both may be present simultaneously in the same patient. Patients who do not respond to empirical antibiotic therapy with improvement in symptoms within 72 hours or have continued fever for more than one week renal imaging is suggested. It is usually difficult to ascertain radiologically which of the many cysts is infected. Diagnostic information may be derived via percutaneous drainage of the suspicious cyst for documentation of the infecting organism and/or drainage the abscess cavity. **Patients and method:** 3 patients (2 F) aging 42-61 years old with flank pain and fever arrived to the nephrology department. Because they did not respond to antibiotic therapy within 72 hours, renal imaging with spiral CT with intravenous contrast was performed without finding the cause of the symptoms. ^{67}Ga -scintigraphy was performed, it was injected just after dialysis and the images were obtained just before the next dialysis. **Results:** In the 3 cases, 4 studies, the images with ^{67}Ga showed pathological uptake in the abdominal region. After the re-evaluation de CT images with ^{67}Ga images and with the gamma hand-probe /ultrasound, the complicated cyst was localized and percutaneous drainage with clinical improvement of the patient. **Conclusion:** In patients with ADPKD and with clinical suspicion of kidney infection, who do not respond to antibiotic therapy and conventional renal imaging, the

ultrasound and the spiral CT are not diagnostic, the ^{67}Ga -scintigraphy is useful for the diagnosis of the suspicious cyst and allow to perform percutaneous drainage.

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Prospective comparison of ^{111}In -labelled leucocyte scintigraphy and ^{18}F -FDG PET in the management of fever of unknown origin (FUO)

L. I. Sonoda, N. Seshadri, C. Solanki, M. Halim, A. Lever, K. Balan; University of Cambridge, Cambridge, UNITED KINGDOM.

Aim: To compare the diagnostic performance of ^{18}F -FDG-PET (PET) and ^{111}In -labelled leucocyte scintigraphy (LS) in the work-up of patients with fever of unknown origin (FUO). **Methods:** Twenty-one consecutive patients with FUO were prospectively studied using whole-body LS and PET within a week of each other. Performance of the two modalities for identifying the aetiology of FUO was evaluated. Final diagnosis was based on biopsy, microbiological tests, and clinical and imaging follow-up. **Results:** Abnormal tracer uptake was seen on LS in 3/21 (14%) patients and on PET in 8/21 (38%) patients, suggesting a higher sensitivity for the latter (McNemar's test, $p < 0.01$). All LS positive cases were identified on PET and confirmed as infection. The causes of FUO on PET in others were: benign ($n=2$), infection ($n=2$) and vasculitis ($n=1$). Of 13 patients with normal investigations, 10 made spontaneous recovery during the follow-up period and no definite cause for FUO was found following further investigations. One patient was diagnosed with Still's disease, one polymyalgia rheumatica and another died of meningoencephalitis. **Conclusion:** PET has a higher sensitivity than LS in the assessment of FUO. PET, where available, may be used as the non-invasive diagnostic modality of choice in the assessment of FUO.

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Semiquantitative Assessment of ^{99m}Tc -Methylene Diphosphate and ^{99m}Tc -IgG Scintigraphy in Diabetic foot

I. Neshandar Asli¹, H. Javadi², H. Sedigh¹, M. Mogharrabi², S. Jalalati², M. Babaei¹, N. Beyraghi¹, M. Assadi³; ¹Department of Nuclear Medicine, Taleghani Hospital, Shahid Beheshti University of Medical Science, Tehran, IRAN, ISLAMIC REPUBLIC OF, ²Department of Nuclear Medicine, 5th Azar Hospital, Golestan University of Medical Science, Gorgan, IRAN, ISLAMIC REPUBLIC OF, ³Bushehr Research Center for Nuclear Medicine, The Persian Gulf Biomedical Sciences Institute, Bushehr University of Medical Sciences, Bushehr, IRAN, ISLAMIC REPUBLIC OF.

Aim: Diabetic foot infection is the most common etiology of nontraumatic amputation of lower extremities and early diagnosis is of great importance in its management. The aim of this prospective study was to evaluate the strength of ^{99m}Tc -MDP and ^{99m}Tc -IgG in the diagnosis of osteomyelitis in diabetic foot. **Materials & Methods:** A prospective university hospital based study was performed over 24 months. Eighteen patients with type II diabetes and foot ulcers (15 men and 3 women; age range: 45-80 y) were referred for imaging because of clinically suspected osteomyelitis in diabetic foot. **Materials & Methods:** A prospective university hospital based study was performed over 24 months. Eighteen patients with type II diabetes and foot ulcers (15 men and 3 women; age range: 45-80 y) were referred for imaging because of clinically suspected osteomyelitis. Early (5h) as well as late (24 h) IgG scan and 3 phase bone scintigraphy were completed for all patients with a 3-4 day interval. Regions of interest were drawn over the abnormal bony sites and the contralateral normal sites, and the abnormal-to-normal uptake ratios (A/N ratios) were obtained for both studies. **Results:** From a total of 23 lesions we observed 10 sites of osteomyelitis, 10 sites of cellulites and 3 sites of aseptic inflammation confirmed by clinical evaluation, radiography and histology. Both ^{99m}Tc -IgG and ^{99m}Tc -MDP scans showed excellent sensitivity for diagnosis of osteomyelitis but the specificity was significantly lower (69.2% & 53.8% respectively). The accuracy of 5h ^{99m}Tc -IgG, 24 hr ^{99m}Tc -IgG and also ^{99m}Tc -MDP in diagnosis of osteomyelitis was 82.60%, 69.5 % and 73.9 %, respectively. There was no significant difference between the indices of early and late ^{99m}Tc -IgG scans for inflammation, cellulites and osteomyelitis. **Conclusion:** These results show that both ^{99m}Tc -IgG and ^{99m}Tc -MDP scans have ideal sensitivity for diagnosis of osteomyelitis but the specificity is significantly dissatisfactory; Early 5h image seems to be adequate in ^{99m}Tc -IgG scintigraphy and there is no need for 24h Images.

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Diagnostic accuracy of ^{99m}Tc -HMPAO-labeled leucocyte scan for osteomyelitis underlying diabetic foot ulcers: a retrospective study in 101 pedal ulcers

S. Georga¹, C. Manes², D. Skoutas², I. Iakovou¹, D. Lo-Presti¹, M. Psallas², V. Nikos¹, T. Christoforidis¹, A. Doumas¹, N. Karatzas¹; ¹3rd Dept of Nuclear Medicine, Aristotle University Medical School, Papageorgiou Hospital, Thessaloniki, GREECE, ²Diabetes Center, Papageorgiou Hospital, Thessaloniki, GREECE.

Introduction-Aim: Accurate diagnosis of osteomyelitis (OM) underlying diabetic foot ulcers remains a challenge. The aim of this study was to evaluate the diagnostic accuracy of ^{99m}Tc -HMPAO-labeled leucocyte scan, alone and in combination with bone scan, for the diagnosis of OM underlying diabetic foot ulcers. **Patients and methods:** We retrospectively reviewed ^{99m}Tc -HMPAO-labeled leucocyte scans (LS) and three phase ^{99m}Tc -MDP-bone scans (BS) performed in 92 consecutive diabetic patients who had a total of 101 pedal ulcers raising concern for contiguous OM. LS images were interpreted alone and in conjunction with BS images according to the following criteria: LS images alone were classified as positive for OM when focally increased uptake at the site of suspected bone infection was greater than surrounding soft tissue uptake or when focally increased leucocyte uptake of approximately the same intensity on both dorsal and plantar views was observed (in cases of suspected OM in the forefoot). When LS were interpreted together with BS, spatially congruent BS/LS findings were considered positive for OM. Final diagnosis was based on long-term clinical and radiological follow-up or bone biopsy. **Results:** Among the 101 pedal ulcers investigated, 45 foci of underlying OM were finally diagnosed (44.5%), while simple soft tissue infection was identified in the rest 56 cases (in 5 cases with concomitant acute Charcot arthropathy). Sensitivity, specificity, PPV, NPV and accuracy of LS alone for diagnosing OM underlying diabetic foot ulcers were: 93.3%, 97.9 %, 96.6 %, 95.9% and 96.1% respectively. In two cases of OM proven by histopathology LS falsely suggested that the

infection was confined to overlying pedal ulcers. The addition of BS didn't change LS interpretation in these cases. There was only one false positive LS result (a case of extraosseous leucocyte uptake which mistakenly attributed to bone). The addition of BS changed LS interpretation in this case. Sensitivity, specificity, PPV and NPV of combined LS/BS were 89.3%, 100%, 95.5 and 100% respectively. The diagnostic accuracy of LS alone or in combination with BS was nearly identical (96.1% versus 95.5%). **Conclusion:** ^{99m}Tc -HMPAO-labeled leucocyte scan is a highly accurate radionuclide test for diagnosing OM underlying diabetic foot ulcers. Diagnostic accuracy of LS is not affected by whether or not the patients have bone scan. Consequently, we suggest that LS should be the first, and in the most cases the single, radionuclide imaging performed in suspicion of OM underlying diabetic foot ulcers.

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SPECT/CT in the detection of osteomyelitis in patients with diabetic foot syndrome - a pilot study

O. Lang, H. Balon, I. Kunikova, R. Pichova, H. Krizova, L. Treslova, E. Silhova, K. Petrova, A. Kratochvil, M. Andel; Charles Univ., 3rd Medical Faculty, Prague 10, CZECH REPUBLIC.

Background: Bone scan (BS) combined with leucocyte scan (LEU) is usually used to diagnose osteomyelitis (OM) in patients with diabetic foot syndrome. Accurate differentiation of cellulitis (C) and OM is crucial for patient management. Introduction of SPECT/CT has brought new possibilities to this field. **Method:** 9 patients, 8 male and 1 female, average age of 62 (48-79) years, suspected of having OM were evaluated. All pts were examined with Tc-99m labeled leucocytes; in 4 pts BS was also done. Planar and SPECT/low-dose CT (LDCT) images were performed. Inflammation (inflm) was considered to be present when focal accumulation of leucocytes was seen. Results were expressed as negative, suspicious or positive for C or OM for each method separately and for their combination. These results were expressed in percent. **Results:** Differentiation of C and OM was not possible on planar LEU images; combination with BS enabled localization of all inflammatory sites to bones. We were unable to differentiate C and OM only in 3 pts using SPECT. The best results were encountered with SPECT/LDCT - see table.

patient	LEU planar		BS		LEU SPECT		LEU SPECT/LDCT	
	inflm	localization	inflm	localization	inflm	localization	inflm	localization
1	no				susp		yes	OM
2	yes	C/OM			yes	C/OM	yes	C
3	yes	C/OM	yes	OM	yes	OM	yes	OM
4	yes	C/OM	yes	OM	yes	OM	yes	OM
5	no		yes		yes	C/OM	yes	C
6	no		susp		yes	C	yes	OM
7	susp				yes	C	yes	OM
8	yes	C/OM	yes	OM	yes	C/OM	yes	C
9	susp				yes	C	yes	OM

Conclusion: LEU SPECT/LDCT improved detection of inflammation in 5/9 pts (56%), the differentiation of C from OM was possible in all pts (100%). We believe LEU SPECT/LDCT is the method of choice in patients with diabetic foot syndrome for inflammation detection and differentiation of cellulitis from osteomyelitis. Bone scan could be omitted, thus the radiation could be reduced and the diagnosis could be made earlier.

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Can F-18 FDG PET/CT detect gastrointestinal mucosa and arterial involvement in Behcet's syndrome?

S. Jeong, B. Song, H. Lee, S. Kang, S. Lee, B. Ahn, J. Lee; Kyungpook National University Hospital, Daegu, KOREA, REPUBLIC OF.

Purpose: Behcet's syndrome is a multisystem disorder presenting with recurrent oral and genital ulcerations as well as ocular involvement. Behcet's syndrome can involve other organs such as gastrointestinal mucosa and artery. The purpose of this study is assessment of organ involvement using F-18 FDG PET/CT in patients with Behcet's syndrome. **Methods:** 8 patients with Behcet's syndrome were enrolled. All patients underwent F-18 FDG PET/CT, gastrointestinal endoscopy (esophagogastroduodenoscopy and colonoscopy) and radiologic study (chest and abdominal CT scan) for assessment of gastrointestinal mucosa and arterial involvement. Pathologic confirmation of suspicious lesions was performed. We compared the detectability of F-18 FDG PET/CT, gastrointestinal endoscopy and radiologic study for the gastrointestinal mucosa and arterial involvement. **Results:** On F-18 FDG PET/CT, 2 patients showed hypermetabolic lesion in ileocecal valve and 1 patient showed hypermetabolism of abdominal aortic wall. On colonoscopy, 3 patients showed aphthous ulcer in colon. On abdominal CT, 1 patient showed abdominal aortic aneurysm. Three patients with hypermetabolic lesion on F-18 FDG PET/CT were diagnosed involvement of Behcet's syndrome by pathologic study. One patient among 3 patients with aphthous ulcer on colonoscopy was diagnosed as chronic colitis by pathologic study. This case is false positive. Two patients among 5 patients without hypermetabolic lesion on F-18 FDG PET/CT were diagnosed gastrointestinal involvement 1 and 2 years ago and have been treated. Follow up colonoscopy and colonoscopic biopsy of the two cases showed normal mucosa of gastrointestinal tract at the same time period of F-18 FDG PET/CT. **Conclusion:** F-18 FDG PET/CT detects accurately gastrointestinal mucosa and arterial involvement and can be used assessment of treatment response in patients with Behcet's syndrome. This study has limitation, however, by small patient number. Further large study is needed for confirm the results.

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Could ^{99m}Tc -sulesomab immunoscintigraphy be the method of choice in the evaluation of infection in patients with deep brain stimulation?

H. Fernandes, P. Linhares, R. Real, P. Oliveira, T. Vieira, A. Oliveira, T. Faria, J. Pereira, R. Vaz; Hospital de S. João, Porto, PORTUGAL.

Aim: Deep brain stimulation (DBS) of the subthalamic nucleus is an effective therapy for advanced Parkinson's disease (PD). Infection is one of possible serious complications. It is potentially fatal, and often leads to removal of the stimulation system. Tc-99m-sulesomab consists of anti-granulocyte monoclonal murine antibody Fab' fragments labeled with technetium-99m. It can be used in the detection of infection/inflammation with an accuracy comparable to that of white blood cells scintigraphy. There are no data reporting the efficacy of immunoscintigraphy in this particular clinical setting. Our aim was to evaluate the role of ^{99m}Tc -sulesomab immunoscintigraphy in the assessment of the infection extent with the purpose of rationalizing the therapeutic approach of postoperative infection in PD patients with DBS. **Materials and Methods:** Immunoscintigraphy with ^{99m}Tc -sulesomab was performed on seven consecutive patients with clinical evidence of skin infection whom, depending on its results, were further submitted to wound debridement alone or in combination with either partial or complete removal of the stimulation system. Planar scans and SPECT-CT were acquired 4h and 24h after injection, using a dual-head gamma-camera coupled with a low-power x-ray tube. **Results:** According to the location of wound dehiscence patients were divided into two groups. The first group comprised six patients that had chronic retroauricular wound dehiscence while the second included the one patient with subclavicular wound dehiscence only. Among the first group of patients, 3 different patterns were detected: one patient had a normal distribution of radiolabeled anti-granulocyte monoclonal antibody fragments and was offered wound debridement alone; other two patients with retroauricular wound dehiscence were shown to have abnormal uptake over the retroauricular wounds and were subjected to partial stimulation system removal that spared only the electrodes; and the three last patients in this group presented with diffuse uptake that included the retroauricular and right frontal wounds, as well as along the extracranial trajectory of the corresponding electrode, which resulted in a complete removal of the stimulation system. Among the second group of patients, a focal uptake was observed over the subclavicular wound, and the patient was subjected to partial removal of the stimulation system at that level. **Conclusion:** These preliminary data pretend to emphasize the possible role of immunoscintigraphy with ^{99m}Tc -sulesomab in the assessment of skin infection extent in patients submitted to DBS. This study suggests that this method of imaging could be useful on an algorithm of diagnosis and treatment for this specific group of patients.

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Diagnostic Performances of 18F-FDG Positron Emission Tomography in Large Vessels Vasculitis : Meta-analysis

F. Besson¹, J. Parienti¹, J. Prio², B. Bienvenu¹, S. Costo¹, G. Bouvard¹, D. Agostini¹; ¹CHU Caen, Caen, FRANCE, ²CHUV, Lausanne, SWITZERLAND.

Aim : To perform a meta-analysis of FDG-PET performances in the diagnosis of large vessels vasculitis (Giant Cell Arteritis (GCA) associated or not with Polymyalgia Rheumatica(PMR), Takayasu). **Materials and methods :** The MEDLINE, Cochrane Library, Embase were searched for relevant original articles describing FDG-PET for vasculitis assessment, using Mesh terms ("Giant Cell Arteritis or Vasculitis" AND "PET"). **Criteria for inclusion were:**(1)FDG-PET for diagnosis of vasculitis(2)American College of Rheumatology criteria as reference standard(3)control group. After data extraction, analyses were performed using a random-effects model. **Results :** Of 184 citations (database search and references screening),70 articles were reviewed of which 12 eligible studies were extracted (sensitivity range from 32% to 97%). 7 studies fulfilled all inclusion criteria. Owing to overlapping population, 1 study was excluded. Statistical heterogeneity justified the random-effects model. Pooled 6 studies analysis(116 vasculitis,224 controls) showed a 81% sensitivity (95%CI:70-89%);a 89% specificity (95%CI:77-95%);a 85% PPV(95%CI:63-95%); a 90% NPV(95%CI:79-95%);a 7.1 positive LR(95%CI:3.4-14.9); a 0.2 negative LR(95%CI:0.14-0.35) and 90.1 DOR(95%CI: 18.6-437). **Conclusion :** FDG-PET has good diagnostic performances in the detection of large vessels vasculitis. Its promising role could be extended to follow up patients under treatment, but further studies are needed to confirm this possibility.

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Tc99m-HMPAO-labeled leucocyte scan in the evaluation of painful knee arthroplasty

S. Georga¹, T. Christoforidis¹, I. Iakovou¹, M. Potoupnis², V. Nikos¹, K. Badiavas¹, A. Doumas¹, D. Lo-Presti¹, G. Kapetanios², N. Karatzas¹; ¹3rd Dept of Nuclear Medicine, Aristotle University Medical School, Papageorgiou Hospital, Thessaloniki, GREECE, ²3rd Clinic of Orthopaedic Surgery, Aristotle University Medical School, Papageorgiou Hospital, Thessaloniki, GREECE.

Aim: To evaluate the value of Tc99m-HMPAO-labeled leucocyte scan (LS), alone and in combination with Tc-99m-phytate-colloid bone marrow scan (BMS), and with the addition of semiquantitative analysis, in the diagnosis of infected knees arthroplasties. **Patients and methods:** Fifty five patients with painful total knee arthroplasties who underwent LS and BMS were enrolled in the study. LS images were acquired 1 and 4 hours post injection and were interpreted alone (late LS images alone and combined with early LS images) and in conjunction with BMS images according to the following criteria: a) Increased periprosthetic leucocyte activity on late LS images was considered positive for infection. b) When leucocyte uptake increased in intensity or in extent with time, LS was compatible with infection. c) Incongruent late LS/BMS images indicated infection. In addition to visual interpretation, mean counts per pixel in the area of suspected infection (SA) and in the contralateral area (CA) were recorded and SA-to-CA ratios for early and late LS and for BMS were calculated (early LSR, late LSR and BMSR respectively). Furthermore, late LSR to BMSR ratios were calculated. Final diagnosis was based on surgical, histological and bacteriological data or clinical follow-up. **Results:** Among the 55 knee prostheses investigated, 23 infected and 32 uninfected prostheses were finally diagnosed. Sensitivity, specificity and accuracy of late LS alone for diagnosing periprosthetic infection were 95.6%, 84.4% and 89.1% respectively. The addition of early LS imaging wasn't improved the results. Sensitivity, specificity and accuracy of combined early and late LS were 69.2%, 86.9% and 80.6% respectively. The same parameters for combined late LS/BMS were 82.6%, 90.6% and 87.3% respectively. Early LSR and late LSR ratios as well as late LSR to BMSR ratios were significantly different ($p < 0.05$) between infected and uninfected prostheses (2.73 ± 0.85 versus 1.38 ± 0.52 , 3.02 ± 1.43 versus 1.36 ± 0.62 and 1.80 ± 0.80 versus 1.05 ± 0.37 respectively). **Conclusion:** Our

results suggest that late (4hour) imaging with Tc99m-HMPAO-labeled leucocytes is an effective method for diagnosing infected knee prostheses. The additional performance of BMS may slightly improve the specificity of LS, although the diagnostic accuracy of combined late LS/BMS for diagnosing infected knee prostheses is nearly identical to that of late LS alone. The addition of early LS imaging isn't found to be helpful. Conversely, the addition of semiquantitative analysis seems to be helpful in discrimination infection from aseptic loosening of knee prostheses.

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Evaluation of 2-deoxy-2-[¹⁸F]fluoroacetamido-D-glucopyranose as a infections imaging agent for PET

M. E. Martinez Pozo, Y. Kiyono, T. Ido, S. Noriki, K. Inai, K. S. Mandap, V. T. Tiwari, Y. Fujibayashi; University of Fukui, Fukui, JAPAN.

Aims: Early diagnosis of infection and the capacity to distinguish between infection and inflammation is of primary importance for the management of patients. Localization of bacterial infections by positron emission tomography (PET) has gained interest in recent years, but still few radiopharmaceuticals are available for use. *N*-acetylglucosamine and its derivatives including peptidoglycan are unique and obligatory structural components of bacterial cell wall. In this study we evaluated the potential of 2-deoxy-2-[¹⁸F]fluoroacetamido-D-glucopyranose ([¹⁸F]FAG) as a bacterial infection imaging agent for PET. Furthermore the uptake of [¹⁸F]FAG and [¹⁹F]FDG was evaluated at sites of bacterial infections or inflammation in rats. **Methods:** Radiofluorination of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-bromoacetamido-D-glucopyranose (TA-BrAG) was performed using microwave heating followed by alkaline hydrolysis with NaOH and purification on HPLC. Whole-body biodistribution of [¹⁸F]FAG was determined in mice using the dissection method. PET scans were performed using a small-animal PET. **Results:** The [¹⁸F]-fluorination proceeded with a labeling efficiency of 75.5 ± 4.2% (n=3) for optimized conditions. Moreover, alkaline hydrolysis of TA-[¹⁸F]FAG and purification by HPLC provided a final decay-corrected [¹⁸F]FAG yield of 9.7±2.8% (n=5), a radiochemical purity of 98.7±1.5% (n=5), and a reaction time of 62 min. These conditions were used in a semi-automated system to produce after purification [¹⁸F]FAG for animal experiments. Biodistribution study showed similar patterns to previously reported studies for [¹⁸F]FAG. PET images showed significant accumulation at sites of infection of both tracers. Sites of inflammation showed significant accumulation of [¹⁸F]FDG while not significant accumulation of [¹⁸F]FAG was observed. Induction of infection or inflammation at site of accumulation of radioisotope was confirmed by histopathological analysis. **Conclusions:** Using a new precursor microwave mediated fluorination of [¹⁸F]FAG was accomplished. [¹⁸F]FAG showed its usefulness to discriminate between bacterial infections or sterile inflammation while [¹⁸F]FDG accumulated on both sites.

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Demonstration of Transdiaphragmatic Passage of Intraperitoneally Injected Labeled E.Coli Through the Diaphragm

O. Cavdaroglu¹, M. S. Eren², M. Karaman³, O. Ozdogan², O. Ulker², T. Unek¹, C. Arslan¹, S. Karademir¹; ¹Dokuz Eylul University School of Medicine Department of Surgery, Izmir, TURKEY, ²Dokuz Eylul University School of Medicine Department of Nuclear Medicine, Izmir, TURKEY, ³Dokuz Eylul University School of Medicine Department of Microbiology and Clinical Microbiology, Izmir, TURKEY.

INTRODUCTION: The diaphragm is a functional structure arises from muscle fibers. The stomach, which is a functional space between mesothelial cells permits the passage of peritoneal fluid to the lymphatic lacunas readily. The lymphatic drainage of the diaphragm primarily reaches to the lymph nodes of the mediastinum by retrosternal lymphatic pathways and also reaches to the systemic circulation by thoracic duct as a minor path. The same transdiaphragmatic pathway was also accused for the transfer of intraperitoneal infections to the systemic circulation and was demonstrated indirectly. In this study we aimed to demonstrate this pathway both directly and indirectly. **MATERIALS AND METHODS:** Seven male Wistar albino rats (280-300 gm) were anesthetized with intramuscular ketamine and xylazine. A laparotomy was performed in sterile conditions. The liver was separated from the diaphragmatic surface by cutting off the falciform ligament using a surgical micro scissors. A 45 degrees trendelenburg position was applied to achieve a direct contact of E-Coli solution with the diaphragm. A solution containing 1x10⁹ colony forming unit per milliliter (CFU/ml) of E-Coli (ATCC 25922) was labeled with Tc-99m Perchnetate. One ml of this solution was injected to the infra diaphragmatic surface. The laparotomy incision was sutured immediately and the rats were imaged at trendelenburg position 3-4 minutes after the injection. We obtained a dynamic image of one minute per frame for 20 minutes to demonstrate the transport of bacteria through the diaphragm. A laparotomy and a thoracotomy were performed at sixth hour. Intracardiac blood was obtained to calculate the systemic activity in the blood stream and for obtaining a blood culture. The liver and the spleen were dissected to demonstrate the uptake of microorganisms by the reticuloendothelial cells and the activity in these organs were counted. **RESULTS:** Transdiaphragmatic passage of radioactivity was detected in all rats as 2 vertical lines of activity entering the thorax in the first 6 minutes. Bacterial growth was observed in all cultures. High counts of radioactivity were detected in blood samples, in liver and spleen. **CONCLUSION:** Particles in the peritoneal cavity with a size smaller than 10 µm was declared to enter systemic circulation using stomach and subperitoneal lacunas but was not demonstrated directly. We demonstrated this passage both directly and indirectly using Tc-99m labeled E-Coli solution in this study. We did not observe a prominent cardiac activity although a vertical intense activity due to the passage was clear.

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Clinical value of PET/CT in bacteraemia of unknown origin. Results from an observational pilot study.

S. Hess¹, S. H. Vind², S. Skarphédinsson³, C. Pedersen⁴, H. J. Kolmos⁵, O. Gerke¹, P. F. Højlund-Carlson¹; ¹Dept. of Nuclear Medicine, Odense University Hospital, Odense C, DENMARK, ²Dept. of Nuclear Medicine, Næstved Hospital, Næstved, DENMARK, ³Dept. of Infectious Diseases, Odense University Hospital, Odense C, DENMARK, ⁴Medical Department O,

Herlev Hospital, Herlev, DENMARK, ⁵Dept. of Clinical Microbiology, Odense University Hospital, Odense C, DENMARK.

AIM Locating the source of bacteraemia in febrile patients is important to institute correct treatment, but may be difficult despite a multitude of diagnostic procedures. We conducted a pilot study to test the clinical value and logistics of PET/CT scans in bacteraemia of unknown origin. **MATERIALS AND METHODS** We prospectively included in-patients with a novel diagnosis of bacteraemia from gram positive cocci. Patients < 18 years of age, pregnant or lactating women, and patients unable or unwilling to give informed consent were ineligible. Retrospective chart reviews gave us dates of admission and discharge, dates and conclusions of all diagnostic procedures performed, and all antibiotic regimes instituted. The final diagnosis was established as a composite of all available chart information and the conclusions stated in the discharge reports. **RESULTS** Of 22 patients screened for inclusion six gave no consent, and one patient had no gram positive cocci on final classification. Of the remaining 15, four were excluded because the PET/CT scan was cancelled. Thus, 11 patients were available for data analysis: two females and nine males, median age 65 years. All patients were on antibiotics for a median period of six days prior to the PET/CT scan. The final diagnoses were infectious spondylodiscitis (n=4), uresepsis (n=4), infective endocarditis (n=2), and one without a definitive infectious focus. PET/CT correctly diagnosed all four cases of spondylodiscitis, whereas MR initially missed one of these. PET/CT identified a case of infected pacemaker electrodes missed by repeat echocardiography, but failed to diagnose a case of aortic valve endocarditis diagnosed correctly by transeofageal echocardiography. This patient was heavily pre-treated with antibiotics prior to the PET/CT scan, whereas echocardiography was performed before the start of antibiotic therapy. In the patients with uresepsis, imaging including PET/CT was of little help in diagnosing infection. In one case, however, PET/CT showed activity in a known case of chronic lymphocytic leukemia. In the last patient, infection was not identified by any imaging modality, but PET/CT demonstrated a prostate cancer and venous thromboembolism. **CONCLUSION** PET/CT shows promise in patients with bacteraemia of unknown origin especially if urinary tract infection has been ruled out. Futile diagnostic procedures (in our patients a median of four times imaging) may be saved. However, further and larger prospective trials are needed to establish the role of PET/CT in this particular clinical setting.

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Role of ¹⁸F-FDG PET/CT in the clinical decision making of idiopathic retroperitoneal fibrosis

D. Proserpi, V. Lanni, R. Pirisino, D. Familiari, A. Festa, P. Pizzichini, G. Capriotti, F. R. Festuccia, C. Fofi, P. Menè, F. Scopinaro; University of Rome "Sapienza" Sant'Andrea Hospital, Rome, ITALY.

BGK: Idiopathic retroperitoneal fibrosis (IRF) is a rare disease probably due to a systemic autoimmune process, characterized by an inflammatory mass which often surrounds abdominal aorta and/or neighbouring structures (i.e. ureters). **AIM:** To evaluate the role of ¹⁸F-FDG PET/CT in the management of patients affected by IRF, and to correlate metabolic assessment of the disease with laboratory findings such as erythrocyte-sedimentation rate (ESR) and C-reactive protein (CRP). **PATIENTS AND METHODS** Between 2006 and 2010 we studied 7 patient with IRF [3 F, 4 M]. Follow-up was performed with the same methods: due to lack of standardized protocols, timing was decided according to patient's clinical requirements. Acute-phase reactants evaluation was made in the meantime of every PET. Patients with discordant PET and laboratory data

Patient	Sex	Age, years	IRF Diagnosis	Distribution of IRF	PET/LAB findings	Ureteral Involvement	Therapy
1	M	50	TC	Periaortic/periliac	PET+/LAB-	Yes	CCS/IMS
2	F	49	Biopsy	Para-caval	PET+/LAB-	Yes	CCS/IMS
3	M	41	Biopsy	Right iliac fossa	PET+/LAB-	No	CCS
4	F	76	TC	Periaortic/periliac	PET-/LAB+	Yes	Ureteral stenting

CCS: Corticosteroids; **IMS:** Immunosuppressors **RESULTS** In patients with newly diagnosed IRF (pts 1, 2, 3) PET/CT revealed an increased uptake of FDG with discordant laboratory data thus allowing to start a proper immunosuppressive therapy. These three pts were followed-up with PET controls till a clearly decreased uptake, showing complete response to therapy. Such results permitted clinicians to give up or taper therapy, avoiding overtreatment. Patients 4, 5, 6, 7 with a not recent diagnosis (years) underwent PET/CT to evaluate disease's metabolic assessment. They all showed no FDG uptake in the retroperitoneal mass and normal laboratory findings were recorded in all but one (pt 4). These patients were classified as PET negative (silent disease): so not eligible for an immunosuppressive therapy. **CONCLUSIONS** PET is a useful tool for clinical decision making in IRF, allowing to evaluate the eligibility and the efficacy of the pharmacological treatment and to detect early recurrences thus modifying the therapeutical approach. Acute phase reactants are not reliable for the management and the follow-up as they are often not concordant with metabolic assessment of the disease. Furthermore, PET could be useful to guide surgeons during biopsy, helping to select active inflammatory areas in order to avoid the removal of wrong histological samples.

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The Clinical Value of ^{99m}Tc-HMPAO Labelled White Blood Cell Scintigraphy in Detection of Occult Infection in Patients with Fever of Unknown Origin

C. Oliveira, H. Fernandes, A. Moreira, T. Santos, R. Silva, G. Costa, J. Pedroso de Lima; Servico de Medicina Nuclear. Hospitais da Universidade de Coimbra, Coimbra, PORTUGAL.

Aim: Fever of unknown origin (FUO) is a diagnostic challenge. ^{99m}Tc-HMPAO labelled white blood cell (WBC) scintigraphy can help to identify a focus of active infection, mainly in an acute context. Our aim was to evaluate the clinical utility of the WBC scintigraphy in detecting or excluding an infectious origin in patients with FUO. **Materials and Methods:** Between February/2008 and March/2010, 43 patients (16 female and 27 male, age range 18-88 years,

mean 55 years) with FUO were submitted to WBC scintigraphy. The scintigraphic study consisted of whole-body (sweep) and/or static planar images on a dual head gamma camera equipped with low energy high resolution collimators, and included SPECT/CT acquisition in 10 patients. In face of the scintigraphic results, individual patient data (concerning complete history and physical examination, blood counts, biochemistry, cultures, viral and collagen vascular disease serology and radiological data) was reviewed to identify the cause of the fever. Scintigraphic results were considered to be true negatives whenever a non-infectious cause was found or in the absence of a definitive diagnosis, during a follow-up period of 1,5 months. Finally, the sensitivity, specificity, negative and positive predictive values of the study were determined. Results: True positive results were obtained in 8 patients (19%): 2 for infection of prosthetic vascular graft, 1 for septic arthritis with abscedation, 1 for acute appendicitis, 1 for splenic abscess, 1 for hepatic abscesses and 2 for infected hepatic cysts. There was 1 false positive (2% of the patients), corresponding to arthritis without signs of infection. The scan was found to be true negative in 29 patients (67%). In 5 patients (12%), the scan was false negative, but in 4 of them we would not expect a significant neutrophilia: 3 cases of fungal infections in immuno-compromised patients and 1 case of pyelonephritis on antibiotherapy. SPECT/CT had an added value in all cases, by localizing infectious focus (2 patients) or identifying physiological uptake (8 patients). Overall, the calculated sensitivity (taking into account all false negatives) was 62%, and the specificity was 97%. However, excluding the 3 immuno-compromised patients and the patient on antibiotherapy, the sensitivity would rise to 89%. The negative and positive predictive values would be 97% and 89%, respectively. Conclusion: Our results suggest that the leukocyte scintigraphy, preferably with SPECT/CT, is a valuable tool in detecting or ruling out an infectious active focus in the diagnostic work-up of FUO.

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The Use of SPECT/CT Avoids Potential Pitfalls of Planar In-111 WBC Imaging in Suspected Periprosthetic Infection

H. R. Balon¹, M. M. Patel¹, O. Lang², ¹W. Beaumont Hospital, Royal Oak, MI, USA, ²Charles Univ., 3rd Faculty of Medicine, Prague, Czech Republic.

Background: In patients with a painful arthroplasty, it is difficult to differentiate periprosthetic infection from prosthesis loosening. The presence of infection changes pt management. Triple tracer studies (TTS), i.e. Tc-99m sulfur colloid bone marrow (BM) mapping, In-111 leukocytes (WBC) and bone scan (BS) have been used to help with this differentiation. SPECT/CT fusion imaging now enables more optimal anatomic localization of abnormal WBC accumulation. **Objective:** To review our experience with TTS including dual tracer SPECT/CT in suspected infection vs. loosening of orthopedic hardware (HW) **Methods:** We retrospectively studied 100 consecutive pts (M/F=46/54; age 15-89y, median=63y) with painful hip (50 pts), knee (47 pts) or leg HW (3 pts). All had a planar TTS scan (day 1: sulfur colloid bone marrow image, day 2: 24hr In-111 WBC image followed by Tc-99m MDP BS). 21 of 50 pts w hip HW, 5 of 47 pts w knee HW, 2 of 3 pts w leg HW also had simultaneous dual window (Tc-99m and In-111 photopeaks) SPECT/low-dose CT. For the purpose of this study, the results were classified as negative, suspicious or positive for hardware-associated infection based on In-111 WBC images. **Results:** Of the 50 hip scans, 24 were negative (2 w SPECT/CT), 1 positive (w SPECT/CT; TP) and 25 suspicious (18 w SPECT/CT, 7 planar only). Of the 7 suspicious planar scans, 2 were true positive, 5 (70%) were false positive (by culture and/or clin. F/U). All 18 SPECT/CT scans excluded periprosthetic infection (TN) and localized WBC uptake to inguinal and/or external iliac lymph nodes, soft tissue lesions, diverticulitis. Of the 47 knee scans, 42 were negative (2 w SPECT/CT), 4 suspicious (2 w SPECT/CT), 1 positive (w SPECT/CT; TP). Of the 4 suspicious scans, 2 w SPECT/CT had soft tissue pathology, 2 planar were FP. Of the 3 leg scans, 1 planar was negative, 2 were suspicious (both had soft tissue inflammation on SPECT/CT). Of 31 total suspicious scans, all 22 (71%) with SPECT/CT were TN. Without SPECT/CT, 29 of 31 (94%) would have been misinterpreted (FP). **Conclusion:** The differentiation of periprosthetic infection from other causes of WBC accumulation was possible in 100% pts who had SPECT/CT, but was not possible in 70% pts who had planar imaging alone. Adding SPECT/CT increases the specificity, accuracy and diagnostic confidence of labeled leukocyte scans and impacts pt management. SPECT/CT should be used whenever findings on planar images are uncertain.

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Diagnostic value of F-18 FDG PET/CT in patients with fever of unknown origin

F. Aydin, A. Kose, A. Boz, F. Gunseren, A. Yildiz, F. Gungor; University of Akdeniz, Antalya, TURKEY.

Aim: Fever of unknown origin (FUO) identifies a pattern of fever with temperature higher than 38.3°C on several occasions over more than 3 weeks, in which the diagnosis remains uncertain after an initial diagnostic work-up. The identification of the cause of FUO is a challenge in clinical practice despite recent advances in diagnostic techniques. The aim of this study was to assess the diagnostic value of F-18 FDG PET/CT in the diagnostic work up in patients with FUO. **Material and Methods:** The study was conducted between April 2008-March 2010 and the study population comprised 14 patients (6 female, 8 male; mean age 41.1 ± 23.6) with FUO underwent F-18 FDG PET/CT scans. Final diagnosis was based on histopathology, microbiologic assays, or clinical and imaging follow-up. Results: PET/CT detected suggestive foci of increased F-18 FDG uptake in 6 patients (Salmonellosis, Tuberculosis, Still's Disease, granulomatous disease, Hodgkin's Lymphoma, and inflamed diffusely atheroma plaques). F-18 FDG PET/CT was negative in 8 patients. In 7 patients showed spontaneous resolution of the febrile state with no further evidence of a localized inflammatory, infectious, or malignant process for a clinical follow-up period of 12-18 month. The remaining one patient was diagnosed Leishmaniasis with bone marrow biopsy. Conclusion: F-18-FDG PET/CT is a useful imaging tool in patients with FUO. When systemic disease are excluded by other diagnostic tests, a negative PET/CT may avoid the need for further investigations. The synergy of combined anatomic-metabolic information is of incremental value in the diagnostic work-up of FUO. Further, larger well-designed, prospective, studies are needed to validate and to implement the strategy of using this hybrid imaging modality as an initial diagnostic investigation in patients presenting with FUO.

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SPECT/CT has additional value to planar white blood cell scintigraphy in patients with suspected vascular graft

infection

E. Ozalp, C. Goffin, B. Bellens, P. Bergmann; CHU Brugmann, Brussels, BELGIUM.

Aim: To evaluate the utility of SPECT/CT white blood cell scintigraphy (WBCs) in patients with suspected vascular graft infections. **Materials and Methods:** 81 scans with 99mTc HMPAO labeled leukocytes were reviewed retrospectively from 60 consecutive patients (14 women, 46 men; age ranged 25-91 yr; mean age 68 ± 12 yr) with suspected vascular graft infections. Additional information provided by SPECT/CT for the diagnosis of an infectious process and its localization to the graft or soft tissues was assessed. The final diagnosis was based on histopathologic findings and microbiologic assays obtained at surgery or on clinical and imaging follow-up. **Results:** Infection was diagnosed in 33 of these patients (41%). SPECT WBCs has significantly higher sensitivity (88% vs 48%, p<0.05) and accuracy (90% vs 74%, p<0.05) than planar WBCs while specificity (92%) for diagnosing infection was similar. SPECT helped to detect the infection in 13 studies, mainly in pelvic area. SPECT/CT provided additional information to the precise anatomic localization of an infectious process and excluded graft involvement in 8 patients with soft tissues infections in abdominopelvic area. **Conclusions:** In comparison to planar imaging, SPECT /CT improved diagnosis, localization, and definition of extent of disease in patients with suspected vascular graft infections, mainly in abdominopelvic area.

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Possible role of 18F-FDG PET/CT in the tailored management of retroperitoneal fibrosis

A. Cistaro, V. Arena, E. Pelosi, D. Penna, P. Fania, M. Mancini; Positron Emission Tomography Center IRMET S.p.A, Turin, ITALY.

Aim: Retroperitoneal fibrosis is a complex clinical entity, characterised by fibro-inflammatory reaction, around the abdominal aorta and the iliac arteries, extended into the retroperitoneum. No biochemical marker correlates with the disease severity and progression. Imaging data may fail discriminating between quiescent fibrotic tissue and florid lesions. 18F-FDG PET was recently suggested as a promising tool for detecting disease activity. The aim of the study is to report on 8 consecutive cases managed tailoring therapeutic interventions on the metabolic activity detected at the 18F-FDG PET/CT. **Material and Methods:** 9 patients (6 males, 3 females) (age range 41-79) affected by retroperitoneal fibrosis (6 new diagnoses), were referred to our centre. In 3 patients retroperitoneal fibrosis was associated with autoimmune diseases, in 4 with aortic aneurism, in 2 was "idiopathic". Diagnosis was made by CT scan or MRI techniques; all performed PET/CT scan at referral and during follow-up. Patients were underwent to a tailored treatment: medical therapy (tamoxifen, steroids and immunosuppression) according to disease activity, expected side effects and tolerance, and ureteral stenting in case of obstructive uropathy. PET/CT was performed in all cases, both at time of diagnosis and during follow-up. In presence of disease activity at PET the stents were scheduled for routine substitution every 6 months. Instead the stents were removed when PET did not show signs of disease activity **Results:** PET imaging strictly correlated with disease activity. Seven patients needed ureteral stenting, safely removed at time of negativization of disease activity at the PET. **Conclusion:** PET is a promising tool for surveillance of disease activity and for planning removal of ureteral stents in retroperitoneal fibrosis.

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Use of 18F-Fluorodesoxyglucose PET/CT in patients with suspected Spondylodiscitis: Preliminary results

O. Solà, D. Fuster, A. Soriano, X. Setoain, S. Garcia, J. Mensa, I. Navales, A. Perisnotti, F. Lomena, F. Pons; Hospital Clinic de Barcelona, BARCELONA, SPAIN.

Aim: To prospectively evaluate the usefulness of Positron Emission Tomography (PET/TC) using 18F-Fluorodesoxyglucose in the diagnosis of spondylodiscitis (SD) in comparison to Magnetic Resonance (RM) of the spine. **Material and methods:** Twenty-three patients (11 female, 12 male) aged 54±18 years old with clinical symptoms suggestive of active infection in the spine (3 cervical, 6 dorsal and 14 lumbosacral). Selective MR of the spine and whole-body PET/TC using 370 MBq of 18F-Fluorodesoxyglucose intravenously were performed in all patients. Definitive diagnosis of infection was made by microbiological study or following remission of spinal infection after a 3-month course of SD-specific antibiotics. **Results:** SD diagnosis was confirmed in 13/23 cases (4 *M. Tuberculosis*, 3 *S. Aureus*, 2 *E. Coli*, 1 *E. Faecalis* and 3 cases where the pathogen was not identified). In the remaining 10 patients the diagnosis was degenerative spondyloarthropathy (n=5), vertebral fracture (n=2), plasmocytoma (n=1), metastasis from adenocarcinoma (n=1) and sacroiliac joint infection (n=1). The PET/TC showed pathological uptake in the spine in all SD patients (100%) and in 2 other cases (plasmocytoma and metastasis from adenocarcinoma). The spinal MR was suggestive of SD in 11/13 patients (85%) as well as in 6 other cases (3 spondyloarthropathies, 1 fracture, 1 plasmocytoma and 1 metastasis from adenocarcinoma). Both techniques were able to diagnose the case of sacroiliac joint infection. **Conclusions:** PET/TC appears to be useful in the diagnosis of SD, with a higher specificity than that of MR. Studies with larger cohorts are needed to confirm the usefulness of PET/TC in the clinical management of SD.

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Diagnostic add value of whole-body acquisition during 99mTc-HMPAO-labeled leukocyte scintigraphy

M. Sollini¹, P. A. Erba¹, E. Lazzeri¹, R. Doria², U. Conti³, A. Cataldi¹, R. Boni¹, M. Lisanti⁴, A. Signore⁵, G. Mariani¹; ¹Nuclear Medicine, University of Pisa Medical School, PISA, ITALY, ²Division of Infective Diseases, AOUP, PISA, ITALY, ³Division of Cardiology, AOUP, PISA, ITALY, ⁴Division of Orthopedics, University of Pisa medical School, Pisa, ITALY, ⁵Nuclear Medicine, University of Rome La Sapienza, Rome, ITALY.

White blood cells (WBC) scintigraphy is widely used for the assessment of suspected infections. Although early whole-body (WB) images are generally acquired solely for quality control, those images may have a clinical impact since additional sites of abnormal tracer uptake may be

detected and further evaluated by SPECT-SPECT/CT. To quantify the frequency of early radiolabelled WBC accumulation besides the site of primary suspicion, we evaluated retrospectively 915 scans performed between August 2007 and December 2009 in our center. The study population included 915 adult patients (469 men, 446 women, mean age = 61.1 ± 15.1 years) with known or suspected infection referred for WBC scintigraphy. Indications for WBC scintigraphy were: suspected osteomyelitis or prosthesis infection (59.8%), FUO (13%), suspected endocarditis or cardiovascular device infection (9.5%), vascular prosthesis infection (5.7%), IBD (3.8%), post-operative fever (1.6%), and other indications (6.6%). WBCs were labelled with ^{99m}Tc -HMPAO according to standard procedures and images were acquired 30 minutes, 6 h and 24 h after WBC administration. Patients with FUO were excluded from the analysis. Positive scans were stratified into: 1) WBC accumulation limited to the region of primary suspected infection, 2) localized at both the site of primary infection and any distant sites, 3) only at distant site(s). Standard of reference for confirming the presence or absence of infection was either histopathology or clinical/imaging follow-up. WBC scintigraphy was negative in 49% and positive in 51%. Positivity was limited to the site of primary suspected infections in 64% of cases. WBC uptake both at the site of primary suspicion and at other sites was detected in 24% of the scans, while accumulation solely outside the region of suspicion was present in 12% of the patients. This pattern occurred with high frequency in patients with vascular prosthesis (44%, high frequency of bowel and bone uptake), endocarditis and cardiovascular device (28%, mainly represented by lung, bone and CNS infections), post-surgical fever (28%), and less frequently for orthopedic infections (18%). None of the patients with IBD presented significant areas of WBC uptake outside the abdomen. These data confirm the importance of WB acquisitions when performing WBC scintigraphy not only for quality control purpose, but also for the detection of "metastatic" infection sites. This occurrence is especially important in post-surgical fever and in specific clinical conditions characterized by high frequency of septic emboli, such as endocarditis and cardiovascular device infections, but it is also present in patients with orthopedic infections.

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Comparison between ^{111}In -Biotin SPECT/CT versus ^{18}F FDG PET/TC in spine infection

E. Lazzeri¹, C. Tascini², P. A. Erba¹, R. Doria², M. Sollini¹, G. Mariani¹; ¹Nuclear Medicine, University of Pisa Medical School, PISA, ITALY, ²Division of Infective Disease, AOUP, PISA, ITALY.

Early identification and localization of spine infection is mandatory for the adequate therapeutic strategy. Radiological imaging (including MRI) suffers from low specificity, especially in post-surgical spine infection. Although the best-performing nuclear medicine procedure is ^{18}F -FDG-PET/TC, it has nevertheless low specificity for differential diagnosis. Our group extensively evaluated the potential of infection-specific radiopharmaceuticals, in particular ^{111}In -Biotin in this clinical setting. We recently started a pilot study aimed at comparatively evaluating the performances of ^{111}In -Biotin SPECT/CT and of ^{18}F -FDG-PET/TC for the diagnosis and the determination of spine infection burden. During the last six months we have evaluated 6 consecutive patients referred to our centre for suspected spine infection. All patients underwent both ^{111}In -Biotin SPECT/CT and ^{18}F -FDG-PET/TC in a single day. ^{111}In -Biotin SPECT/CT was acquired 4 hours post i.v. injection of ^{111}In -Biotin, and ^{18}F -FDG PET/TC was obtained 1 hour post i.v. injection of ^{18}F -FDG, which was administered immediately after completing single photon imaging. Final diagnosis was based on bacterial cultures and results of both ^{111}In -Biotin SPECT/CT and ^{18}F -FDG PET/TC classified as True Positive (TP), True Negative (TN), False Positive (FP) and False Negative (FN). ^{111}In -Biotin SPECT/CT showed 2 TN results and 4 TP results. ^{18}F -FDG PET/TC showed 1 FP, 2 TP, 2 FN and 1 TN. The patient who was FP positive with ^{18}F -FDG PET/TC and TN with ^{111}In -Biotin SPECT/CT had lumbar spine metastasis of melanoma. The 2 patients who were FN with ^{18}F -FDG PET/TC and TP with ^{111}In -Biotin SPECT/CT had *Staphylococcus Aureus* infection and *Staphylococcus Aureus* oxacillin resistant infection. In one patient, who was TP with both procedures, ^{111}In -Biotin SPECT/CT showed different localization of infection site (anterior region of the vertebral body) in comparison to ^{18}F -FDG PET/TC findings (centre of the vertebral body). In this small series of patients ^{111}In -Biotin SPECT/CT seems to have higher accuracy than ^{18}F -FDG-PET/TC for both spine infection diagnosis and definition of extent of disease. Such pattern is probably related to the low specificity of ^{18}F -FDG as an infection-imaging agent.

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Predictive value of bone SPECT-CT for chronic pain relief after percutaneous vertebroplasty in vertebral fractures.

M. Solá, R. Pérez, P. Cuadras, R. Díaz, P. Puyalto, V. Vallejos, M. Mila, M. Fraile; Hospital Universitari Germans Trias i Pujol, Badalona, SPAIN.

The increase of life expectancy and the improved oncologic therapies, have resulted in a greater frequency of vertebral fractures secondary to osteoporosis. In the context of minimally invasive therapies, percutaneous vertebroplasty (PV) has demonstrated excellent results in the treatment of chronic vertebral pain. The role of pre-intervention bone SPECT-CT in the management of these patients has not been clearly established. OBJECTIVE: To determine the value of bone SPECT-CT in patient selection, treatment planning and prediction of response to PV. METHODS: We performed a prospective study including 33 patients intended for PV. Clinical evaluation, review of MRI and SPECT-CT results and postprocedure outcome measurements of pain, mobility and analgesic use were evaluated. Bone SPECT was done using a Symbia T2 System with a diagnostic CT. RESULTS: 24 out of 33 patients underwent PV. Positive SPECT-CT images predicted clinical improvement in 91% (21/23) of the patients.

24 PV 9 no PV
23 + SPECT-CT 1 - SPECT-CT 7 + SPECT-CT 2 - SPECT-CT
21 improve 1 persist 7 persist 2 persist

Agreement between SPECT-CT and MRI was 80% (20/25).

PV group	SPECT-CT		non PV group	SPECT-CT	
	+	-		+	-
MRI	+ 12		MRI	+ 5	
	- 3	1		- 2	2

SPECT-CT images described other possible cause of pain such as new fractures or multiple coexisting fractures, bone remodeling in a previous cementated vertebra, facet syndrome and discopathy. On the other hand, positive SPECT-CT was mandatory in 8 patients who could not receive MRI evaluation, all of whom improved after PV. CONCLUSIONS: Percutaneous vertebroplasty is a highly efficient therapy for the relief of chronic pain due to vertebral fractures. Bone SPECT-CT seems a good predictor of postprocedural response. It also adds valuable information to the cause of back pain, and facilitates complete patient evaluation in patients that can not receive MRI.

P60 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized Nuclear Medicine: Bone & musculoskeletal

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Whole body ^{99m}Tc MIBI scan: a potentially useful technique for evaluating metabolic bone disease

A. M. Alshammari, A. H. Elgazzar; Department of Nuclear Medicine, Faculty of Medicine, Kuwait University and Mubarak Al-Kabeer Hospital, Kuwait, KUWAIT.

Introduction: Metabolic bone disease due to hyperparathyroidism is characterized by increased bone resorption and new bone formation. ^{99m}Tc -hexakis-2-methoxyisobutylisonitrile (^{99m}Tc MIBI) accumulation is controlled by metabolic function and cell viability. Few case reports showed increased bone uptake in cases of hyperparathyroidism. The precise mechanisms for the increased uptake of MIBI have yet to be elucidated, but it is likely to occur because of increased perfusion, metabolism, and osteoblastic activity. However, none of the case reports have used quantitative analysis to confirm visual results. The aim of this study was to investigate the potential of whole body ^{99m}Tc MIBI for detecting various bony changes associated with hyperparathyroidism. **Methods:** Eighty six patients with biochemically proven hyperparathyroidism were included in this case-control prospective study. All patients were routinely referred for parathyroid localization. An extra whole body image was acquired and images were assessed visually and by drawing regions of interest over the sternum, femur, humeri, spine and the soft tissue adjacent to the bone. The ratios of bone to soft tissue were calculated and compared to ratios drawn in a control group routinely referred for cardiac imaging and injected with ^{99m}Tc MIBI, after confirming the absence of bone disease. **Results:** The visual interpretation of the scans showed forty eight patients to have increased bone uptake. The quantitative assessment showed significant difference between the mean ratios of femurs, humeri, sternum and spine of the case and control groups. Kruskal-Wallis test showed significant agreement between the visual and quantitative ratios drawn from right and left femur and left humerus only ($P < .05$). **Conclusions:** Whole body images using ^{99m}Tc MIBI are useful in detecting bony changes in long bones of metabolic bone disease associated with hyperparathyroidism. Quantitative analysis can help confirm the visual scan findings.

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Bone scan display modes, should more than one be used for interpretation

S. Alfarsi, A. Elgazzar, H. Alshammari, N. Kazem, A. Omar; Departments of Nuclear Medicine, Faculty of Medicine, Kuwait University and Mubarak Al Kabeer hospital, Ministry of Health, Kuwait, KUWAIT.

Introduction and objectives: Bone scan has been around for decades and there is growing awareness of its expanding application in several skeletal diseases, particularly in benign bone disease. The diagnostic ability of such a simple but valuable modality depends on many factors including spatial resolution, which reflects the detail and sharpness of the image, intrinsic resolution, computers that facilitate data manipulations, contrast, noise, the ability to detect the abnormalities by the interpreting physician and the quality of display which can be manipulated in many ways to aid the interpretation. Linear (white/black) and inverse (black/white) are most commonly used and the preferred one varies among department and readers. The objective of this study was to compare two gray scale display modes (linear and inverse) to find the effect on the physicians' interpretation. **Material and methods:** one hundred cases were chosen retrospectively, 59 males and 41 females in a range of age between 6 months- 88years old. The cases were reviewed by 2 qualified nuclear medicine consultants on two display modes of gray scale Black over white (linear) and white over black (inverse) independently. Each physician determined which mode was better in seeing the findings on the whole body bone scans regardless to the actual patient's complaint. Any disagreements were resolved by a third physician blindly to the other two opinions. The data have been displayed using Xeleris functioning work station at nuclear medicine department, Mubarak Alkabeer Hospital. **Results:** Linear display was better in 27 cases (27%) while the inverse display was better in 23 cases (23%). In the remaining 50 cases (50%) there was no difference. Overall, vertebrae, ribs, knees, feet and shoulders showed better contrast in the linear mode. On the other hand, skull and ankle joint lesions were better seen on inverse mode. Additionally, cold lesion in pelvis and spine was better detected in inverse than linear mode. **Conclusion:** To achieve the best possible diagnostic information from a bone scan the two gray scale display modes should be use rather that only one.

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Scintigraphic patterns of bone metastases in 146 patients with different types of cancers

D. Beiki¹, B. Fallahi¹, M. Khodaparast¹, A. Fard-Esfahani¹, M. Eftekhari¹, M. Saghari¹, V. R. Dabbagh Kakhki²; ¹Research Institute for Nuclear Medicine, Tehran University of Medical Sciences, Tehran, IRAN, ISLAMIC REPUBLIC OF, ²Research Center (NMRC), Mashhad University of Medical Sciences, Mashhad, IRAN, ISLAMIC REPUBLIC OF.

Aim: Bone scan as an appropriate procedure with high sensitivity and moderate specificity is currently accepted by many clinicians for early detection of metastasis; however, characterizing scintigraphic patterns of bone metastases in each type of cancer may still help physicians to improve their skills for more accurate and faultless judgment about the scan findings. **Materials and Methods:** A cross-sectional study was conducted to explore the specific patterns of bone metastases in 146 patients with different types of cancers using a multitude of imaging modalities including bone scan. **Results:** The most common locations of bone metastases on scan images of patients with prostate cancer (71 cases) were pelvis, thoracic vertebrae, proximal femur, ribs and lumbar vertebrae, respectively, which in most cases were not accompanied with significant localized pain. Very intense uptake was noted in about 95% of cases with metastases to the thoracic vertebrae and 50% of cases with metastatic lesions in the common sites of metastasis, i.e. lumbar spine and proximal femoral bone. The most common sites of bone metastases in 61 patients with breast cancer were pelvis and hip, lumbar vertebrae, thoracic vertebrae, ribs, sternum and cervical spine. As well, an intensely higher uptake was observed in most of metastases to the sternum (86%), hip (79%), lumbar and thoracic vertebrae (75–78%); however in contrary to the prostate cancer, in most cases of breast cancer, the skeletal metastasis accompanied by significant localized pain. The most common sites of bone metastasis due to gastrointestinal (GI) cancers were cervical (100%), lumbar (100%), thoracic (84%) vertebrae and sternum (50%) with more intense uptake in all cervical spine and sternal metastases. Localized pain was detected in almost all cases with metastases to the lumbar spine and sternum while the other metastatic lesions were associated with localized symptom in more than 50% of cases with GI cancer. **Conclusion:** The pattern of metastases (common sites, association with localized symptoms and intensity of uptake) are important factors for better characterization of lesions on bone scan as to whether this lesion is truly metastatic or represents a benign lesion.

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The Effects of Different Preserving Media on the Viability and Healing of Free Craniotomy Flaps

M. K. Hamamcioglu¹, A. Sarikaya², C. Kilincer¹, M. F. Firat³, ¹Trakya University Medical Faculty Department of Neurosurgery, Edirne, TURKEY, ²Trakya University Medical Faculty Department of Nuclear Medicine, Edirne, TURKEY, ³Siyami Ersek Hospital Department of Nuclear Medicine, Istanbul, TURKEY.

Craniotomy is the main neurosurgical technique to access intracranial vault. Traditionally, the free cranial bone flap is preserved in saline during the operation. After completion of the operation, the bone flap is secured to its original place, and a fusion is expected. Because osteocytic activity of the flap is affected adversely from *in vitro* conditions, the bone flap preserving method may have some effect on subsequent fusion process. This study aimed to if bone flap preserving method effects subsequent osteoblastic activity of the flap, to compare different methods, and identify the best one in terms of subsequent fusion process. **Materials and Methods** 28 patients who underwent craniotomy for various reasons were included in the study. During intracranial surgery, the free bone flaps were kept in either saline (S) (n=15), blood-wrapped gauze (BG) (n=6), or Euro-Collins® solution (EC) (Fresenius Medical Care, St. Wendel, Germany). The room temperature, opening and closure methods were the consistent and the same for all cases. The craniotomy areas of all patients were evaluated using bone scintigraphy. Scintigraphic uptake values of both centers and peripheries of the craniotomy flaps of the three groups were measured and compared using Kruskal-Wallis test. High level of uptake meant continuing osteoblastic activity, thus incomplete fusion process. **Results** Measurements taken from the center of the craniotomy flap were almost the same. However, measurements taken from the periphery (edges) of the craniotomy flap showed some differences: BG group showed the highest uptake measurement (2,55±1,10), revealing its fusion process was still under way. S group showed lower uptake, thus more complete fusion process (2,11±0,59). EC groups showed the least uptake, thus the most complete fusion process between the three groups (1,64±0,49). However, probably due to small sample numbers, the difference did not reach to statistically significant levels (P=0,101). **Conclusion** The results of the current study suggest that craniotomy flap preserving method may affect the viability of the flap, and subsequent fusion process. EC is one of the promising agent, and it seems to be useful to keep the craniotomy flap viable during the operation, protecting it from the harmful *in vitro* conditions. More studies are needed to prove its definite protective effects.

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Accidental Muscular Tracer Uptake in Bone Scintigraphy is Not Related at all to Rhabdomyolysis

H. F. Sinzinger, P. Haber, A. Staudenherz; Medical University Vienna, Vienna, AUSTRIA.

Muscular uptake by bone seeking agents although rare is a long known phenomenon. Nuclear Medicine textbooks explain muscular tracer uptake in bone scintigraphy after strenuous exercise with rhabdomyolysis. A 34-years old man (hobby marathon runner) showing severe tracer uptake in both the pectoral and the biceps muscles when examined for meniscal lesion and suspected fibrous dysplasia stimulated us to examine the underlying mechanism. He did extensive weightlifting 9, 7, 5 and 2 days before the bone scan and showed local aches. The CK was 7840 U/l at the day scintigraphy was performed. 43 adults (37 m, 6 f, aged 25 - 56 years) performing various sports activities at a top national level undergoing bone scintigraphy for various injuries were retrospectively analysed. Type, intensity and interval to exercise, exercised muscles as well as biochemical parameters including CK, myoglobin, etc. were available. In addition, 35 hobby sportsmen (29 m, 6 f, 34 - 59 years) heavily exercising were studied for comparable indications. All of them performed strenuous exercise regularly until Nuclear Medicine exam. No single top athlete, but 9 of the hobby athletes showed a positive muscle uptake in bone scintigraphy (4 of them after weight lifting) in various muscular groups most heavily exercised. Our findings show that abnormal bone seeking tracer uptake after strenuous exercise has nothing to do with rhabdomyolysis or the extent of CK-elevation. It reflects an individual reaction depending on functional stage, training status, as well as site, type, intensity and interval of exercise. The underlying biochemical mechanism will be presented.

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Evaluation of blood flow using three-phase scintigraphy in patients with diabetic foot syndrome

V. Zavadovskaya, M. Zorkaitsev, O. Kilina, K. Popov, M. Ibraev; SSMU, Tomsk, RUSSIAN FEDERATION.

Purpose: to assess efficacy of three-phase scintigraphy in the evaluation of blood flow in patients with neuropathic, ischemic, and mixed forms of diabetic foot. Material and methods. This study includes the results of three-phase scintigraphy with 99mTc-MDP (740 MBq, SPECT Philips Brightview) of 76 patients (36 males and 40 females, aged 55,2±6,4 years) with diabetes mellitus type I and II, and with suspicion of osteomyelitis in diabetic foot (ischemic form n=13, neuropathic form n=25, mixed form n=38). Results were verified with morphological study in 39 patients. The control group included 57 patients (24 males and 33 females, aged 52,3±4,1 years) without pathological changes in the peripheral regions of the lower extremities. Results. Comparison of arterial blood flow in groups with various forms of diabetic foot showed a significant increase of the entrance time in ischemic (26,2±0,4 sec) and mixed (25,4±0,7) forms (p<0,05) and not significant in neuropathic form (22,06±0,4) compared with the control group. In the second phase of the study (blood-pool) the following types of distribution of radiopharmaceutical in soft tissues were determined: a uniform (n=64, 84,2%; ischemic form n=6, 53,8%, neuropathic form n=21, 84,0%, mixed form n=36, 94,7%), among whom were patients with areas of local hyperfixation of radiopharmaceuticals (n=52, 68,4%, ischemic form n=1, 7,7%, neuropathic form n=21, 84,0%, mixed form n=31, 81,7%) and the presence of «silent» zones (n=12, 15,8%, ischemic form n=6, 46,2%, neuropathic form n=4, 16,0%, mixed form n=2, 5,3%). In the bone phase of the study the following types of distribution of radioactivity were identified: normal accumulation (n=76, 100%), among whom were patients with areas of local hyperfixation of radiopharmaceuticals in the bone tissue (n = 61, 80,3%; neuropathic form n=23, 92,0%, mixed form n=38, 100%). Comparison of scintigraphy and morphological studies confirmed the highly informative three-phase scintigraphy in the evaluation of main and peripheral blood flow. Thus, in patients with diabetic foot the depression of the main vessels blood flow and blood flow prevail the changes of intraosseous blood flow. Conclusions. Three-phase scintigraphy is high-performance method in revealing the arterial and peripheral blood flow disorder in patients with diabetes mellitus. The observed preservation of blood flow in bone tissue makes it possible to expand the employment of methods of nuclear medicines and apply scintigraphy with labeled leukocytes for indicating purulent infection in patients with complicated course.

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Increased extraosseous 99m-technetium hydroxy diphosphonate uptake in chronic kidney disease patients with secondary hyperparathyroidism. Correlation with hyperphosphatemia

L. H. Enevoldsen¹, J. Hea², P. Hasbak³, ¹Bispebjerg Hospital, Copenhagen, DENMARK, ²Herlev Hospital, Herlev, DENMARK, ³Rigshospitalet, Copenhagen, DENMARK.

Aim: In bone scan patients with end stage renal disease and hyperparathyroidism, soft-tissue accumulation of ^{99m}technetium hydroxy/methylene diphosphonate (^{99m}Tc-HDP/MDP) have been reported primarily in case reports and usually explained by hypercalcemia and/or hyperphosphatemia. Recent evidence indicates that human vascular smooth muscle cells produce hydroxyapatite during cell culture with increased phosphate levels. As ^{99m}Tc-HDP/MDP primarily binds to hydroxyapatite we hypothesised that soft-tissue accumulation would be found in patients with hyperphosphatemia. **Materials & Methods:** Retrospectively, we identified 63 chronic kidney disease (CKD) patients, who were diagnosed with secondary hyperparathyroidism and consecutively admitted to our department for total body ^{99m}Tc-HDP bone scan over a 3 year period. Age, gender, vintage (time since initiation of dialysis), treatment modality, presence of ischemic heart disease (IHD), peripheral arteriosclerosis and mean concentrations of the biochemical markers (carbamide, creatinine, electrolytes, parathormone, calcium, phosphate, albumin, haemoglobin, bicarbonate, alkaline phosphatase) taken 0-3 months prior to the bone scan were evaluated. Results: Soft tissue uptake were detected in 37/63 (59%) patients. Primary locations were in the heart (27/37 = 73%), muscles (12/37 = 32%), lung (9/37 = 24%) and stomach (6/37 = 16%), whereas 13/37 (35%) patients had simultaneous uptake in more than one location. Regarding biochemical markers, patients with soft-tissue uptake differed from patients without only in terms of plasma phosphate levels (1.95 ± 0.15 (n=37) vs. 1.27 ± 0.08 mM (n=26), p = 0.0012), whereas total plasma calcium (2.12 ± 0.04 vs 2.42 ± 0.07 mM) and ionized plasma calcium concentrations (1.18 ± 0.04 vs 1.30 ± 0.04 mM) were normal, and identical, between groups (p > 0.05). Furthermore, all patients with myocardial uptake (n = 27) had a coronary arteriography verified history of IHD, whereas IHD was present in only 6 of the 36 patients without myocardial uptake. **Conclusion:** In conclusion, CKD patients with secondary hyperparathyroidism have a high incidence of soft-tissue accumulation of ^{99m}Tc-HDP and this finding is strongly correlated to elevated phosphate, but not calcium values.

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Findings of Bone Scintigraphy After Hirudotherapy

S. Ozyurt, G. Koca, A. Comak, M. Korkmaz; Health of Ministry, Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara, TURKEY.

INTRODUCTION: Hirudotherapy is used as an alternative treatment method since years, even though its therapeutic effect hasn't been fully understood. It has a wide field of application in cardiovascular diseases, muscular skeletal system and in many diseases (rheumatologic diseases, tendonitis, arthritis ...) and today most commonly used in treatment of pain. Three-phase or 4 phase dynamic bone scintigraphy is a sensitive distinguishing technique between osteomyelitis / soft tissue infection, which is highly important in the determination of the patient's treatment protocol. CASE: 70 years old female patient with left leg and left ankle pain and swelling complaints was referred to our clinic with pre-diagnosis of osteomyelitis or RSD. She had broken her left ankle 8 years ago and operated two times from her ankle. In physical examination she was obese and there was mild hyperemia in her left leg compared to its symmetry without significant temperature rise in her left leg but she was commonly walking on her right leg. In the

lateral region of her left ankle there was an incision scar and in the 1/3 proximal region of her left leg there was 2 or 3 lesions cruted. In dynamic bone scintigraphy there was increased perfusion and hyperemia in her left ankle and her left leg in collimators field of view compared to their symmetry but there was no significant accumulation of the radiotracer in old fracture region. In late bone static images, taken at 3 and 24 hours, there was no pathologic radioactivity accumulation signifying infection. We commented on the increased perfusion and hyperemia at dynamic and blood pool images in her left ankle and her left leg as a nonspecific uptake related with venous circulation disorders. But in patient's superficial lower extremity and doppler US, the venous structures were totally normal. We decided to ask further questions about her leg and found out that she had her leg hirudotherapy (Leech therapy) application 4 times within last month which could clarify the increased perfusion and hyperemia in dynamic and blood phases of bone scintigraphy. **CONCLUSION:** In nuclear medicine clinics while preparing reports and making interpretation of the scintigraphic findings the contribution of the history and physical examination of the patient is crucial. Depending on dilation effects of hirudotherapy in superficial veins, it may lead an increase in perfusion and hyperemia in blood pool phases of bone scintigraphy which might be confusing in differential diagnosis.

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The value of bone scintigraphy in the postoperative follow-up of patients with renal cell cancer

J. Zhang, R. Wang, Z. Fu, Y. Fan, X. Zhang, F. Guo, Y. Wang, G. Zhao, H. Tian; Department of Nuclear Medicine, Peking University First Hospital, Beijing, CHINA.

Objective: Renal cell cancer(RCC) is the most common malignancy arising from the kidney and bone is a major site of haematogenous spread. Diagnosis of bone metastases could allow the initiation of therapy before skeletal complications occur, thereby possibly delaying their onset. The aim of present study was to investigate the value of bone scintigraphy in the postoperative follow-up of patients with RCC. **Methods:** To analyze the bone scintigraphy of postoperative patients with RCC retrospectively, and to determine bone metastases on the basis of pathology, CT, MRI and bone scintigraphy. **Results:** In all, 26 patients were identified with skeletal metastases among the 78 patients evaluated(33%; 20 men and 6 women, median age 57 years) between March 2002 and December 2008. Renal cell histology was clear cell in 19 patients, papillary type in 4, sarcomatoid RCC in 2 and cystic RCC in 1. Seven patients had single bone metastases, 19 had multiple bone metastases. One patient had osteolytic lesions, 3 cases had osteolytic and osteoblastic lesions, 22 patients had osteoblastic lesions. 22 patients had bone pain, the other 4 patients had no bone pain. The most common sites of bone metastases in order of frequency were lumbar vertebra(13/26), pelvic bones (11/26), ribs (11/26), femur (8/26) , humerus(5/26), thoracic vertebra(4/26), skull(3/26), sternum(2/26), scapula(2/26) and calcaneus(1/26). **Conclusion:** Bone scintigraphy can detect bone metastases of postoperative patients with RCC in the early stage, those who have bone pain should undergo bone scintigraphy as early as possible. [Key words]: Renal cell cancer; Bone scintigraph; Bone metastases; Bone pain

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SUV evaluation of normal bone in oncologic patients undergoing 18F-fluoride PET/CT study

S. Moisan, S. Beaulieu, C. Cohade, L. Boucher; Montreal University Health Centre, Montreal, QC, CANADA.

Objective: 18F-fluoride PET/CT studies are increasingly used for the assessment of oncologic patients. However, SUVs of normal bone are not known in this population. Our main objective was to determine the SUV reproducibility of different bone structures. We also looked for a possible relationship between SUV and some clinical data. **Methods:** We retrospectively reviewed 18F-fluoride PET/CT studies performed on a 3D Philips PET/CT camera of 40 oncologic patients and their medical charts. Bones with visually abnormal 18F-fluoride uptake or structural abnormality on CT were excluded. We chose 26 bony structures throughout the body and multiple SUV (max and mean values) were obtained at each site, with special attention to select the same location for each patient. We collected 108 ROIs on different bone structures for each patient. The ROI was first drawn on the CT image and then copied on the corresponding metabolic PET image. Statistical analysis using intraclass correlation coefficient (ICC) and Pearson's correlation coefficient was performed. **Results :** Overall, there was a better reproducibility for mean SUV compared to max SUV, with significant results for the following structures: lumbar vertebral body (mean SUV: 5.90; ICC 0.918); thoracic vertebral body (6.50; 0.914); femoral head (2.37; 0.913); femoral diaphysis (2.09; 0.906) ischial tuberosity (3.88; 0.899); humeral head (1.88; 0.890); sternum (3.33; 0.847); skull (1.32; 0.844) and humeral diaphysis (1.50; 0.806). There was good reproducibility with Pearson's analysis for femoral neck(mean SUV 2.77; Pearson 0.953) and pubic symphysis (3.93; 0.880). There was a correlation between mean SUV and increasing time between tracer injection and imaging, significant for 9 structures. There was also an inverse correlation between mean SUV and age, significant for 8 structures. **Conclusions :** Mean SUV has proven reproducible for the aforementioned bone structures. Our data may prove useful to differentiate abnormal from normal bone metabolism in various pathological conditions, such as metabolic disease.

P703

Hand bone densitometry correlates well with lumbar and femoral ones in a population of patients with established Rheumatoid arthritis

H. Fernandes, M. Bernardes, P. Oliveira, T. Vieira, G. Terroso, A. Oliveira, M. Perez, F. Simões Ventura, J. Pereira; Hospital de S. João, Porto, PORTUGAL.

Aim: Periarticular osteoporosis is an early finding in the hands of patients with Rheumatoid arthritis (RA), due to the release of bone resorbing cytokines from the inflamed synovium. Hand dual energy x-ray absorptiometry (DEXA) provides a very sensitive tool for measuring bone loss in RA and may be useful in identifying patients at high risk of developing progressive disease. A few studies showed a significative correlation between the bone mineral density (BMD) measurements of hand and lumbar spine/femoral. The purpose of this study was to correlate the

hands BMD values with the ones obtained in the lumbar spine and proximal femur, as well as to determine the osteoporosis prevalence in a population of patients with established RA. **Materials and Methods:** BMD values, T and Z scores were obtained with a LUNAR Expert 1320^o in patients with established RA at lumbar spine, proximal femur, both hands and 2th proximal phalanges. SPSS14.0 was used for statistical data analysis. **Results:** We prospectively evaluated 97 patients, 77 women (79%), with mean ages of 53±12 years, 16±11 years of disease duration and 26,75±4,54 kg/m² of body mass index. All patients were medicated with corticosteroids (dose inferior to 7,5mg/day) and 62 (64%) with biological agents, mainly under TNFalpha blockers. At lumbar spine, 43% (42) of the patients had abnormal results; 10% (10) had mild osteopenia, 4% (4) moderate osteopenia, 16% (15) severe osteopenia and 13% (13) had osteoporosis. At proximal femur, 36% (35) of the patients had abnormal results; 13% (13) had mild osteopenia, 8% (8) moderate osteopenia, 7% (7) severe osteopenia and 7% (7) had osteoporosis. We verified a positive correlation between the BMD obtained in both hands and the second proximal phalanges with the BMD of lumbar spine and femur.

Anatomical sites	Spearman Correlations (BMD) (r = correlation coefficient; p<0,001 = level of significance)			
	Proximal Femur	Femoral neck	Wards triangle	Lumbar spine
Right hand	r= 0,697	r= 0,651	r= 0,620	r= 0,671
Left hand	r= 0,686	r= 0,655	r= 0,615	r= 0,638
2 th right proximal phalange	r= 0,622	r= 0,634	r= 0,631	r= 0,676
2 th left proximal phalange	r= 0,687	r= 0,709	r= 0,708	r= 0,711

We also verified a strong positive correlation between proximal femur and lumbar spine BMD (r=0,693; p<0,001). **Conclusion:** In our patient's population a strong positive correlation between BMD measurements of both hands and the values of BMD of the femur and lumbar spine were found. Other studies are needed to determine the role of the bone loss in the hands as a prognostic factor among patients with RA.

P704

Pilot assay for comparison of bone mineral density and genetic polymorphisms in patients with risk of hip fractures

K. P. Rojo, M. Aguilera, M. Cañadas, J. López, M. Navarro-Pelayo, J. Llamas, A. García, M. A. Calleja; Hospital Virgen de las Nieves, Granada, SPAIN.

Objective: To select a set of single nucleotide polymorphisms (SNPs) putative involved in the risk of hip fractures (HF) according to the recent literature and investigate the association between bone mineral density (BMD) values and these gene polymorphisms in our group patient population. **Methods:** bibliographical search was performed in different databases (PubMed, PharmGKB, among others), focused on the clinical impact of SNPs in Caucasian populations with osteoporosis and HF, affecting femoral neck BMD. Nineteen patients (female) having risk of HF were recruited. Epidemiologic data were collected. The genotypes of the selected candidate SNPs (OPG-163, CaSR986/990/1011; VDR-BsmI) were analyzed by polymerase chain reaction and restriction fragment length polymorphism. **Results:** According to the literature reviews, most relevant SNPs involved in HF-risk and BMD-value belong to pathways related to Osteoclastogenesis (rs3102735; rs9533155), Wnt (rs3736228, rs4988321), Vitamin-D Receptor (rs7975232; rs11568820; rs731236), Estrogen, Collagen-1A (rs1800012), Calcium-Sensing Receptor (rs1801725; rs1042636; rs1801726) and Mevalonate (rs2297480). The mean age of the patients was 65 years. The frequencies for each SNP, classified by the BMD-value, are showed in Table 1, with their respective alleles. Table 1: Frequencies for selected candidate SNPs (number of patients)

	CaSR986 rs1801725	CaSR990 rs1042636	CaSR1011 rs1801726	VDR-BsmI rs1544410	OPG-163 rs3102735											
	GG	GT	TT	AA	AG	GG	CC	CG	GG	GA	AA	CC	CT	TT		
NF	OP	10	3	1	13	2	0	15	0	0	8	7	1	0	0	12
	OT	2	0	0	2	0	0	1	1	0	1	2	0	0	1	6
LS	OP	7	2	1	8	2	0	10	0	0	6	5	1	0	0	16
	OT	5	1	0	7	0	0	6	1	0	3	4	0	0	1	2
Total		16 patients	17 patients	17 patients	19 patients	19 patients										

NF: Neck femoral, LS: Lumbar spine, OP: Osteopenia, OT: Osteoporosis. No statistical association between osteoporosis and the SNPs analyzed was found (p>0.05 in all cases). **Conclusion:** the main candidate pathways involved in HF-risk and BMD-value were Osteoclastogenesis, Wnt, Vitamin-D Receptor, Estrogen, Collagen-1A, Mevalonate. In our population sample, there is not any association between osteoporosis and the SNPs analyzed, maybe due to the small number of patients. It will be necessary to develop larger studies to evaluate this possible association.

P705

Bone mineral density in patients with neurodegenerative versus non-degenerative parkinsonism as diagnosed by ¹²³I-ioflupane brain scintigraphy

A. Arka, T. Exarchopoulos, A. Georgiou, S. Tsiouris, S. Konitsiotis, C. Sioka, A. Papadopoulos, J. Calef-Ezra, J. Al-Boucharali, C. Bougias, A. Kyritsis, A. Fotopoulos; University General Hospital of Ioannina, Ioannina, GREECE.

Aim: Numerous recent reports suggest an increased prevalence of osteopenia and osteoporosis in patients suffering from Parkinson's disease (PD). However, PD in those studies has been established on the basis of clinical criteria (Hoehn and Yahr scale), with no imaging confirmation of neurodegeneration that would also allow its separation from non-degenerative movement disorders like essential tremor (ET) or drug-induced tremor. The aim of this study was to estimate the levels of bone mineral density (BMD) in patients with neurodegenerative parkinsonism (PD and/or the much less frequent parkinson-plus syndromes -- Group A), as compared to non-degenerative parkinsonism (ET, drug-induced tremor etc. -- Group B). **Materials and Methods:**

We studied 66 parkinsonian patients (42 men, 24 women, aged 67.8±11.0 years [mean ± SD]) referred to our department for presynaptic dopaminergic brain scintigraphy by ¹²³I-ioflupane (DaTSCAN™). All participants enrolled were free from any other condition that could affect BMD and were classified in Groups A or B according to brain scan results. Prior to radiopharmaceutical administration for brain imaging we measured the BMD in lumbar spine and hip by dual-energy X-ray absorptiometry (DXA). The Z-score and T-score were calculated to diagnose subnormal BMD (values between -1.5 and -2.5 suggested osteopenia and below -2.5 osteoporosis) and were compared between the two patient groups (independent t-test, level of significance set at 5%). Results: 42 patients were diagnosed as neurodegenerative parkinsonics (Group A); the remaining 24 cases provided normal brain scan (Group B). The two groups were comparable as regards age (68.7±9.7 vs. 66.3±13.0 years respectively) and no significant BMD differences were found between them (Z-score: -[0.55±1.05] vs. -[0.67±0.90] respectively, *p*=0.635; and T-score: -[1.89±0.90] vs. -[1.92±1.00] respectively, *p*=0.917). Conclusion: Neurodegenerative parkinsonism does not seem to have any increased negative influence on BMD when compared to non-degenerative disorders like essential or drug-induced tremor. Limited normal motility is probably responsible for the increased prevalence of osteopenia and osteoporosis associated with such movement disorders.

P706

Gamma probe guided surgery for osteoid osteoma

S. Isgoren¹, G. Daglöz Gorur¹, M. A. Oc¹, E. Alkan Ciftci¹, M. Gur¹, H. Demir¹, L. Buluc²; ¹Kocaeli university department of nuclear medicine, Kocaeli, TURKEY, ²Kocaeli university department of Ortopedics, Kocaeli, TURKEY.

Osteoid osteoma is a benign skeletal tumor. Approximately two thirds of them are located in the appendicular skeleton. The classic presentation is that of focal bone pain at the site of the tumor. The pain worsens at night and increases with activity; it is dramatically relieved with small doses of acetylsalicylic acid. Radiography and radionuclide bone scan are effective to show the nidus and to diagnose the osteoid osteoma. Radionuclide bone scan demonstrates a fairly intense radiotracer accumulation at the nidus. Complete nidus resection is the standard treatment of this tumor. Nevertheless, localization of nidus may be difficult, and may require more invasive procedures to ensure complete resection. In this study, we report 5 osteoid osteoma cases that the nidus detected intraoperatively by gamma probe guided and surgically removed. Five patients those had osteoid osteoma localization verified preoperatively by radionuclide bone scan were included. Characteristics of the patients are summarized in Table 1. Two hours before the surgery Tc-99m MDP was injected and patients were escorted to the surgical room. The affected bone region was uncovered with retractor and the area giving a maximum counts is detected by using gamma-probe and resected. The detected counts were recorded (Table 1). Gamma probe guided surgical removal of the tumors allowed pain relief of all the patients without any complication. Gamma probe guided surgical excision facilitates accurate localization of lesion and perform an effective removal of the nidus. This less invasive approach warrants minimal bone resection, reduces risk of pathological fracture and the recurrence rate.

Table 1: Patient characteristics and gamma probe counts per second (cps)

Patient	Patient characteristics			Gamma probe counts (cps)			
	age	sex	region	Nidus (in vivo)	Normal bone (in vivo)	Nidus (ex vivo)	Post-resection region area
1	43	M	Femur	1880	520	923	610
2	10	M	Femur	580	335	180	340
3	18	M	Femur	635	270	280	250
4	35	M	Humerus	1880	420	712	490
5	13	F	Femur	422	186	220	200

P707

Prediction of bone loss using biochemical markers of bone remodeling in patients with multiple sclerosis

M. Assadi¹, H. Salimipour², I. Nabipour¹, Z. Samani¹, R. Nemati², M. Seyedabadi¹; ¹Bushehr Research center for Nuclear Medicine, The Persian Gulf Biomedical Sciences Institute, Bushehr University of Medical Sciences., Bushehr, IRAN, ISLAMIC REPUBLIC OF, ²Department of Neurology, Faculty of Medicine, Bushehr University of Medical Sciences, Bushehr, IRAN, ISLAMIC REPUBLIC OF.

Aim: Bone mineral density (BMD) was known to be lower in multiple sclerosis (MS) patients at both the lumbar spine and hip. Several factors have been shown to be related to osteoporosis and MS including Matrix metalloproteinase 9 (MMP-9), Osteopontin (OPN), Osteocalcin (OC), receptor activator of nuclear factor Kappa-B ligand (RANKL), osteoprotegerin (OPG), C-reactive protein (CRP), PTH and Vitamin D. Interferon beta-1b (IFN beta 1-b) is one of the medications that is applied in the management of MS and has been shown to ameliorate disease activity and inhibit osteoporosis. The aim of this study was to investigate the effects of IFN-1b1 and IFN-1ba plus Ca-Vit D3 on BMD, EDSS and the abovementioned factors in MS patients. Materials & Methods: Thirty-six patients with chronic progressive MS who have been receiving IFN beta-1b or IFN beta-1b plus VitD3-Ca were enrolled as a target group and 38 age and sex matched cases were considered as a control group in the study. The level of serum CRP, MMP-9, OPN, OC, RANKL and OPG were investigated by ELISA. BMD was measured by dual-energy x-ray absorptiometry. Results: BMD of L4 were lower in MS patients receiving IFN beta-1b or IFN beta-1b and VitD3-Ca in comparison to control (*p*<0.01), but there were no significant difference in BMD of femur neck, wards triangle, greater trochanter, L2, L3, L4 and total lumbar. We did not observe any difference in hsCRP, MMP-9, OPN, OPG, RANKL, OC and Vit D3. However PTH levels were significantly lower in MS patients receiving IFN-1ba plus Ca-Vit D3 compared to control (*P* < 0.05). Multiple linear regressions revealed that BMI was positively correlated with BMD in femur neck ($\beta=0.27$; *p*=0.026), greater trochanter ($\beta=0.32$; *p*=0.007), L2 ($\beta=0.31$; *p*=0.01), L4 ($\beta=0.4$; *p*=0.0) and lumbar ($\beta=0.4$; *p*=0.001). In multivariate linear analysis, after BMD adjustment for BMI as covariate, it was observed that OPG were independent predictor of BMD in L4 ($r=0.78$; *p*=0.02) and Lumbar ($r=0.74$; *p*=0.03), MMP-9 was correlate with lumbar BMD ($r=0.731$; *p*=0.046), and PTH with BMD L3 (0.647; *p*=0.008). Conclusion: We found that patients receiving

IFN-1b1 or IFN-1ba plus Ca-Vit D3 show ameliorated BMD and other factors associated with osteoporosis in MS.

P708

The Evaluation of Three-phase Bone Scintigraphy in Diagnosis and the Efficiency of the Treatment in Reflex Sympathetic Dystrophy

I. Alic Ozaslan¹, F. Uzun Yenici²; ¹Bagcilar Training and Research Hospital, Istanbul, TURKEY, ²Sisli Etfal Training and Research Hospital Nuclear Medicine Clinic, Istanbul, TURKEY.

Objectives: To investigate the quantitative evaluation of three phase bone scintigraphy in diagnosis and in the efficiency of the treatment patients having reflex sympathetic dystrophy (RSD) at the upper extremity. **Material and Methods:** Three-phase bone scintigraphy is performed to 17 prediagnosed patients who suffer from stage-1 RSD at upper extremity and to 10 people who don't have any upper extremity pathology from control group. After one month therapy, three-phase bone scintigraphy of 17 prediagnosed patients is repeated. Images are evaluated visually and quantitatively in the late static phase. In the quantitative evaluation of two different methods are applied. The first method: Symmetrical region of interest (ROI) from wrist and MKP (metacarpofalangeal) region mean count ratios are calculated and compared with the ones before the treatment and with the ones of control group. The second method: Symmetrical rectangular ROI is taken, mean count ratios are calculated and compared with the ones before the treatment and with the ones of control group. **Results:** In the statistical evaluation of, mean count rates are observed as below; **Wrist ROI** pretreatment: 2,76 post treatment: 2,29 (*p* < 0.001) ; **MKP** (metacarpofalangeal) pretreatment: 2,35 post treatment: 2,12 (*p*<0.001). **Symmetrical rectangular method** pretreatment: 2,11 post treatment 1,82 (*p*<0.001). Pretreatment and post treatment mean count rates are high compared to control group. Wrist counts and symmetrical rectangular counts significantly decrease compared to pretreatment counts but the change of MKP (metacarpofalangeal) counts aren't appreciable compared to pretreatment ones. Symmetrical rectangular method is more considerable than the others. **Conclusion:** As the results are found concordant with the clinical signs, three-phase bone scintigraphy and late static phase quantization are significant in the diagnosis and the evaluation of treatment efficiency of stage-1 reflex sympathetic dystrophy at upper extremity.

P61 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Conventional/Specialized Nuclear Medicine: SLN (Sentinel Lymph Node)

P709

Size of colloid particles: how it can influence efficacy of sentinel lymph nodes biopsy?

S. Kanaev, S. N. Novikov, M. Girshovich, L. Jukova, A. Barbashov; N.N. Petrov Inst. Oncol., St. Petersburg, RUSSIAN FEDERATION.

Aim of the study: to evaluate efficacy of sentinel and second echelon lymph nodes (LN) visualisation in relation to diameter of injected radiocolloids. **Material & Methods:** Lymphoscintigraphy was performed in 122 patients (pts) with breast cancer: nanocolloids (NC) (d<80 nm) were used in 89 pts, large particles (LP) with diameter 200-1000 nm - in 33 pts. Early (3-60 min) and delayed (240-720 min) LN images were obtained after intratumour injection of 75-150 MBq (0.5-1 ml) of radiocolloids. Afterward we compared results of LN and lymph flow visualisation with LP and NC. **Results:** After NC injection sentinel LN detected in 83/89 cases. 5 of this 6 pts with non-visualised LN had extensive LN invasion by metastases. In in 1 case the reason for lymph flow block was unknown. Efficacy of NC for detection of sentinel LN without massive invasion reached 98.9%. LN visualisation after LP injection was successful in 27 of 33 pts. Only 1 of 6 pts with non-visualised LN had sings of metastatic invasion. Efficacy of LP for sentinel LN detection (84.8%) was significantly lower than efficacy of NC (*p*<0.05). Lymph flow patterns visualised with NP were as follows: only axillary (AX) region in 44.2%, AX +sub-supraclavicular (SCL) - 24.4%, AX + internal mammary (IM) - 16.3%, AX + IM + SCL - 15.1%. After LP injection most pts (85.1%) had lymph flow only to AX region, 11.1% - AX + IM, 3.7% - AX + SCL. Differences are highly significant ([[Unsupported Character - р]] = 0.0104). **Conclusion:** Size of radiocolloids strongly influences patterns of lymph flow from the tumor and efficacy of sentinel LN visualization. We recommend NC for routine use in clinical practice.

P710

Visualisation of internal mammary (IM) lymph nodes (LN) in patients with breast cancer: correlation with primary tumour localisation.

S. Novikov, M. Girshovich, S. Kanaev, O. Zotova, A. Barbashov, V. Semiglazov; N.N. Petrov Inst. Oncol., St. Petersburg, RUSSIAN FEDERATION.

Aim of the study: to evaluate hypothesis that localisation of primary breast cancer influence topography of sentinel LN revealed in internal mammary region. **Material and methods:** LN visualisation was performed in 84 primary breast cancer patients. LN scintigraphy in anterior projection was performed 30-60 and 240-360 min after intratumoural injection of 75-150 MBq (0.5-1 ml) of 99mTc-nanocolloids. All LN visualised in internal mammary region were considered as sentinel LN. Their topography was determined as number of LN in each intercostals space. The tumour location was classified as inner or outer in the upper or in the lower quadrant. **Results:** Lymph flow to IM LN revealed in 27 of 84 (32.1%) evaluated patients. In absolute values most of them (15) had tumours in external and 12 - in internal quadrants. Relative frequencies of lymph flow to IM LN were as follows: 39% - for tumours localised in internal and 22.9% - in external quadrants. It is assumed that lymph flow from lower quadrants is limited by III-V intercostals spaces. We found that 2 of 4 patients in this group had IM LN in I-II intercostals spaces. On the contrary, 10 of 22 patients (45%) with tumour in the upper quadrants had IM LN in the III-V intercostals spaces. In absolute values distribution of visualised IM LN in patients with tumour in

the lower quadrants was as follows: I intercostals space -1, II-2, III - 3, IV - 1, V - 0 IM LN. In patients with tumour in the upper quadrants: I intercostals space - 4, II-9, III -9, IV -6, V - 2 IM LN. In 24 of 27 (89%) cases IM SLN were localised only on the side of primary tumour and in another 3 - on both sides from the sternum. **Conclusion:** 1. More than a half of patients with sentinel LN visualised in IM region had primary tumour in external quadrants of the breast. 2. IM LN more frequently detected in patients with tumours localised in internal quadrants. 3. There are no significant differences in frequencies of lymph flow to each intercostals space from tumours of upper and lower breast quadrants.

P711

Sentinel lymph node biopsy for staging oral squamous cell carcinoma

S. Rodríguez Martínez de Llano¹, I. Candal Casado¹, B. Patiño Seijas², P. Pais Silva¹; ¹Centro Oncológico de Galicia. Nuclear Medicine., La Coruña, Galicia, SPAIN, ²Hospital Universitario Juan Canalejo. Maxillofacial Surgery., La Coruña, Galicia, SPAIN.

Introduction The presence of lymph node metastases in oral squamous cell carcinoma is the most important prognostic factor. 30% -40% of patients with cN0 (clinical node negative) staging, obscure lymph node metastases. Objectives To determine whether sentinel node biopsy reduces the incidence of elective neck dissection required in management of patients with cN0 staging and to determine the sensitivity and negative predictive value of this technique. **Material and Methods** 67 patients with oral squamous cell carcinoma (cN0) were included. Preoperative lymphoscintigraphy was performed in all cases within 24 hours of surgery. A total volume of 0.4 ml of radiocolloid was injected into submucosa around the primary tumor (37 MBq) in four sites. 30 patients underwent resection of the primary tumor and sentinel node biopsy, the other 37 patients held elective neck dissection (END) in addition to this. Results The tongue was the most frequent location (55.2%) followed by the floor of the mouth (17.9%), lower lip (10.4%), gingiva (2.98%) and buccal mucosa (13.4 %). 31 patients had stage T1, 32 had T2 and 4 had T3. The overall identification rate was 58/67 (86.5%). 86 sentinel nodes were detected in 58 patients (1.48 per patient). 9 of them had tumor-positive sentinel nodes, with primary tumor in the tongue (N = 8) and oral mucosa. Histological examination showed sentinel node micrometastases in 5 cases and one case was positive after immunostaining. In 9 patients where the sentinel node was located, 3 had occult metastases. The occult metastasis rate was 16,41%. The sensitivity of the technique was 90% and negative predictive value (NPV) was 96%. The false negative rate was 2.7% when associated with END and 3.3% when not. **Conclusions** Our study seems to confirm the utility of sentinel node biopsy in squamous cell carcinoma of the oral cavity. In our opinion, the technique in the staging is technically feasible, accurate and minimally invasive, with a high NPV, which supports its sole use.

P712

The role of sentinel node biopsy (SNB) in breast cancer.

E. Del Giudice, G. Pontone, G. Rauli, A. Pellegrini, R. Bonsanto, C. Cappelli, C. Corbelli; Faenza Hospital, FAENZA, ITALY.

Aim: Axillary lymph node status represents the most important prognostic indicator of progression and survival in breast cancer. The aim of this study was to identify the patients with breast cancer and sentinel node metastases who will benefit by axillary lymph node dissection. **Materials and methods:** From January 2006 to December 2009, we examined 900 consecutive patients that presented a breast lesions with a diameter between 3-20 mm, with clinically negative axillary node. 220 patients presented non palpable breast lesions: in this patients the day before intervention we injected 7-10 MBq of human albumin macroaggregates (MAA) labelled with 99mTc in 0.2 ml of saline, under ecographic guide. In all patients we injected 20 MBq of nanocolloid-99mTc in 0.4 ml of saline. Lymphoscintigraphy was performed after 30 minutes to 1 hours taking planar anterior and lateral views to reveal SN. The skin projection of SN and the injection site were marked on the skin with ink. **Results:** gamma probe was used to locate the breast lesion and guide its removal; breast lesion was localized in all cases and were removed radically with negative margins in 855 (95%). Non palpable breast lesions were excised in all (220) patients. The definitive histology revealed 750 ductal invasive carcinomas (83%), 85 lobular carcinomas (9%), 25 mucinous carcinomas (3%), 22 fibroadenomas (3%) and 18 ductal carcinoma in situ (2%). SN was detected in 878 cases (100%). SN was positive in 216 of 878 pts (24%). Occult metastases included isolated tumor cells (ITC) and micrometastasis (MM) were detected in 51 of 216 patients (23%) and macrometastasis in 165 of 216 (77%): in this last patients complete three-level lymphadenectomy were performed. Of the 51 patients ITC+ and MM+ 40 had axillary complete dissection (AD); 39 had metastatic tumor cells in only one lymph node (SN); 1 patients had micrometastasis in sentinel node and macrometastasis were found in 2 other axillary lymph node. 11 patients had only systemic adjuvant therapy. **Conclusions:** sentinel node biopsy provide accurate staging information in breast cancer and reduce morbidity compared with complete axillary lymphadenectomy. Our experience confirm that radio-guided surgery is a simple and fast technique that enables the lesion to be safely excised. Breast lesion and SN can be carried out in the same intervention with satisfactory results and several advantage. The clinical relevance of isolated tumor cell and micrometastasis in axillary lymph node remain unknown.

P713

Fully automated sentinel-lymph-node detection software for breast- and prostate-cancer patients using SPECT/CT-studies

U. Luetzen¹, N. Zsoter², E. Bernhard¹, I. Garai³, M. Zuhayra¹, C. Arslanemir¹, L. Papp²; ¹University Clinic Kiel, Nuclear Medicine Department, Kiel, GERMANY, ²Mediso Medical Imaging Systems Ltd., Budapest, HUNGARY, ³PET-CT Medical Diagnostic Ltd, Medical University of Debrecen, Debrecen, HUNGARY, ⁴University Clinic Heide, Nuclear Medicine Department, Heide, GERMANY.

Aim: In nuclear medicine sentinel-lymph-node (SLN) examinations are standard procedures. The common way of interpretation is the visual analysis of the images by nuclear medicine specialists. The SPECT/CT-data analysis depends solely on the examiner's experience and is very time-

consuming. Therefore our goal was to design a fully automated post-processing-method which detects, classifies and quantifies SLN on SPECT/CT-studies. The clinical investigation of the method was performed on data, taken from breast- and prostate-cancer patients. Results show that the method successfully fulfilled its requirements on both patient groups. **Methods:** We collected 72 reconstructed SPECT/CT-datasets of each entity. The SPECT/CT-data were acquired 0.5-2 hours after injection of 30-150 MBq of 99mTc-Nanocolloid, by using a SPECT/CT-camera-system (Symbia T, Siemens). The implementation and the validation of the automated method were performed in InterView Fusion software manufactured by Mediso. Two masks were automatically segmented from the CT representing the region of the body and the bones. Based on the body mask a threshold for the background noise level was determined in the SPECT. In order to merge separate hot spots of the injection into one region, another threshold value was determined and applied automatically by the method. The rest of the detected hot spots in the SPECT were quantified by calculating their volume/mean/std.dev/min/max. Two indices were calculated for every individual hot spot: weighted probability (mean*(std.dev/volume)) and bone ratio (volume laid on bone regions / total volume). Separator functions were calculated on the 2D feature space of the above indices to automatically classify the SPECT hot spots as true and false lymph-nodes. The determination of the separator functions was based on trials given by two experienced nuclear medicine specialists independently. The result of the automated method was compared to corresponding previous reports. Results: 98.3% and 99.5% of previously reported lymph nodes were determined automatically for the studies of prostate- and breast-cancer patients respectively by using the InterView Fusion software. The whole post-processing-method took an average time of 2 minutes for a patient's SPECT/CT-dataset to gain all marked lymph-nodes and their quantitative values. **Conclusions:** The fully automated SLN detection and quantification algorithm can be applied on SPECT/CT-data of prostate- and breast-cancer patients. The clinical validation of the method indicates that it is a fast and accurate tool for SLN detection. Therefore it can support physicians in daily routine sustainably.

P714

Sentinel lymph node biopsy in Breast ductal carcinoma "in situ"

C. Sampo¹, M. Giménez¹, J. Torrecabota², C. Peña¹, C. Serra², E. Hernandez¹, R. Canet³, A. Pozo¹, A. Graner⁴, F. Serra¹, M. Galmes¹; ¹Department of Nuclear Medicine. Son Dureta Hospital, Palma de Mallorca, SPAIN, ²Department of Gynaecology. Son Dureta Hospital, Palma de Mallorca, SPAIN, ³Department of Anatomopathology. Son Dureta Hospital, Palma de Mallorca, SPAIN, ⁴Department of Radiology. Son Dureta Hospital, Palma de Mallorca, SPAIN.

INTRODUCTION In spite of Sentinel lymph node biopsy (SLNB) in the nodal staging of the Breast Cancer is nowadays considered an standard of care, it's utility in the Breast Ductal Carcinoma *in situ* (DCIS) is still controversial because of the low risk of metastatic involvement of the axilla. **AIM** The aim of our study is to present our experience in the application of the SLNB in high risk Breast DCIS previous to surgery. **MATERIALS&METHODS** We included 38 patients (p) with a diagnosis of Breast DCIS after biopsy, considering high risk criteria big tumour size, high histological grade or if the patient had to be submitted to a mastectomy. A 2-day protocol was used to localise the sentinel node (SN) after the injection of 99mTc-Nanocolloid (peritumoral or subareolar), obtaining images after 2-4h. The day of the surgery, after anatomopathological analysis of the SN, the patient underwent a complete axillary lymph node dissection (ALND) just in case of infiltration of the node. **RESULTS** Out of 38p included, in 6 the definitive tumour size is unknown, with an average tumour size of 18.6 mm (range 6-120mm). A total of 73 sentinel nodes were removed with an average of 1.92 SN/p. Of the 38p, 20 tumours were invasive at the definitive analysis, 1 was a carcinosarcoma, 2 were microinvasive and 15 were non-invasive, being negative all the sentinel nodes removed in this last group. In 1 patient we didn't found a SN after lympho-gammagraphy and in another patient the sentinel node wasn't removed at the surgery room. In both cases, an ALND wasn't done and both were non invasive at the definitive pathological analysis. A positive SN were seen in 7p (7/36), 5 with macrometastatic involving, 1 micrometastatic and 1p with isolated tumoral cells (ITC). After 28 month follow-up all the patients are alive and free of disease, exceptuating the one with the carcinosarcoma who died after a year from the diagnosis (positive SN). **CONCLUSION** The SLNB is a useful method to check the axillary nodes in patients with non invasive Breast Carcinoma, improving the staging of the disease and the planning of the surgery treatment.

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Comparison between two different sentinel node and occult lesion localization protocols for non palpable breast lesions

F. Armas, M. Hernández, J. Herrera, A. Santana, C. Isla, J. Miranda, M. Ochoa, R. Chirino, V. Vega; Hospital Insular de Gran Canaria, Las Palmas de Gran Canaria, SPAIN.

AIM: To evaluate the differences between two different protocols used for performing the sentinel lymph node biopsy (SLNB) and the radioguided occult lesion localization (ROLL) in the same surgical act (SLNB+ROLL=SNOLL). **MATERIAL AND METHODS:** 59 consecutive patients with suspected occult breast carcinoma (non palpable) were studied. Group I (33 pts) underwent a double injection in the same day of the surgery: albumin macroaggregates within the suspicious breast lesion for the ROLL and albumin nanocolloids subdermally for the SLNB. Group II (26 pts) were injected only intralesionally with albumin nanocolloids the day before surgery and the scintigraphy was performed 24 hours later. In this second group, a subdermal reinjection was done in case of no drainage to the sentinel node. **RESULTS:** Histopathological analysis revealed breast carcinoma in 53 patients (thus 10% of the lesions resulted benignant). In 56 cases the SLN was properly visualized (Group I: 32/33, Group II: 24/26). Mean SLN resected: 2.62. Axillary metastases were proved in 28.3%. No statistically significant differences were found between both groups regarding the number of SLN visualized or resected (p: 0.75) or the percentage of lymphatic involvement (p: 0.12). 15% of the patients required a second intervention due to the presence of disease in the surgical margins. **CONCLUSIONS:** The design of SNOLL protocols for non palpable breast lesions is flexible and can be adapted to the logistics of the different institutions. In our study we analyzed two protocols and no significant differences in efficiency were found.

P716**The benefits of SPECT/CT on sentinel node mapping in breast cancer**

H. Fernandes, F. Osorio, T. Vieira, P. Oliveira, A. Oliveira, M. Perez, J. Pereira, M. Cardoso; Hospital de S. João, Porto, PORTUGAL.

Aim: Accurate lymph node staging is essential for the prognosis and treatment of patients with breast cancer. For patients staged as NO, both clinically and echographically, it is common practice to biopsy the sentinel node. The precise anatomic localization of the sentinel lymph node(s) allows to programme minimal invasive surgery and to avoid its incomplete removal. Conventional planar lymphoscintigraphy does not always define the exact lymphatic drainage pattern, and does not give precise anatomic information about the sentinel lymph node(s) location. Recently, to help overcome these difficulties, it was introduced the hybrid technology of SPECT/CT, which gives images with better contrast and resolution and also provides a better anatomic detail. The aim of this study was to determine the advantages of using SPECT/CT instead of planar scintigraphy in presurgical localization of sentinel lymph nodes. **Materials and Methods:** We prospectively included 24 consecutive patients with breast cancer staged as NO. All patients were administered 4 intradermal injections of ^{99m}Tc-nanocolloid (100µCi each) and had planar and SPECT/CT images acquired. **Results:** Preoperatively, SPECT/CT identified the sentinel lymph node in all patients. Planar images failed to detect the sentinel lymph node in 2 of the 24 patients, resulting in a 8.3% false-negative rate. Globally, planar images allowed the identification of 24 sentinel lymph nodes (in 22 patients), whereas SPECT/CT identified 27 sentinel lymph nodes, 3 more (11.1%) than conventional evaluation. Intraoperatively the combined technique with both vital dye and gamma probe guided sentinel node biopsy was used. Vital dye identified 29 sentinel nodes, while gamma probe identified 33 "hot" nodes, 4 more (12.1%) than the vital dye. **Conclusion:** In our preliminary series, SPECT/CT had higher accuracy and identified more sentinel lymph nodes than conventional planar lymphoscintigraphy (11% more), and provided additional anatomic information. The hybrid SPECT/CT has the potential to make image fusion a routine clinical tool that improves lymphatic mapping in patients with breast cancer.

P717**Intraoperative Imprint Cytology in Sentinel Lymph Nodes Obtained by Radioguided Sentinel Node Biopsy in Breast Cancer Patients**

M. Lazar¹, S. Hamar², L. Kaizer², G. Lazar, Jr.³, Z. Simonka³, K. Ormandi¹, A. Paszt³, T. Sera⁴, A. Palko⁴, T. Miko², L. Pavics⁴; ¹Euromedic Diagnostics Szeged Ltd., Szeged, HUNGARY, ²Department of Pathology, Szeged, HUNGARY, ³Department of Surgery, Szeged, HUNGARY, ⁴Department of Nuclear Medicine, Szeged, HUNGARY, ⁵Department of Radiology, Szeged, HUNGARY.

Introduction: Axillary lymph node clearance can be avoided in the majority of breast cancer patients by using radioguided sentinel lymph node biopsy, though it has to be performed by a second operation in about one fifth of patients. The number of these second operations can be decreased by applying intraoperative imprint cytology, therefore we decided to introduce this method. The aim of this study was to evaluate the feasibility and efficacy of imprint cytology. **Material and methods:** Eighty-five patients with breast tumour (one bilateral) were enrolled in the study. The technique of radioguided sentinel node biopsy was not changed (intra- or peritumoural administration of 150 MBq ^{99m}Tc-Senti-Scint, sentinel node mapping, intraoperative gamma probe detection), and we continued to combine it with blue dye technique. However, sentinel node removal was performed first, which were directly carried to the Department of Pathology for imprint cytology, and tumour removal was carried out after all this. We were informed about the result by phone. In case a positive result was reported, we performed axillary block dissection as well. **Results:** Imprint cytology was positive in 13 cases, which were all proved by later full examination, but final results showed metastatic involvement in additional 7 cases. **Conclusions:** If well organized, the method is well applicable, although it slightly extends the time of surgery. In spite of providing false negative result in 8% of cases, imprint cytology made it possible to avoid second operation in 15% of all patients, and no unnecessary intervention was made due to false positive result.

P718**Sentinel lymph node detection with ^{99m}Tc-Nanocolloid in differentiated thyroid carcinoma**

I. Banzo, I. Martinez-Rodriguez, R. Quirce, J. Jimenez-Bonilla, M. de Arcocha, H. Portilla-Quattrociochi, P. Medina-Quiroz, A. Rubio-Vasallo, R. del Castillo, J. M. Carril; H.U. Marques Valdecilla. Servicio de Medicina Nuclear. Universidad de Cantabria, Santander, SPAIN.

Aim: The extent of lymph node dissection in differentiated thyroid carcinoma (DTC) remains controversial. The aim of this study was to evaluate the feasibility and the usefulness of sentinel lymph node (SLN) mapping and SLN biopsy in patients with DTC. **Materials and Methods:** **Patients:** A prospective study was carried out in 8 patients who were scheduled to undergo total thyroidectomy for DTC. Six patients were females and two patients were male. Patients ranged in age from 19 to 86 years old. The mean patient age was 49.6 years. All patients were correctly diagnosed with DTC before surgery by fine-needle aspiration cytology. Median tumor size was 41.5 mm. **Lymphoscintigraphy.** Three hours before the start of surgery patients underwent a lymphoscintigraphy after a single intratumoral injection of 4-9 MBq ^{99m}Tc-Nanocolloid in 0.1-0.2 ml saline under ultrasound guidance. Dynamic study was acquired in anterior view (120 sec/frame for 30 min) followed by static planar images (10 min/frame) in anterior, lateral, and oblique views up to 2-3 hours postinjection. Detected SLN were marked on skin with a pen. **Surgery.** At surgery thyroidectomy was performed first. Then, central and lateral neck compartments were scanned with a hand-held gamma probe for the identification of the SLN. One identified all foci of increased radioactivity were removed and submitted for histological study. **Results:** Among the 8 patients with DTC, papillary carcinoma was found in 7 and Hürthle cell carcinoma in 1 patient. **SLN detection.** SLN was detected in 7 of the 8 patients. The number of identified SLN ranged from 1 to 6. Five of the 7 patients had a metastasis positive SLN. Of these 5

patients, 3 had lymphatic metastasis in additional lymph nodes. Two of the 7 patients had negative SLN in histological analysis. There was no patient with negative SLN and metastasis in non-SLN. **No SLN detection.** SLN was not detected in 1 of the 8 patients. In this patient both lymphoscintigraphy and intraoperative gamma probe localization were normal. A locoregional lymphadenectomy was performed. Histological examination discovered metastasis in 2 of the 8 lymph nodes. **Conclusion:** SLN mapping and SLN biopsy are feasible for evaluating lymph node metastasis in patients with DTC. The use of a hand-held gamma probe for the intraoperative detection after removal of primary tumour increases the identification rates of SLN.

P719**Can age be relevant in breast cancer sentinel node biopsy?**

R. Ruano¹, M. Ramos², F. Gomez-Camirero¹, P. Tamayo¹, A. S. Rosero¹, J. Gonzalez-Orus², J. R. Garcia-Talavera¹; ¹Nuclear Medicine, University hospital of Salamanca, SPAIN, ²General Surgery, University hospital of Salamanca, SPAIN.

Background: the use of sentinel node biopsy (SNB) in breast carcinoma (BC) is a widespread technique where nuclear medicine plays the main role for its successful development. It is the aim of this study to present our experience in the therapeutic approach of the SNB in patients classified according to age to find out if this factor influences SN detection and SN histological results. **Methods:** we studied 821 consecutive T1-T2<5cm BC with performed SNB in the period 2002-2009. Age groups considered were: <35y (18pts), 35-49y (212pts), 50-69y (386pts), ≥70y (205pts). Preoperative lymphoscintigraphy was performed with ^{99m}Tc-colloidal rhenium sulphide (nanocis); the sentinel node was located with a gamma ray detection probe (europrobe) and periareolar isosulfan blue dye (lymphazurin). Axillary lymph node dissection (LND) was completed only when the SLN was positive for metastasis or not located. **Results:** We found no statistical differences in axillary detection (global detection 98.78%). Internal mammary chain was visualized in 22% <50y vs 12% in >50y (p<0.05). Non-palpable lesions were more common in 50-69y group (30%vs19% p<0.05). BC family history decreased among age (33% <35y vs 12%>70y). No statistical differences in number of SN excised nor in tumor hormonal receptor status. SNB histopathology results were not different among groups (p>0.05), finding a greater amount of SN metastasis in palpable lesions vs non-palpable lesions (31% vs 19%, p<0.05). SN was the only node affected in up to 65% pts. Conservative treatment of the breast was feasible in 72% cases. 226 cases underwent a mastectomy, with a greater proportion in >70y BC (p<0.05). Breast reconstruction occurred in 60% pts <50y vs 43% 50-69y and only 3% >70y (p<0.05). **Conclusion:** SNB detection and results are not age-related although a greater amount of visualized internal mammary drainage can be expected in younger patients. Age selection for BC screening programs should take into account family history. Early BC detection with an important amount of nonpalpable lesions must be the main goal in radiological screening to reduce the percentage of axillary metastasis and to permit a conservative surgery treatment.

P720**Sentinel Lymph Node Biopsy in the Course of IntraOperatory RadioTherapy: a Feasible and Indispensable Procedure both for the Surgeon and for the Radiotherapist**

L. Castorina¹, A. Di Grazia², M. Lipera³, I. V. Patti², A. Seca², M. Tamburo², G. Cocchiara¹, M. A. Da Costa Vieira²; ¹Nuclear Medicine, Rem, Catania, ITALY, ²Radiotherapy, Rem, Catania, ITALY, ³Surgery, Mediterranean Institut of Oncology, Viagrande (Catania), ITALY.

Aim. The use of the sentinel node biopsy (SLNB) has vastly reduced the area of surgery. The intraoperative radiotherapy (IORT) is a form of partial breast radiotherapy which, according to studies that have been carried out so far, produces the same results as total breast irradiation after quadrantectomy. By combining these two procedures it is possible to minimize the patient's physical and mental stress. Moreover, the SLNB is necessary for the radiotherapist to determine the right treatment in the case of metastatic or non-metastatic sentinel nodes. **Methods.** The two procedures were carried out on 26 women aged between 28 and 86, with a tumour size of up to 2 cm. The day before surgery a preoperative lymphoscintigraphy was performed by means of a periareolar subdermal injection of 350 MBq ^{99m}Tc-labeled nanocolloid. Scintigraphic images were taken up to 1 hour after the injection. On the operating table, the gamma probe signalled the radioactive nodes, which were all removed. Surgery was quadrantectomy in 19 cases and mastectomy nipple-sparing in the other 7 cases. IORT was carried out after tumorectomy by an electron accelerator NOVAC 7, giving a 21 Gys dose when only IORT was necessary or a 16 Gys dose if a boost was required (when the sentinel node was metastatic) or after a nipple-sparing mastectomy. **Results.** Sentinel lymphnodes (SL) were detected in all 26 cases, both by lymphoscintigraphy and by gamma probe in the course of surgery. Out of the twenty-six patients three metastatic nodes were found and in these women axillary nodes were removed, too. These patients had fortunately metastasis only in the SL. They received IORT in a boost of 16 Gys and then entered a programme of external radiotherapy over the axillary cavity. **Conclusions.** The surgical treatment of most breast cancer cases has changed from radical mastectomy to quadrantectomy and from axillary node dissection to SLNB (but not in all centers yet). The oncological radicality of these surgical operations has been assured by post-operative radiotherapy. Our Breast Unit is able to execute all the surgical and radiotherapy treatments in the course of only one operation. If SLs are not metastatic, the patient may have already been discharged with a propitious long-term prognosis. If SLs are metastatic, the radiotherapists must change their treatment plan giving a boost in the course of the surgery and, later, external radiotherapy over the axillary cavity.

P721**Utility of axillary sentinel lymph node biopsy before neoadjuvant chemotherapy for breast carcinoma**

S. Sanz Viedma, T. Amrani, J. Jimenez Hoyuela, E. Ramos, A. Sanchez, S. Ortega, M. Martinez del Valle; Hospital Clínico Virgen de la Victoria, Malaga, SPAIN.

The timing for performing sentinel node biopsy (SNB) is still a controversial issue in patients undergoing neoadjuvant chemotherapy (NC). **AIM:** To evaluate the utility of SNB before NC in

clinically negative axillae node breast cancer patients. MATERIAL AND METHOD: Retrospective study from October 2008 to January 2009. We evaluated 15 women, mean age 45.8 y and histological diagnosis of invasive breast carcinoma with stage II (T2-T3N0M0). All patients were candidates to NC for breast conserving surgery. Axillary ultrasound and fine needle aspiration were performed for indeterminate or suspicious axillary lymph nodes, being negative in all cases. The protocol consisted of performing the SLNB before NC and axillary node dissection (ALND) only when the sentinel node was positive for disease. Lymphoscintigraphy was performed on the day before surgery (exeresis of the sentinel node) after the periareolar injection of 37 MBq ^{99m}Tc labelled nanocolloid. After NC (4 cycles adriamycin /cyclophosphamide and 4 cycles of docetaxel) lumpectomy was performed and ALND was made if the sentinel node was positive. Pathological assessment of the tumour was graded according to the Miller and Payne scale. The pathological axillary response was determined by comparing the pre-treatment axillary status with the results on the nodes removed into the ALND. For patients with negative SN before treatment the response with respect to the axilla was not applicable. RESULTS: The histological subtype was the following: 13 invasive ductal carcinoma, 1 papillary, and 1 mucinous. The mean tumour size was 3.3 cm (range 2-6). The identification rate of the sentinel node was 93%. 1/15 patients (6%) the sentinel node was not found. The mean number of axillary sentinel node removed was 1.3 (1-4). 5/15 patients (34%) had node-negative disease. In the follow up of these patients no early axillary relapses were detected. The remaining 9 patients (60%) with node-positive disease before treatment underwent ALND at the time of definitive breast surgery after the NC. All patients were pathological node negative in the ALND. The pathological response (M&P scale) of the primary tumour was: grade 1-3 in 4 patients and grade 4-5 in 11 patients CONCLUSION: SNB before NC has a high identification rate and it is an accurate procedure to predict the pretherapeutic axilla status. It can also determine the pathological axilla response to NC. Pre and post treatment axillary staging provides an important prognosis value.

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Surgical Behavior Impact of Sentinel Lymph Node Biopsy (SLNB) in Intraductal Breast Cancer

V. Castillo, M. E. Rioja, O. Gutierrez, L. Diez, U. C. Vera, E. Diaz, L. Cabañas, C. Sánchez, M. V. Collado, A. Crespo; Ramon y Cajal, Madrid, SPAIN.

Aim: Analyze the impact of SLNB in final surgical attitude in patients with pre-surgical diagnosis of intraductal breast cancer. Material and Methods: We have retrospectively reviewed our database of 660 patients with breast cancer diagnosis and SLNB. Of these we selected 96 (14,5%) whose preoperative diagnosis by core biopsy (BAG) was CID The day before surgery were performed intratumoral injection of Nanocoll-Tc99m stereotactic/ultrasound guided (111 MBq/0.2 ml) in 34 non-palpable lesions (36%), peritumoral injection (4 x 28 MBq/0.5 ml) in 36 palpable lesions (37%) and pericentricital in 26 patients (27%). Moreover 23 patients in which no lymphatic drainage was observed on the scintigraphy received an extra retroareolar injection (37 MBq/1 ml). Sixty one patients (63%) underwent to mastectomy and the rest of them to breast-conserving surgery. Results The sentinel lymph node detection rate was 99%. No axilar or extraaxilar lymphatic drainage was identified in one patient. The histological final diagnosis was invasive carcinoma in 28/96 patients (29%). Of these, twelve (43%) presented metastasis in at least 1 of the sentinel lymph nodes (8 macrometastases and 4 micrometastases). No evidence of invasive carcinoma was identified in the other 68 patients (71%). However, 3 patients presented metastases in the sentinel lymph node (2 macrometastases and 1 micrometastasis); one more patient showed isolated tumoral cells in two sentinel lymph nodes. A second surgery was avoided in 28/96 with invasive carcinoma final diagnosis and in the 4 patients with metastases in the sentinel lymph node, even though the lack of invasive carcinoma component. Unnecessary axilar lymphadenectomy was avoid in 6/61 (10%) who presented invasive carcinoma in the mastectomy specimen and negative sentinel lymph node. In sixteen patients (16%) internal mammary sentinel lymph node was identified in scintigraphy; no metastases were found in any of the nine that could be biopsied. Conclusions 1. The SLNB performed in patients with pre-surgical diagnosis of intraductal breast cancer has saved a new surgery in 34% of our patients and unnecessary axilar lymphadenectomy by 10%. 2. The internal mammary sentinel lymph node biopsy has doubtful impact of the intraductal breast cancer final treatment.

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Long term validation of sentinel node technique in malignant melanoma - a five-years follow-up.

M. Papós¹, J. Oláh², M. Lázár³, J. Varga², E. Varga², G. Mohos², E. Kis², I. Korom², T. Séra¹, L. Kemény², L. Pávics¹; ¹Department of Nuclear Medicine, University of Szeged, Szeged, HUNGARY, ²Department of Dermatology and Allergology, University of Szeged, Szeged, HUNGARY, ³Euromedic Diagnostics Ltd., Szeged, HUNGARY.

Radioguided sentinel lymph node (SN) biopsy in patients with malignant melanoma (MM) by now is a well accepted method however the validation of the method has to be proven on the basis of long-term follow-up. Aim: The aim of this study was to analyse the follow-up data of SN negative patients concerning to the later lymph node involvement. Patients and methods: Between September of 1999 and March of 2005 SN localisation was performed in 337 patients suffering from MM preoperatively by gamma-camera technique using ^{99m}Tc-nanocolloid (Senti-Scint), and intraoperatively with gamma-probe. The Breslow thickness of MM was more than 1 mm, or less than 1 mm, but grade Clark IV, or ulcerated or regressed. All patients were clinically in N0 stage. and the later lymph node status. The follow-up period was longer than 5 years in all patients (60-127 months). Results: SN was identified in 313 patients in one region and in 24 cases in more than one region. In 202 patients (60%) SN was MM free, and in 135 cases (40%) MM positive. More than 5-yers clinical follow up was possible in 248 patients. In this group of patients 152 had negative SN. In SN negative patients MM associated mortality was 10% (15/152). The survival rate with active disease in SN negative cases was 5% (8/152). During the follow-up lymph node metastasis was detected in SN negative patients in 5% (7/146, lymphatic status of 6 patients is unknown) therefore these patients were classified as false-negative cases in concerning the SN biopsy. Conclusion: The low false negative rate confirms the validity of SN biopsy technique.

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Blue dye versus d Tc-99m Nanocolloid methods in breast cancer.

O. M. Emer, Ö. Almus, R. Yıldız, A. Ayan, E. Öztürk, T. Tufan, M. A. Özgüven; Gülhane Military Medical Academy, Ankara, TURKEY.

BACKGROUND: Sentinel lymph node biopsy (SLNB) is commonly performed using radioisotopes and/or blue dye. However, it is still undefined which reagent is more suitable for identifying sentinel lymph nodes (SLN). PATIENTS AND METHODS: A consecutive series of 125 breast cancer patients who had undergone SLNB at the Gulhane Military Medical Academy Hospital from 2005 to 2010 was analyzed. The SLN was identified by blue dye in Group A (72 patients), by Tc99m nanocolloid in Group B (40 patients) and Group C (33 patients) with a combination of technetium-99m nanocolloid and isosulfan blue dye. The correlation between clinicopathological factors and the distribution of radioisotopes and blue dye was analyzed. Patients with metastatic disease, breast skin infiltration, inflammatory cancer and the ones who had satellite lesions were not included to the study. RESULTS: In Group A 10/18 patients who had positive SLNB had positive lymph nodes except SLN, in a patient who had negative SLN, a metastatic lymph node was found in axillary dissection. In Group B 15 patients had positive SLN and 2 patients with negative SLN had axillary lymph node metastasis. In Group C 5 patients had positive SLN and there were no additional metastatic lymph node in axillary dissection material. Table below shows sensitivity, specificity, positive and negative predictive values .

Groups	Sensitivity	Specificity	PPV	NPV
A	90.9%	75.5%	55.5%	96.15%
B	88.2%	100%	100%	91.3%
C	100%	100%	100%	100%

CONCLUSION: These data suggest that combination of radioisotope and blue dye combination has better results in detecting SLN in breast cancer. Besides in frozen section negative SLN clinical and radiologic features must be evaluated carefully in order to decide axillary dissection

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Sentinel lymph node biopsy in breast cancer using combined method

U. Yararbas¹, B. Zengel², A. Şirinocak², O. Bingolballı², A. G. Denecli²; ¹Ege University Hospital, Izmir, TURKEY, ²Izmir SB Bozyaka Research and Training Hospital, Izmir, TURKEY.

Aim: Sentinel lymph node biopsy (SLNB) can be performed using radiocolloid, blue dye or the combination of two. The aim of our study is to review our experience in SLNB using combined method and compare success rate of radiocolloid and blue dye. Material and Method: Ninety-one patients with T1-2N0M0 breast cancer that underwent SLNB using combined method between March 2007-January 2010 in Izmir SB Research and Training Hospital were included in the study. Four patients had bilateral breast lesions, so far a total of 95 SLNB procedures were performed. Age range was 36-86 years. Fifteen patients (15.7%) had prior excisional biopsy. All patients underwent lymphatic mapping using radiocolloid and isosulphan blue. For this purpose, a total of 1 mCi of tin colloid in 17 and nanocolloid in 78 patients was injected intradermally at 4 quadrants of periareolar region the day before surgery, lymphoscintigraphies were obtained in all patients in anterior and lateral projections 1 hr after the injection. Blue dye (Isosulphan blue) was injected to subareolar space in 5ml volume after the induction of general anesthesia. All nodes bearing radioactivity and/or blue dye were harvested. Results: In 94 of 95 SLNB, 1 or more SLN were identified (98.9%). Radiocolloid identified SLN(s) in 94 (98.9%) and blue dye in 70 (73.6%) cases. The patient with failed SLN localization using combined method had a recent (14 days) prior excisional biopsy at upper outer quadrant. Mean SLN number was 4 in patient group. In 36 of 94 procedures with successful SLN identification, metastasis in SLNs were detected (38.2%). Conclusion: Our results show that combined method using periareolar radiocolloid and subareolar blue dye injection yields very high SLN identification rates. However radiocolloid is superior to blue dye (98.9% versus 73.6%) and success of the method is mainly based on radiocolloid . In the literature, various SLN detection rates are given for blue dye. Our study group is mainly consisted of patients without prior excisional biopsy and validation of the malignancy of the breast lesion by frozen section analysis is needed in this group of patients. This procedure causes a 30-45 minutes of delay during which clearance of the blue dye may occur. In the light of this observation, protocols using only blue dye for lymphatic mapping are not recommended especially in patients with potential delays during surgery. Additionally use of blue dye can be omitted if radiocolloids are used in SLNB.

P62 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Therapy & Clinical Trials: RIT

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Indium-111-Zevalin and FDG uptake in association with tumor response in radioimmunotherapy for B-cell non-Hodgkin's lymphoma

K. Hanaoka, M. Hosono, Y. Yamazoe, Y. Komeya, N. Tsuchiya, K. Usami, M. Sumita, Y. Tatsumi; Kinki University School of Medicine, Osaka-sayama, JAPAN.

Objectives The purpose of this study was to clarify quantitative tumor accumulations of ¹¹¹In-Zevalin* (In-Zevalin) and ¹⁸F-FDG (FDG) on SPECT/CT and PET/CT, respectively, as compared to tumor response in B-cell non-Hodgkin's lymphoma patients receiving Zevalin therapy. A count recovery coefficient technique was adopted for In-Zevalin to correct the partial volume effect and to precisely quantify tumor accumulation. Methods Fourteen patients having confirmed non-Hodgkin B-cell lymphoma who underwent Zevalin therapy along with In-Zevalin SPECT/CT and FDG PET/CT between January 2009 and February 2010 were enrolled in this prospective study.

Volumetric regions of interest (VOI) were placed over lymphoma lesions on PET and SPECT images by referring to CT images. On PET/CT images, maximum standardized uptake value (SUV_{max}) of FDG was measured. On SPECT/CT images, tumor accumulations expressed as percent of injected dose per gram (%ID/g) of In-Zevalin were measured at 48 h after injection. To obtain count recovery coefficients, a NEMA image phantom containing ¹¹¹In solution was imaged with the SPECT/CT scanner. %ID/g was corrected for size on CT images with relevant recovery coefficients (c%ID/g). All lesions (n=38) were classified into responders and non-responders according to International Workshop Criteria on pre- and post-therapeutic CT images. Results: Pretherapeutic lesion long diameter was 15.5±3.4 mm and 17.1±6.6 mm (not significant), and reduction rate in size (product of diameters) was 86.8±15.2% and 10.9±23.7%, respectively, for responders (n=23) and non-responders (n=15). Pretherapeutic SUV_{max} was 6.3±3.0 and 9.1±4.9 (p<0.05), and reduction rate in SUV_{max} was 70.3±15.7% and 38.8±42.6% (p<0.01), respectively, for responders and non-responders. Tumor accumulation of In-Zevalin was 0.0022±0.0006 and 0.0021±0.0006%ID/g (not significant), and 0.0064±0.0039 and 0.0060±0.0023 c%ID/g (not significant), respectively, for responders and non-responders. All 3 lesions with the lowest accumulation (<0.001%ID/g) showed high reduction rates in size of more than 80%. Conclusions: Pretherapeutic FDG accumulation was predictive of tumor response in Zevalin therapy. Tumor response was independent of In-Zevalin accumulation in consistent with previous reports even if the partial volume effect correction was applied to perform more precise quantification. Low In-Zevalin accumulation does not preclude 90Y Zevalin therapy.

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Syndecan-1 antigen targeting using Iodine-131-labeled anti-CD138 B-B4 antibody in Multiple Myeloma patients

C. Rousseau¹, L. Ferrer¹, M. Bardies², F. Davodeau², A. Faivre-Chauvet³, P. Baumgartner⁴, J. Wijdenes⁵, J. Barbet², P. Moreau⁶, F. Kraeber-Bodéré¹, M. Chereh¹; ¹CRCNA Inserm UMR 892 Cancer Center Nuclear medicine, Nantes-Saint Herblain, FRANCE, ²CRCNA Inserm UMR 892, Nantes, FRANCE, ³CRCNA Inserm UMR 892 University hospital Nuclear medicine, Nantes, FRANCE, ⁴Cancer Center Nuclear medicine, Nantes-Saint Herblain, FRANCE, ⁵Diaclone, Besançon, FRANCE, ⁶Hematology Department, University hospital, Nantes, FRANCE.

Aim: Multiple myeloma (MM) is characterized by high expression of syndecan-1 (CD138), a heparan sulfate proteoglycan expressed by 100% myeloma cells. The continued over expression of syndecan-1 in progressive forms of MM suggests that radioimmunotherapy (RIT) using anti-CD138 monoclonal antibody (mAb) could be effective even on refractory forms of the disease. A feasibility study has been carried out to assess toxicity, absorbed doses to critical organs and tumours of the anti-CD138 -¹³¹I-B-B4 mAb (complete IgG1). Preliminary results obtained for the first four patients are reported here. **Methods:** MM patients previously treated by Velcade® chemotherapy, with recurrence documented by imaging (MRI, PET/CT) and a rise of monoclonal immunoglobulin level were enrolled in the study. All patients received two injections of 20 mg/m² of ¹³¹I-B-B4 mAb one week apart: a first injection of 370 MBq for the dosimetry study and a second injection of 555 MBq/m² for the treatment. For dosimetry purpose, each patient underwent a whole body (WB) CT scan and four WB emission scans at days D0, D1, D3-4 and D7. Images were corrected for attenuation and scatter to assess organs and bone marrow (BM) absorbed doses. Clinical, biological and imaging (MRI, PET/CT) follow-up was carried out for one year after treatment. **Results:** Images obtained one hour after the first ¹³¹I-B-B4 injection showed high BM and liver uptake but no kidney uptake was observed. Bone marrow uptake confirmed BM involvement as detected by pre-RIT FDG PET/CT. Absorbed doses were calculated for the liver (0.3±0.3 mGy/MBq), the kidneys (1.10±0.9 mGy/MBq) and BM (0.52±0.23 mGy/MBq). No hepatic nor renal toxicity could be observed, as suggested by the relatively low absorbed doses. No haematological toxicity was observed, apart from a thrombopenia, always reversible with symptomatic treatment. The highest platelet toxicities (duration and level) were observed for the highest BM absorbed doses. **Conclusion:** MM RIT with B-B4 antibody seems promising, with acceptable dosimetry and toxicity results. We are now planning a new RIT phase I/II trial with humanized B-B4 mAb.

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Radiation dosimetry of ¹¹¹In-Trastuzumab used for HER2-SPECT

J. R. de Jong, T. Oude Munnink, A. H. Brouwers, R. A. J. O. Dierckx, P. J. Perik, E. G. E. de Vries, M. N. Lub-de Hooge; University Hospital Center Groningen, Groningen, NETHERLANDS.

Aim: Trastuzumab is a monoclonal antibody targeted at the human epidermal growth factor receptor-2 (HER2). Overexpression of HER2 is found in 20-25% of all breast cancers. With HER2-SPECT using ¹¹¹In-trastuzumab we detected new lesions in 13 out of 15 patients (Perik et al J Clin Oncol.2006). In order to assess the biodistribution and radiation burden of ¹¹¹In-trastuzumab, a dosimetry study was performed. **METHODS:** Whole-body planar scintigraphy scans were acquired at days 0, 1, 5 and 7 post injection of 100 MBq ¹¹¹In-trastuzumab. SPRIND, a dosimetry software package for whole-body scintigraphy, was used to draw regions of interest for source organs and to calculate residence times. The radiation dose of organs, as well as the effective dose were subsequently calculated according to the MIRD method using OLINDA. **RESULTS:** Seventeen HER2 positive breast cancer patients were included and received 100 MBq of ¹¹¹In-trastuzumab. The effective dose of ¹¹¹In-trastuzumab was determined to be 0.18 ± 0.02 mSv/MBq. This corresponds to an average radiation burden of 18 mSv for the reference adult with a dose of 100 MBq of ¹¹¹In-trastuzumab. The organ receiving the highest radiation dose is the liver with 0.63 ± 0.20 mGy/MBq. Other organs receiving a radiation dose of note are the spleen (0.35 ± 0.09 mGy/MBq), the heart wall (0.33 ± 0.05 mGy/MBq), the osteogenic cells (0.29 ± 0.04 mGy/MBq), the lungs (0.29 ± 0.05 mGy/MBq), the gallbladder wall (0.28 ± 0.04 mGy/MBq) and the kidneys (0.26 ± 0.05 mGy/MBq). Preliminary data on blood dosimetry indicate that the dose on red bone marrow through blood perfusion may be as high as 0.3 mGy/MBq. The total dose on red marrow then sums up to 0.42 mGy/MBq. Moreover, this increases the estimate for the effective dose to 0.22 mSv/MBq. **CONCLUSION:** The combination of slow kinetic behavior and excretion of trastuzumab and the long lived radionuclide ¹¹¹In results in a relatively high effective dose for ¹¹¹In-trastuzumab. This is however in agreement with known results from literature with

other ¹¹¹In labeled antibodies. Limiting the administered dose to 60 MBq will prevent individual organ dose from exceeding 50 mGy in patients under suspicion of breast cancer.

P729

Radiation dosimetry of ¹¹¹In-bevacizumab used for VEGF-SPECT in melanoma patients

J. R. de Jong, F. J. Warnders, W. B. Nagengast, R. A. J. O. Dierckx, G. A. P. Hospers, A. H. Brouwers, E. G. E. de Vries, M. N. de Hooge; University Hospital Center Groningen, Groningen, NETHERLANDS.

AIM: Increased production of VEGF in melanoma lesions allows for visualizing these lesions by VEGF-SPECT using ¹¹¹In-bevacizumab. In order to assess the biodistribution and radiation burden of ¹¹¹In-bevacizumab, a dosimetry study was performed alongside a research trial in melanoma patients. **METHODS:** Nine patients, with stage III/IV melanoma who presented nodal lesions, were included and received 100 MBq of ¹¹¹In-bevacizumab (8 mg). Whole-body planar scintigraphy scans were acquired at day 0, 4 and 7 post injection for dosimetry and biodistribution. Bloodsamples were taken at several time-points for dosimetry of the red bone marrow. SPRIND, a dosimetry software package for whole-body scintigraphy, was used to draw regions of interest for source organs and to calculate residence times. SPRIND includes a red marrow module based on the method of Shen et al. The radiation dose of organs, as well as the effective dose were subsequently calculated according to the MIRD method using OLINDA. As bevacizumab is not renally excreted, no voiding bladder model was employed. **RESULTS:** The effective dose of ¹¹¹In-bevacizumab was determined to be 0.20 ± 0.01 mSv/MBq. This corresponds to an average radiation burden of 20 mSv for the reference adult with a dose of 100 MBq of ¹¹¹In-bevacizumab. The organs receiving the highest radiation dose are the liver with 0.44 ± 0.06 mGy/MBq and the heart wall with 0.41 ± 0.06 mGy/MBq. Other organs receiving a radiation dose of note are the kidneys (0.38 ± 0.03 mGy/MBq), the spleen (0.37 ± 0.10 mGy/MBq), the osteogenic cells (0.34 ± 0.03 mGy/MBq), the testes (0.34 ± 0.01 mGy/MBq) and the lungs (0.32 ± 0.04 mGy/MBq). Preliminary data on blood dosimetry indicate that the dose on red bone marrow through blood perfusion may be as high as 0.3 mGy/MBq. The total dose on red marrow then sums up to 0.45 mGy/MBq, making it a dose limiting organ. Moreover, this increases the estimate for the effective dose to 0.24 mSv/MBq. **CONCLUSION:** The combination of slow kinetic behavior and excretion of bevacizumab and the long lived radionuclide ¹¹¹In results in a relatively high effective dose for ¹¹¹In-bevacizumab, which is however consistent with literature data from other ¹¹¹In labeled antibodies. Limiting the administered dose to 100 MBq will prevent individual organ dose from exceeding 50 mGy.

P63 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Therapy & Clinical Trials: Radiosynovectomy

P730

Radioisotopic synovectomy in chronic inflammatory joint disease

C. Paniagua Correa, M. P. Garcia Alonso, M. A. Balsa Breton, S. I. Vasquez Tineo, A. Mendoza Paulini, A. Mariana Monguia, L. Castillejos Rodriguez, A. Ortega Valle, F. J. Penin Gonzalez, C. Pey Illera; Hospital Universitario de Getafe. Medicina Nuclear., Getafe (Madrid), SPAIN.

Radioisotopic synovectomy (RS) is a local intra-articular injection of beta-emitting radionuclides that radiate the synovium with the aim of destroying it selectively, in patients with chronic arthropathies without response to other local or systemic treatments. **OBJECTIVE:** To evaluate the usefulness of RS in the treatment of various chronic inflammatory arthritis and villonodular synovitis. **METHODS:** From October/96 to October/99 we performed RS in 63 patients (35 females and 28 males) with a mean age of 46,6 years (21-84) with chronic inflammatory joint disease (19 rheumatoid arthritis, 2 palindromic rheumatism, 13 inflammatory seronegative spondyloarthropathies, 1 juvenile chronic arthropathy, 11 undifferentiated seronegative spondyloarthropathy (9 was oligoarthritis), 6 chronic monoarthritis and 11 villonodular synovitis). These patients had been treated with traditional therapy consisting of systemic steroid or no steroid drugs and intra-articular steroid injection without response. Seventy-one RS were performed (63 knees, 5 ankles, 2 elbows and 1 wrist), using the radionuclide suitable for each type of joint. **RESULTS:** RS was performed without any periprocedural complication in all treated joints. With regard to the clinical success, we assessed an early clinical evaluation (6-8 weeks) finding a good clinical condition in 47/71 cases (66.19%) and a later evaluation (6-12 months) showing that only 38/71 cases (53.52%) remained asymptomatic at this moment. 66/71 RS performed were followed for 2 years. In 34/66 cases (47.88%) the clinical outcome was good and in 32/66 it was unfavourable. A new sinoviortesis was practiced over 14/32 joints (good response in 5 cases), 7/32 were involved surgically and 11/32 cases remain with an expectant attitude. Apparently we did not observe relationship between the outcome of the technique and the patient's underlying disease, except in villonodular synovitis, in which 7 / 11 (63.63%) had good response even after more than 2 years follow-up. **CONCLUSION:** Radioisotopic synovectomy (RS) is an effective treatment option for chronic joint diseases without response to local or systemic therapy and can delay surgery when needed. We observed the best results of RS in villonodular synovitis with better long-term evolution.

P731

166 Holmium-Phytate-Radiosynoviorthesis in rheumatoid arthritis. Five years clinical results. Phase III prospective study.

M. Szentesi¹, Z. Nagy², P. Géher¹; ¹Semmelweis Univ., Chair of Rheumatology and Physiotherapy, Budapest, HUNGARY, ²Polyclinic of the Hospitaller Brothers of St. John of God., Budapest, HUNGARY.

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:** Examination of anti-inflammatory effect of 166-Holmium-phytate injection. **Methods:** Phases III, prospectiv study. 30 patients suffering from chronic synovitis, rheumatoid arthritis were examined. The protocol commenced with screening. The patients were selected according to inclusion and exclusion criteria. **Holmium phytate injectable suspension marked by 600 MBq ¹⁶⁶Holmium phytate injectable suspension**, and 40 mg of 1 ml triamcinolone acetoneide and 1 ml of lidocaine 1 %. There were 60 month follow-up period after the administration of the isotope. Inflammatory activity of the affected knee-joint was tested prior to treatment, and the 3rd and 3, 6, 9, 12, 24, 36, 48 and 60 months after the treatment. Evaluation was based on the criteria as described by Müller, Rau and Scütte the score system was developed by the authors. **Results:** During the study period, inflammation decreased. In the first five years excellent and good results were recorded in 93.3%. Five years after radiosynoviorthesis 93.3% of patients did not need another puncture. Administration of Holmium-166 phytate is a safe procedure. We did not detect any symptoms of radiation sickness. We found no deviations in either haematological or chemical parameters during the study period. **Conclusion:** Holmium-166 phytate isotope is an effective radiopharmacy treating synovitis. Due to its physical parameters it is optimal to treat large joints (knee) and medium size joints (hips, shoulder, elbow, wrist, ankle). Effective dosage is 555-925 MBq. **References:** Szentesi M.,¹ Környei J.,² Antalfy M.,² Török 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 Farbaký Zs.,¹ Nagy E.,¹ Környei J.,² Antalfy M.,² Török J.,² Tóth Gy.,² Jánoki Gy.,³ Balogh L.³ Géher P.,³ 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. Szentesi M.,¹ Takács S.,¹ Farbaký Zs.,¹ Nagy E.,¹ Környei J.,² Antalfy M.,² Török J.,² Jánoki Gy.,³ Balogh L.,³ Géher P.,³: Radiosynoviorthesis with ¹⁶⁶Ho-phytate - First clinical results Phase I-IIa, randomized, increasing dosage, single-blind, placebo-controlled comparative study Eur. J. Nucl. Med. Suppl. 2. 500. 2003.

P732

BIOLOGICAL HAZARDS OF RADIATION SYNOVIOCTOMY II. LEAKAGE ¹⁶⁶Holmium-phytate-radiosynoviorthesis in rheumatoid arthritis. Phase III prospectiv study

M. Szentesi¹, Z. Nagy², P. Géher¹; ¹Semmelweis Univ., Chair of Rheumatology and Physiotherapy, Budapest, HUNGARY, ²Polyclinic of the Hospitaler Brothers of St. John of God, Budapest, HUNGARY.

Isotopes traditionally used cause whole body radiation of 10 Rad. 60 % leakage was found after using 198-Au for 24 hours by Oka and Topp. 10 % leakage was measured by Stewenson following administration of 5-15 mCi of 198-Au or Y-90. Specialists working with radiosynovectomy have aspired to produce an isotope incurring lower radiation loads. **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:** Examination of the pharmacokinetics and leakage of ¹⁶⁶Ho phytate injection into the joint, its tolerability, local irradiation and anti-inflammatory effect to the joint. **Methods:** Phases III, prospectiv study. 30 patients suffering from chronic synovitis, rheumatoid arthritis were examined. The protocol commenced with screening. The patients were selected according to inclusion and exclusion criteria. **Patients:** Gender (male/female): 7-23; Age: 57,13 (37-77) Stage of knee joint x-ray (I / II): 7/23; Duration of synovitis (years): 7,38 (0,5-27); Duration of disease (years): 9,1 (1-27); Number of punctures before the Ho-166 treatment: 12,8; Number of steroid injections before the treatment: 12,9 **Holmium phytate injectable suspension marked by 600 MBq ¹⁶⁶Holmium phytate injectable suspension**, and 40 mg of 1 ml triamcinolone acetoneide and 1 ml of lidocaine 1 %. **Results:** 1. 98% of 166-Ho applied intraarticularly can be measured back in the treated knee joints; 2. Leakage tests established that less than 0,5% of injected activity appears in the liver and less than 1% in the regional lymphatic glands; 3. We did not find any radioactivity nor in the serum and neither in the urine; 4. We did not detect any general or local symptoms of radiation sickness; 5. Inflammation decreased significantly; 6. We did not find any abnormalities in the bone marrow (or no radiotoxic effect) function; 7. Hepatic or renal functions did not show any abnormalities after 166-Ho injection. The applied doses caused neither hematological nor renal damage. **Conclusion:** Ho-166 isotope is an effective radiopharmacy treating synovitis. Due to its physical parameters it is optimal to treat large joints (knee) and medium size joints (hips, shoulder, elbow, wrist, ankle). Effective dosage is 600 MBq. **Bibliography:** Szentesi M.,¹ Környei J.,² Antalfy M.,² Török 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.

P733

Effects of radiation synovectomy in the hemophilic joints as evidenced by MRI

A. Polat¹, G. Buyukdereli¹, I. Sasmaz², O. Sargin¹, C. Özkan³, M. Kibar⁴, B. Antmen², K. Bıcağcı⁵; ¹Department of Nuclear Medicine in Cukurova University Faculty of Medicine, Adana, TURKEY, ²Department of Pediatric Hematology in Cukurova University Faculty of Medicine, Adana, TURKEY, ³Department of Orthopedics and Traumatology in Cukurova University Faculty of Medicine, Adana, TURKEY, ⁴Department of Nuclear Medicine in Acibadem Hospital, Adana, TURKEY, ⁵Department of Radiology in Cukurova University Faculty of Medicine, Adana, TURKEY.

Aim: Hemophilic arthropathy most commonly and severely affects the knee, followed by the elbow and ankle. The aim of this study was to evaluate the effects of radiosynovectomy (RS) in the hemophilic joints by using Magnetic Resonance Imaging (MRI). **Materials & Methods:** A total of 20 hemophilic patients ranging in age 6-18 years underwent RS due to recurrent bleedings in 26 joints (knee; n:14, elbow; n:9, ankle; n:3). RS of the knee was performed using Y-90 (4-4.5 mCi), all other joints were treated with Re-186 (2-2.5 mCi). In order to detect the effects of RS in the hemophilic joints, MRI was performed before and after treatment. Mean follow-up period after the RS was 21 months (range: 7 months to 30 months). For MRI evaluation of hemophilic arthropathy, joints were scored using 'Denver' scoring scheme both prior to and following RS. Denver MRI scale includes joint effusion, haemarthrosis, synovial hypertrophy, haemosiderin deposition, erosions, cysts and cartilage loss. **Results:** After a mean observation period of 21

months, there were no any joints with worsened Denver score. MRI showed that joint effusion, haemarthrosis, synovial hypertrophy, haemosiderin deposition and mean Denver score improved significantly after RS (P<0.05). However, the findings of erosions, cysts and cartilage loss were not change to a significant extent. **Conclusion:** This study suggest that RS with Y-90 and Re-186 is effective in terms of improving the findings of hemophilic arthropathy as shown by MRI.

P734

Effectiveness and Safety of Radiosynovectomy in Patients with Hemophilia - Initial Experience

J. A. B. Silva¹, P. T. Aguiar², A. M. D. Gomes², B. J. Amorim², M. C. L. Lima², E. C. S. C. Etchebehere², R. M. Filho², M. F. Barbosa³, J. Mengatti³, R. Pagnano¹, M. C. Ozelo¹, E. V. Paula¹, E. T. I. Sakuma², A. O. Santos², C. D. Ramos³; ¹Haematology & Haemotherapy Center, University of Campinas, Campinas, BRAZIL, ²Nuclear Medicine Division of the Department of Radiology, University of Campinas, Campinas, BRAZIL, ³Nuclear and Energy Research Institute, São Paulo, BRAZIL.

BACKGROUND: Haemophilia is characterized by hemarthrosis and hemorrhage into muscles, other tissues and cavities. Hemarthrosis results in debilitating chronic hemophilic arthropathy. Intra-articular injection of radioisotopes (radiosynovectomy - RS) in hemophilic patients with "joint target" (3 or more recurrent joint bleedings in a period of 6 months) could prevent joint destruction and reduce bleeding episodes. In the acute phase of hemarthrosis, treatment consists mainly of clotting factor replacement. **OBJECTIVES:** To prospectively evaluate the efficiency and safety of RS with ⁹⁰Y-hydroxyapatite (⁹⁰Y-HA), ⁹⁰Y-colloid and ¹⁵³Sm-Hydroxiapatite (¹⁵³Sm-HA). **METHODS:** Inclusion criteria consisted of hemophilic patients with "joint target" and chronic synovitis (defined by clinical criteria and diagnostic imaging). Efficiency was determined by comparing the frequency of hemarthrosis before and after RS. Safety of RS was assessed by the frequency of adverse effects such as transient sinovitis, bleeding and infection. The occurrence of radiopharmaceutical articular extravasation, was assessed by acquiring images after 72 hours of injection. **RESULTS:** Thirty-eight joints were submitted to RS (26 knees, 5 ankles and 7 elbows) in 34 patients (4-37 years of age, mean age 14 years). All knees and 2 ankles were treated with either ⁹⁰Y-colloid or ⁹⁰Y-HA, and 3 ankles and all elbows with ¹⁵³Sm-HA. After 6 months of RS, the mean monthly frequency of hemarthrosis was reduced from 1.42 ± 0.21 to 0.54 ± 0.19 (p < 0.001) in the whole group, from 1.08 ± 0.39 to 0.31 ± 0.28 (p = 0.0025) in the subgroup of patients treated with ¹⁵³Sm-HA and from 1.54 ± 0.25 to 0.62 ± 0.25 among patients treated with ⁹⁰Y-HA/⁹⁰Y-colloid (p < 0.001). Transient synovitis occurred in the first few weeks after RS in 17% of patients treated with ⁹⁰Y-HA in 2 patients and ⁹⁰Y-colloid in 3 patients - 3 knees and 2 ankles). No patient treated with ¹⁵³Sm-HA presented synovitis. Extra-articular leakage occurred in 10% of patients among them 2 ankles (1 with ⁹⁰Y-colloid and 1 with ¹⁵³Sm-HA) and 2 elbows (with ¹⁵³Sm-HA). The reduction in hemarthrosis episodes in the whole group would potentially result in a reduction of approximately US\$ 190.000 cost with clotting factor consumption during this 6-month period. **CONCLUSIONS:** In this preliminary analysis, RS was effective in decreasing hemarthrosis episodes in hemophilic patients and may significantly reduce clotting factor consumption.

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Biological hazards of radiation synovectomy I. Chromosomal analysis of periferal lymphocytes of patients before and after radiation synovectomy with 166-Holmium-Phytate

M. Szentesi¹, Z. Nagy², P. Géher¹; ¹Semmelweis Univ., Chair of Rheumatology and Physiotherapy, Budapest, HUNGARY, ²Polyclinic of the Hospitaler Brothers of St. John of God, Budapest, HUNGARY.

Background: Radiation synovectomy may be indicated for the treatment of chronic synovitis. A number of factors may affect its current use, including availability, limited evidence for its efficacy compared to intra- glucocorticoid, and concerns regarding the potential long term effects of radiation exposure, particularly in younger patients. Specific chromosome-type abnormalities in peripheral lymphocytes can be useful indicators of whole-body radiation exposure. The frequency of these aberrations has been shown to increase in patients who have had radiation synovectomy using Yttrium-90 /Y-90/ by up to five times compared to baseline levers. **166-Holmium-phytate /166-Ho/** is a new radiopharmaceutical currently on trial which appears to have less extra-articular leakage than Y-90 compounds. **Objectives:** The aim of this study was to identify any increase in specific chromosome-type abnormalities, using published criteria, in patients following 166-Ho synovectomy of the knee. **Patients:** Gender (male/female): 7-23; Age: 57,13 (37-77) Stage of knee joint x-ray (I / II): 7/23; Duration of synovitis (years): 7,38 (0,5-27); Duration of disease (years): 9,1 (1-27); Number of punctures before the Ho-166 treatment: 12,8; Number of steroid injections before the treatment: 12,9 The cytogenetic analysis was performed in each patient before and 4 weeks after the RSO. **Method:** Conventional cytogenetic analysis was performed on the peripheral blood sample. Cells were incubated for 72 hours in RPMI 1640 containing 20% fetal calf serum, antibiotics and 0,1 ml Phytohemagglutinin. Colcemid was subsequently added for 1 hour. 100 metaphases were analyzed from each sample. The following chromosomal aberrations were scored: ring chromosome, gap lesion, terminal and interstitial deletion, translocation ring chromosome. **Results:** The normal range of the structural deviation is 0-4%. Pathologic rate of the chromosomal aberrations are above 5%. In our study in only one case a ring chromosome was identified in the post-therapy sample/0,00055%/ **Conclusion:** There was no increase in the scored chromosome- type abnormalities after 166-Ho RSO. This study further support the relative safety of 166-Holmium-phytate compared to other radiopharmaceuticals. **References:** Stevenson A. C., Bedford J., Hill A. G. S., Hill H.: Chromosoma damage in patients who have had intra-articular injections of radioactive gold. Lancet 4. 24. 837-839. 1971.

P736

Comparison between 153-samarium or 90-yttrium synovectomy in knees of hemophilic patients

J. U. M. Calegario¹, J. Machado¹, M. Sayago², D. C. Landa¹, J. S. C. Almeida², J. Menghati³, A. P. Paula⁴; ¹Hospital de Base do DF, Brasília,

BRAZIL, ²Hospital de Apoio, International Hemophilia Training Center, BRAZIL, ³Radiopharmacy Center, IPEN-CNEN-SP, BRAZIL, ⁴Hospital Universtário de Brasília, Brasília, BRAZIL.

Aim—To compare the use of 740 MBq of ¹⁵³Sm and 185 of ⁹⁰Y, both labelling hydroxyapatite (HA), in the synovectomy of hemophilic patients to assess the possible equivalence. **Material and Methods**—Twenty seven patients, 26 males, and 31 knees, were divided in two groups: 1-treatment with intra-articular dose of 740 MBq of ¹⁵³Sm-HA: 15 knees of 13 patients, average age=22,3 years (range from 7 to 57 years old) and arthropathy evolution of 6,8 years; 2-treatment with 185 MBq of ⁹⁰Y-HA: 16 knees of 14 patients, average age=26,4 years (range from 9 to 45 years old) and arthropathy evolution of 10,2 years. The evaluation before and after 1 year of synovectomy used the following criteria: reduction in the number of haemarthrosis and pain by visual analogic scale and improvement in articular motility. The occurrence of adverse effects were considered also. Early scintigraphic studies (1–2 h) were made after the synoviorthesis. **Results**—We did not found significant difference in the reduction of frequency of haemarthrosis ($p=0,37$) and pain ($p=0,60$) that were, respectively: group 1: 53,6% and 34,8%; group 2: 74,3% and 29,6% (Fisher test). The improvement in articular motility was not significant in both groups. Three cases of mild synovitis were observed in each group. The scintigraphic control showed no articular escape and homogenous distribution of the injected material. **Conclusions**—The beta energy=2.2 MeV of ⁹⁰Y is better for knees synovectomy, but the use of higher activities of ¹⁵³Sm (beta=0,80 MeV) have similar biological effect in hemophilic patients. This may be useful in places that have only production of ¹⁵³Sm.

P737

The Effectiveness of Radioisotope Synovectomy for Chronic Synovitis

G. Koca¹, B. Alioglu², H. Ozsoy³, K. Demirel¹, H. I. Atilgan¹, M. Korkmaz¹, ¹Health of Ministry, Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara, TURKEY, ²Health of Ministry, Ankara Training and Research Hospital, Department of Pediatric Hematology, Ankara, TURKEY, ³Health of Ministry, Ankara Training and Research Hospital, Department of Orthopedics, Ankara, TURKEY.

AIM: Hemophilia is the most common congenital coagulation disorder. Hemophilic arthropathy, caused by chronic synovitis is the most common musculoskeletal complication in hemophilia patients. The aim of this study was to evaluate the efficacy of radioisotope synovectomy (RS) for chronic hemophilic arthropathies. **MATERIAL METHOD:** Between January 2006 and February 2010, 37 radioisotope synovectomies (RS) in 18 severe hemophilic patients (factor 8 < 1%) have been performed at our centre. Their mean age was 12 years (range: 8 - 20 years). Hemophilic patients with grade-II or III synovitis were selected for RS in our study. We preferred to use Y90 for all large joints and Re186 for small joints. Mean follow-up period after procedure was 22.6 months (range: 6 months to 33 months). **RESULTS:** The distribution of joints injected was as follows; rhenium-186 [Re186] 19 joints (ankles, 8 and elbows, 11) and yttrium-90 [Y90] 18 joints (knees, 18). RS was performed in 8 ankles for 7 patients, 11 elbows for 7 patients, and 18 knees for 13 patients. Mean bleeding rate before the procedure and after the procedure were as follows: Ankles, 3.43 vs 0.62 ($P=0.002$); elbows, 3.12 vs 0.55 ($P=0.000$); and 3.83 vs 0.62 ($P=0.011$). No major complication requiring secondary treatments has been observed. **CONCLUSION:** An early RS is the best way to halt the evolution of chronic hemophilia synovitis to devastating hemophilic arthropathy. RS is very effective and safe in the treatment of chronic synovitis of children with hemophilia. We highly recommend this procedure for developing countries to prevent joint disabilities. For a better and a healthier generation, RS has to be introduced in all the developing countries.

P738

Sm-153 EDTMP in chronic multifocal arthritis; initial results of a prospective study

A. Zafeirakis¹, I. Karfis², M. Lyra³, M. Paphiti⁴, A. Stavrakas⁴, A. Gouliamos⁴, G. Limouris⁵, ¹401 Military Hosp, Athens, GREECE, ²NIMTS Military Hosp, Athens, GREECE, ³Aretaieion Univ Hosp, Athens Medical Faculty, Athens, GREECE, ⁴Aretaieion Univ Hosp, Athens Med. Faculty, Athens, GREECE.

Purpose: To evaluate the effect of systemic radiation therapy with Sm-153 EDTMP on pain and disease activity in patients with Idiopathic Multifocal Polyarthritits (IMP). **Material and Methods:** Seven patients (2 men, 6 women; mean age, 64.2 years, age range, 68-76 years) with long life history of painful IMP, non-responding to the classical symptomatic therapies (anti-inflammatory schemes) and with a total of 38 diseased joints (mean number, 5.04; range, 4-7 joints), 11 proximal and 27 distal interphalangeal, were treated by systemic application of Sm-153 EDTMP (Quadramet, GE Health Care) in a dosage of 16 MBq / kgr BW (0.5 mCi / kgr BW) intravenously, at onset. The follow up period covered 18 months. The efficacy of the treatment was assessed by a pain and performance question-naire that patients were asked to complete daily, including the parameter of the tender and swollen joint count number as well as the acute phase reactant value. **Results:** In 6 out of 7 patients (85.7 %) the single Sm-153 EDTMP was adequate to lead to obvious clinical improvement of the disease activity, i.e. pain relief plus swollen decrease in 2, simple pain relief in 5 (average relief in of 5.2 joints) and simple swollen decrease in 3 (average decrease in 1.8 joints) patients, respectively. An erythrocyte sedimentation rate drop was observed in 6 cases. Repetition of the scheme was performed in 2 patients leading to a pain relief prolongation. **Conclusions:** These preliminary results show that systemic low dose treatment with Sm-153 EDTMP decreases the disease activity in patients suffering from IMP. The methodology is simple to be performed by any, even inexperienced nuclear physician, painless, and shows promising preliminary results that have to be followed by longer patients' series. Repetition of the scheme prolongs the analgesic period. Investigations with other radiopharmaceuticals, already used for cancer palliative therapy such as Re-186/Re-188 HEDP and Sn-117 m DTPA should be performed and compared for final evaluation.

P64 — Tuesday, October 12, 2010, 16:00 — 16:30, Hall Z

Therapy & Clinical Trials: Miscellaneous

P739

Usefulness of Fluorine-18-Fluorodeoxyglucose Positron Emission Tomography for Predicting Outcome of Sorafenib Treatment in Patients with Hepatocellular Carcinoma

J. Lee¹, H. Choi², H. Kim¹, Y. Choi¹, W. Kang¹, J. Lee¹, ¹Division of Nuclear Medicine, Department of Radiology, Yonsei University Health System, 254 sungsan-ro seodaemun-gu seoul, KOREA, REPUBLIC OF, ²Division of Oncology, Yonsei Cancer Center, 254 sungsan-ro seodaemun-gu seoul, KOREA, REPUBLIC OF.

Purpose Sorafenib (Nexavar) is an orally active multikinase inhibitor that is approved in the EU for the treatment of hepatocellular carcinoma (HCC). Monotherapy with sorafenib prolongs overall survival and delays the time to progression in patients with HCC who are not candidates for potentially curative treatment or transarterial chemoembolization. In this study, we used [18F]-2-fluoro-2-deoxyglucose [FDG] with positron emission tomography combined with computed tomography (PET/CT) to predict the treatment response of sorafenib in patients with advanced HCC. **Materials and Methods** 29 patients, 22 males and 7 females, with a mean age of 61 years (27-79 years), with advanced HCC were enrolled. Sorafenib was given 400mg twice daily orally. Nine patients underwent primary tumor resection, 19 had extrahepatic metastases; eleven with metastatic lymphadenopathy, eight with metastatic lung lesions, and eight with skeletal metastasis. The [18F] FDG-PET/CT was performed before treatment for each patient. A region of interest (ROI) was placed over every primary and metastatic lesion using 3D isocount at 41% of the maximum pixel value, measuring the maximal and mean uptake values within each ROI. Based on the maximal and mean SUVs, we chose the most hypermetabolic lesion and calculated its ratios, SUVmax and SUVmean ratios, using the cerebellum as the reference. We statistically analyzed the correlation between the calculated ratios and overall survival (OS) and progression-free survival (PFS) of the involved patients. **Results** The average OS and PFS were 6.1 ± 5.5 and 4.0 ± 4.2 months, respectively. Treatment response based on RECIST criteria was as follows; SD in fourteen patients, PD in twelve, and PR in one (not available in two). OS and PFS correlated significantly with SUVmax ratio ($r = -0.511$, $p < 0.01$, and $r = -0.413$, $p < 0.05$, respectively). OS showed significant relationship with SUVmean ratio ($r = -0.435$, $p < 0.05$) but PFS showed marginal relationship with SUVmean ratio ($r = -0.319$, $p = 0.06$). On the basis of SUVmax ratio, the patients were divided into two groups: group A (n=10), SUVmax ratio of ≤ 1.0 ; and group B (n=19), SUVmax ratio of > 1.0 . The OS and PFS were significantly higher in group A than in group B. **Conclusion** [18F] FDG-PET/CT may be useful for prediction of outcome of sorafenib treatment in patients with HCC.

P740

Hepatic falciform ligament Tc99m-macroaggregated albumin activity on SPECT/CT prior to Yttrium-90 microsphere radioembolization: Prophylactic measures to prevent non-target microsphere localisation via patent hepatic falciform arteries

Y. Kao, A. Tan, A. Goh; Department of Nuclear Medicine and PET, Singapore General Hospital, Singapore, SINGAPORE.

AIM: Yttrium-90 (Y-90) intrahepatic arterial microsphere radioembolization may be used in selected cases of unresectable hepatocellular carcinoma. Non-target delivery of Y-90 resin microspheres along the hepatic falciform ligament have been reported to cause acute radiation dermatitis of the anterior abdominal wall. We describe two patients where hepatic falciform ligament Tc99m-macroaggregated albumin (MAA) activities were found on SPECT/CT during pre-therapy planning and its impact on treatment strategy. **MATERIALS AND METHODS:** Two patients with hepatocellular carcinoma underwent routine pre-therapy Tc99m-MAA liver-lung shunting study and abdominal SPECT/CT. In both patients, hepatic falciform ligament Tc99m-MAA activity were seen on SPECT/CT leading to active measures being taken to prevent non-target Y-90 resin microsphere localisation. **RESULTS:** The first patient underwent prophylactic coil embolization of the patent hepatic falciform artery; the second patient underwent super-selective infusion of Y-90 resin microspheres to avoid the patent hepatic falciform artery. Both patients experienced no acute post-therapy complications. **CONCLUSION:** SPECT/CT provides valuable diagnostic information for treatment planning prior to Y-90 resin microsphere therapy. Careful evaluation of the Tc99m-MAA SPECT/CT is essential to identify any extrahepatic radiotracer activity. In our patients the finding of hepatic falciform ligament Tc99m-MAA activity led to appropriate treatment strategy and intervention. The outcome was the safe and uneventful delivery of Y-90 resin microspheres.

P741

Selective internal radiation therapy (SIRT) with Yttrium-90 (90Y) radiomicrospheres in the treatment of unresectable hepatocellular carcinoma

N. Arslan¹, M. Emi², E. Alagoz¹, B. Ustunsoz³, K. Oysul⁴, M. Beyzadeoglu⁴, S. Gorgulu⁵, M. A. Ozguven¹, ¹Gulhane Military Medical Academy and Medical Faculty, Department of Nuclear Medicine, ANKARA, TURKEY, ²Gulhane Military Medical Academy and Medical Faculty, Department of Radiology, ANKARA, TURKEY, ³Gulhane Military Medical Academy and Medical Faculty, Department of Radiology, ANKARA, TURKEY, ⁴Gulhane Military Medical Academy and Medical Faculty, Department of Radiation Oncology, ANKARA, TURKEY, ⁵Gulhane Military Medical Academy and Medical Faculty, Department of General Surgery, ANKARA, TURKEY.

OBJECTIVE Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide with few treatment options. The therapeutic benefit and safety of 90Y microspheres is well supported in the literature. The aim of this study is to review the role of liver directed radiotherapy with 90Y microspheres for unresectable HCC. **MATERIAL AND METHOD** Twelve patients with HCC were considered for SIRT. All patients had PET/CT scan to detect any extra hepatic metastases. Patients with sufficient liver function had pre-treatment visceral angiography to define and

occlude non-target arteries and Technetium-99m macro aggregated albumin scan to detect lung shunting, and also simulate SIRT. The Body Surface Area method was used to calculate the prescribed radiomicrospheres activity. Bremsstrahlung imaging was performed to confirm delivery of Y-90 microspheres to the desired hepatic arterial territory in all patients after the delivery of microspheres. **RESULTS** The administered activity ranged from 1 to 2,5 GBq (mean 1,71 GBq). The absorbed doses to tumour masses ranged between 44 Gy to 1640 Gy (mean 476,2 Gy), while the absorbed doses to normal liver and lung ranged between 12.6 Gy to 227,7 Gy (mean 53,4 Gy) and 2,4 to 11,4 Gy (mean 6,5 Gy), respectively. Overall response rate was 66,6 % for 9 patients out of 12 who had follow up results so far. **CONCLUSION** Y-90 radiolabelled microspheres can be effectively used for the treatment of HCC with little side effects. The selective nature of microsphere distribution allows the delivery of high doses of radiation to tumors while keeping the exposure of the healthy liver at a minimum.

P742

Comparison of 153-Samarium and 89-Sr in pain palliative therapy efficacy in patients with bone metastatic prostate cancer. Do plasma markers HER-2, TNF- α or IL2 work as prognostic factors?

I. I. Iakovou¹, A. Dumas¹, T. Christoforidis¹, M. Siabanopoulou², V. Nikos¹, D. Lo Presti¹, S. Georga¹, K. Badiavas¹, A. Psarakou², D. Pantoleon¹, N. Karatzas¹; ¹3rd Nuclear Medicine Dept. of the Aristotle University, General Hospital "G. Papageorgiou", Thessaloniki, GREECE, ²2nd Nuclear Medicine Dept. of the Aristotle University, AHEPA Hospital, Thessaloniki, GREECE.

Aim: The study compares the efficacy of palliative treatment using Strontium-89-chloride (89Sr) or 153-Samarium Lexidronam (153Sm) on pain symptoms, quality of life and bone marrow function, in men with painful bone metastases due to prostate cancer and investigates the role of specific plasma markers as prognostic factors. **Method:** A total of 32 men suffering from prostate cancer and widespread bone metastatic disease enrolled in this prospective study. Fifteen patients were treated with 153Sm and 17 patients with 89Sr. Pain palliation was evaluated on the basis of the Wisconsin pain test improvement and response was graded as complete, partial, minimal or absent. All patients were interviewed using standardized sets of questions before and after therapy weekly for 3 months. Blood counts tests were performed weekly for the first 6 weeks and then after 3 months. Haematological toxic side effects were reported according to WHO guidelines. The correlation between response to therapy and human epidermal receptor-2 (HER2), serum interleukin-2 (IL-2) and tumor necrosis factor- α (TNF- α) levels was also studied. **Results:** Treatment efficacy was complete in 15 men (47%), partial in 11 (34%) and none in 6 (19%) patients. The global response rate was 83% for 89Sr and 80% for 153Sm. There was two patients with a thrombocytopenia grade I and only one with grade III. Platelet and white blood cell counts returned to pre-therapy levels within 6-12 weeks after therapy. Patients who responded to palliative therapy had higher IL-2 and lower HER2 and TNF- α concentrations, than the non-responders. **Conclusion:** Both radiopharmaceuticals appear to be equally effective in pain palliation, without induction of severe side effects or significant differences in therapeutic efficacy or toxicity. HER2, IL-2 and TNF- α are plasma markers proved to be useful indicators of patient response to palliative treatment.

P743

Safety and Efficacy of Repeated Samarium-153- EDTMP Treatment in Patients With Painful Bone Metastasis

I. Siim, L. Zaabar, I. Meddeb, D. Ben Sellem, B. Letaief, A. Mhiri, F. Ben Slimene; Nuclear Medicine Dept., Salah Azaiez Institute, Tunis, TUNISIA.

Introduction: Bone metastases are a major complication of several different cancers and are a source of considerable morbidity including pain. Bone seeking radiopharmaceuticals are an effective and well tolerated treatment for painful bone metastases. **Aim:** The purpose of the analysis was to assess the safety and efficacy of repeated doses of Samarium-153- EDTMP in patients with metastatic bone pain. **Patients and Methods:** Data were collected retrospectively for 76 patients treated with Samarium-153- EDTMP (1mCi/kg) for painful bone metastasis. Particular emphasis was placed on analysis of data from 11 patients receiving ≥ 2 doses. Patients were eligible for retreatment with Samarium-153- EDTMP if pain improved after initial treatment but subsequently recurred by Week 8 or later, provided adequate hematologic function was present (leukocyte > 3,000/mL and thrombocyte >75,000/mL). Pain scores, adverse events, and hematologic parameters were assessed after each dose. **Results:** A total of 11 patients received more than 1 dose of Samarium-153- EDTMP, 5 received 3 infusions, 3 received 4 infusions, 3 received 5 infusions, and 1 received 6 infusions (mean: 3,09 doses per patient). The mean interval between the first and second infusions and between infusions after the second was ≈ 14 weeks. Mild, transient suppression of platelets and white blood cell counts was the most common adverse event after treatment. Both WBCs and PLTs decreased to a nadir value of approximately 36%, 38% and 43% of baseline after 1 dose, 2 doses and ≥ 3 doses, respectively. Recovery to PLT >75,000/mL and WBC >3,000/mL (toxicity grade 1 or less) occurred in 86% after a second or greater administration. The incidence of grade 3 hematologic toxicity was 5% and 8% in patients who received 2 and ≥ 3 administrations, respectively. A Significant decreases in pain ($p < 0.05$) were observed in 64% and 77% of patients, respectively, after 2 doses and ≥ 3 doses. **Conclusion:** Repeated dosing of Samarium-153- EDTMP was both safe and effective and is a reasonable treatment option in patients whose bone pain recurs after an initial injection provided that adequate hematologic function is present at the time of drug administration.

P744

Comparison of strontium-89 imaging with Bremsstrahlung to bone scintigraphy

M. Yoshimura, K. Okamoto, K. Uchida, J. Park, K. Saito, N. Kanesaka, K. Koizumi, K. Tokuyue; Tokyo Medical University, Shijuku-ku, Tokyo, JAPAN.

Introduction: Strontium-89 is suggested to act as a calcium mimic and accumulates at sites of osteoblastic lesions through incorporation into the mineralizing collagen during new bone formation. In most cases, the accumulation of strontium-89 and bone scintigraphy resembles, but in some cases there is great discrepancy between them, and as a result, favorable effect is not

obtained. In this study, we compared strontium-89 imaging with bremsstrahlung (Sr-89 imaging) to bone scintigraphy semiquantitatively and investigated the cause of the discrepancy of these imagings. **Subjects & Methods:** (Subjects) Twenty patients with 55 lesions of multiple bone metastases were treated with intravenous Sr-89 of 2.0MBq/kg. Sr-89 imaging was obtained 2-6 weeks after injection, using a gamma camera fitted with a multi-purpose collimator: a 50% energy window was centered over the 71-keV photopeak. Bone scintigraphy before Sr-89 therapy was obtained 4 hours after intravenous injection of 740MBq of Tc-99m MDP/HMDP. (semiquantification method) Regions of interest (ROIs) were placed over the affected sites on both Sr-89 imaging and bone scintigraphy. S-index was calculated by dividing the counts/pixel of the each affected site by the counts/pixel of the non-affected femur on Sr-89 imaging, and B-index was calculated by dividing the counts/pixel of the each affected site by the counts/pixel of the non-affected femur on bone scintigraphy. Then the S-index and the B-index of each region were compared. **Results:** S-index ranged from 1.3 to 5.4. B-index ranged from 2.1 to 51.8. S-index and B-index of each region correlated in most cases. All the regions with lower S-index compared with B-index were metastases from breast cancer, which had been treated with bisphosphonate priorly for at least one year. **Conclusion:** Lower Sr-89 accumulation rather than expected from bone scintigraphy might be caused by breast cancer and/or bisphosphonate. It was impossible to distinguish which factor is more important to reduce the accumulation of Sr-89, because there was no case with therapeutic history of bisphosphonate priorly for at least one year except for breast cancer. It is important to realize the localization and retention of Sr-89 activity to make more effective use of Sr-89.

P745

External Radiotherapy and Radionuclide Therapy of Bone Metastases: a Feasible and Synergic Combination

L. Castorina¹, G. Mazzone², A. Di Grazia², ¹Nuclear Medicine, Rem, Catania, ITALY, ²Radiotherapy, Rem, Catania, ITALY.

Aim: To assess the feasibility, the safety and the efficiency of the combination of external radiotherapy and radionuclide therapy of painful bone metastases. **Patients and methods.** Twenty-nine patients with painful bone metastases were treated both with external radiotherapy and radionuclide therapy. There were 15 women (14 with breast cancer) and 14 men (12 with prostate cancer), aged between 44 - 80 (average 64), who received 60 treatments in total with radiotherapy (20 - 30 Gy spread out over 5 - 10 days) and 32 treatments with ¹⁵³Samarium-EDTMP (2000 - 2500 MBq). 19 of the 29 patients were treated firstly with external radiotherapy (28 irradiated seats), while 10 patients were initially injected with the radionuclide and then subjected to radiotherapy with external beams (32 irradiated seats). All the radiotherapy treatments were provided with 3DCRT, using an electron accelerator LINAC 6 - 15 MV energy. **Results and Conclusions.** Most of the patients who firstly received external radiotherapy at that moment had only one or two painful bone metastases; when they were suffering from disseminated metastases, they were rightly referred to radionuclide therapy. However, when patients with multiple bone metastases were still in pain, they completed their treatment with a palliative cycle of radiotherapy with external beams. So, we had favourable clinical outcomes and the pain palliation was accompanied by an improvement in mobility and a decrease in the dosage of analgetics. The haematological toxicity was mild and transient and the patient's compliance was very high.

P746

Graves' ophthalmopathy aggravation after radioiodine treatment; is the preventive corticosteroid administration useful?

I. I. Iakovou, A. Dumas, K. Badiavas, V. Nikos, T. Christoforidis, D. Lo Presti, S. Georga, N. Karatzas; 3d Nuclear Medicine Dept. of the Aristotle University, General Hospital "G. Papageorgiou", Thessaloniki, GREECE.

AIM: Radioactive sodium iodine (131-I) administration is a well established method for Graves' disease treatment, despite of the aggravation of ophthalmopathy seen in some of the patients. The aim of our study was to investigate if the use of corticosteroids could inhibit the worsening of ophthalmopathy. **METHODS:** We retrospectively studied 39 patients suffering from Graves' disease and mild ophthalmopathy, who received 131-I treatment during the last 2 years in our department. Twenty patients (41 \pm 8 yrs) formed Group A and 19 patients (37 \pm 10 yrs) Group B. TSH mean blood levels was 0.006 μ g/dl \pm 0.001 μ g/dl in group A and 0.005 μ g/dl \pm 0.001 μ g/dl in group B while iodine thyroid uptake was 8,3% \pm 4,2% and 7,8 % \pm 4,9% respectively. Methylprednisolone was administered in group A patients for 7 days before and for 7 days after the iodine treatment. All the patients were evaluated every three months up to one year by clinical and biochemical examinations. **RESULTS:** Seventeen patients (85%) from group A became euthyroid after 12 months, while ophthalmopathy worsened just in 1 (5%) of them. In group B 15 (79%) patients finally returned to normal thyroid function even though in 4 (21%) ophthalmopathy worsened. It is notable that TRAb, TgAb and TPOAb levels were especially high in patients with Graves' eye disease aggravation. **CONCLUSION:** Corticosteroid therapy proved extremely useful in patients with Graves' disease before therapy with 131-I, since it can inhibit the worsening of ophthalmopathy, especially in these with high levels of thyroid antibodies.

P747

Differentiated Thyroid Cancer : empirically treating high serum thyroglobulin levels and negative morfo-funtional findings .

F. Capocchetti¹, B. Crisculi¹, G. Theodorou¹, D. Tsevas¹, G. Rossi², C. Manni¹, P. Nicolli¹, S. Remediani¹, A. Spini¹, S. Fattori², S. Ancidei¹, E. Brianzoni¹; ¹Nuclear medicine division, ASUR ZT 9, Macerata, Italy, Macerata, ITALY, ²Medical Physic Unit, ASUR ZT 9, Macerata, Italy, Macerata, ITALY.

Aim: Some Authors proposed in Differentiated Thyroid Cancer use of empiric radioiodine treatment (ERT) in patients with dosable thyroglobulin serum levels and negative diagnostic findings. In literature is reported that ERT have shown 59-94% positive post-treatment WBS and a

decrease of serum thyroglobulin levels in about two-third of cases. Aim of this work is to investigate retrospectively success of radioiodine therapy and if exist a predictive factor of response to ER T. **Material and methods** 25 patients (10male;15female; aged 36-83 years) with DTC submitted to, at least one treatment with 131I, with dosable serum thyroglobulin and negative morpho-funtional findings (WBS, US and 18F-FDG PET/CT) were submitted, after adequate thyroid hormone withdrawal to high dose of radioiodine (range 4440-7437; mean 5428). Post-treatment WBS was performed 3 and 7 days later. Liver uptake, if present, was evaluated with a visual assessment. Serum levels of TSH (U/ml), thyroglobulin (ng/ml), AbhTg, urinary iodine and ematochemical routine. Median follow-up from RI was 10 months through diagnostic WBS after rh-TSH stimulation (with thyroglobulin and Antibodies levels) and US. **Results:** Based on WBS findings patients were divided into two groups: -Group A 13/25 (52%) with evidence of pathological foci: mean thyroglobulin levels 111, range 13-642; mean TSH value 87, range 47-218; 4/13 (30%) patients with positive AbhTg and 7/13 (54%) with altered liver enzymes. -Group B: 12/25(48%) with negative WBS associated in all cases to liver uptake: mean thyroglobulin 179, range 11-1575; mean TSH 103, range 42-148; 2/12 (17%) with positive AbhTg; 8/12 (67%) with altered liver enzymes. Follow-up: Group A, 3/13 (23%) complete remission, 1/13 (7%) progression disease and 9/13 (70%) stable or partial remission. In Group B (based mainly on serum thyroglobulin levels): 6/12 (50%) undosable, and 6/12 (50%) partial decrease or persistent levels. No significant correlations were found between Group A and B concerning age, Histology, serum thyroglobulin levels, activity administered, liver uptake also related to liver function and follow-up. **Conclusions:** In our series we found a positive WBS in 52% of cases with undosable thyroglobulin in 9/25 (36%), stable or partial decrease in 15/25 (60%) and increased levels in 1/25 (4%) at the successive follow-up. As previous reported in literature do not seems be a predictive factor of response to radioiodine therapy so use of 131I should be selected individually and the potential advantages of treatment balanced with immediate and long-term complications.

P748

RhTSH-aided 131I ablation in thyroid cancer: Effect of short term L-thyroxin withdrawal (10 days) on pre-therapy evaluation

M. Chianelli¹, V. Todino¹, F. Graziano¹, C. Panunzi¹, R. Guglielmi¹, A. Signore², E. Papini¹; ¹Regina Apostolorum Hospital, Albano - Rome, ITALY, ²University Sapienza, Rome, ITALY.

We have recently reported that rhTSH-aided low-dose 131I thyroid ablation is effective but does not allow thorough evaluation of thyroid remnants by neck scintigraphy (131I given after only 1 rhTSH injection). We have therefore developed an alternative protocol based on short term L-T4 withdrawal (10 days) in an attempt to enhance pre-therapy 131I uptake. Low risk patients who underwent total thyroidectomy for differentiated thyroid cancer were enrolled; all patients on the day of treatment underwent 131I uptake, neck scintigraphy and US of the neck. Patients were prepared to 131I ablation by administration of rhTSH; patients from group A (n=20) did not stop L-T4, patients from group B, (n=20) stopped L-T4 for 10 days. In patients from both groups TSH, Tg and TgAb were measured on the day of treatment and after two days. Post-therapy WBS was acquired. Efficacy of ablation therapy was assessed after 6-12 months by WBS, Tg and TgAb measurement, off L-T4. No patient from either group became biochemically hypothyroid. All patients showed visible uptake in the thyroid bed at the post-therapy WBS. In group A five patients did not show any visible uptake in the thyroid bed at the pre-therapy scan and, on average, lower neck uptake was observed (1.3±1.4% vs 4.7±4.5%, group A vs group B, p=0.004; Mann Whitney U test). In patients showing high uptake (>10%) at pre-therapy scan, treatment with prednisone was started to prevent local side effects. High ablation rates have been observed in both groups of patients for both ablation criteria (Tg and WBS off L-T4) with no statistical differences between the two groups (Fisher exact test). Short term L-T4 withdrawal (10 days) allows thorough pre-therapy scintigraphic evaluation of thyroid remnants without inducing signs or hypothyroidism.

P749

Clinical analysis of papillary thyroid carcinoma in elderly patients with radioiodine ablation

Z. Gao, W. Chang; Huazhong University of Science and Technology, Union Hospital, Wuhan, CHINA.

Objective Papillary thyroid carcinoma (PTC) is the most common type in thyroid carcinoma, and its incidence is more than 80%. The overall prognosis of patients with PTC is excellent, but the prognosis in elderly patients is worse. The aim of this paper was to analyze the clinical features and evaluate the outcome and the safety of radioiodine treatment in older patients with PTC. **Methods** Thirty-six cases of post-operative elderly PTC patients (14 men, 22 female; age range, 60~80years, mean age 63.4 years) were included. ALL patients had a histologically confirmed diagnosis of PTC. All of them underwent total or near-total thyroidectomy. Twenty-two patients had regional lymph nodes metastatic lesions, and 9 had distant metastasis. All patients had undergone iodine-131 remnant ablation therapy in 3-4 weeks after thyroidectomy. Serum FT3, FT4, TSH, TgAb, TPOAb, Tg, cervical ultrasound and other laboratory examinations were essential in every return visit. The efficacy of the therapy was assessed by a diagnostic iodine-131 whole body scan and stimulated Tg level in 6 months postablation. And the ablation therapy was considered to be successful if the iodine-131 scan was negative and stimulated Tg was less than 2 ng/ml. **Results** The median follow-up period was 32.5 months, with a range from 12 to 65 months after radioiodine therapy. Ten patient were complete remission, 14 were partial remission, 6 were stable diseases, and 6 were progressive diseases. **Conclusions** The prognosis of elder PTC gets worse with advancing age, extra-thyroid extension and distant metastasis. Postoperative radioiodine-131 therapy should be the standard approach of treatment for the elderly patients to improve the fate.

P750

A Population Kinetic Model for 18F-Choline in Prostate Cancer Patients

A. Giussani¹, T. Janzen¹, F. Tavola², H. Uusijärvi-Lizana³, S. Mattsson³, M. Zankl¹, M. C. Cantone², C. Hoeschen¹; ¹Helmholtz Zentrum München,

Neuherberg, GERMANY, ²Università degli Studi di Milano, Milano, ITALY, ³Lund University and Skane University Hospital, Malmö, SWEDEN.

AIM The MADEIRA Project (Minimizing Activity and Dose with Enhanced Image quality by Radiopharmaceutical Administrations) aims to improve the efficacy and safety of 3D functional imaging by optimizing, among others, the knowledge of the temporal variation of the radiopharmaceuticals' uptake in and clearance from tumor and healthy tissues. The aim of the present study was to optimize the time schedule for data collection and improve the evaluation of the organ doses to prostate cancer patients undergoing investigation with 18F-choline. **MATERIALS AND METHODS** Biokinetic data were collected at Malmö University Hospital in 10 patients undergoing screening with 18F-choline for recurrence or metastasis after prostate cancer. Activity concentrations in liver, kidneys, spleen, and (if present) tumour were quantitatively determined up to four hours post-administration by means of PET and PET/CT imaging. Additionally blood and urine samples were collected at different times post-administration and the activities in those samples were measured with a gamma counter. Starting from these data, a compartmental model was developed using the forcing function method and the population kinetic approach with the pharmacokinetic/pharmacodynamic modelling software ADAPT 5, and reference radiation dose values for a typical patient were estimated. **RESULTS** The developed model structure consists of one central compartment, representing the blood, and seven compartments, which describe the peripheral organs and the elimination pathways. The population standard deviation was found to be lower than 60% for all model parameters, indicating that this general structure is able to describe successfully the biodistribution of the radiopharmaceutical in a typical patient. The organ receiving the highest radiation dose is the kidney (0.083 mGy/MBq). Doses to liver and spleen were estimated at 0.062 mGy/MBq and 0.042 mGy/MBq respectively. On the basis of the model calculations, it was also shown that PET scans taken later, between 90 and 120 minutes after injection of 18F-choline, have the potential to improve the detection of malignant lesions during diagnostic examinations. **CONCLUSIONS** The population kinetic model developed in this study was successfully used to describe the biodistribution of 18F-choline in prostate cancer patients. With the help of the model, reliable estimates of the organ doses to the patients were calculated, and suggestions for an improved diagnostic protocol introduced. **ACKNOWLEDGEMENTS** The work was carried out within the Collaborative Project "MADEIRA" (www.madeira-project.eu), cofunded by the European Commission through EURATOM Seventh Framework Programme (Grant Agreement FP7-212100).

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Kinetic model analysis for absorbed dose calculation applied to brain in 18F-FDG PET imaging

E. F. G. Laffon¹, M. Bardies², J. Barbet², R. Marthan³; ¹Hôpital Haut-Lévêque, Pessac, FRANCE, ²Université de Nantes, INSERM U892, Nantes, FRANCE, ³Université de Bordeaux 2, INSERM U885, Bordeaux, FRANCE.

A kinetic model analysis is proposed to assess absorbed dose to an arbitrary tissue in [¹⁸F]-FDG PET imaging, whose efficiency is demonstrated in physiological brain, by comparing calculated estimates with human literature data. First, an analytic solution for the tissue [¹⁸F]-FDG time-activity curve (TAC) has been derived from kinetic model analysis assuming reversible radiotracer trapping. Then, integrating this solution from the time of tracer administration to infinity, yielded analytic solutions for cumulated activity, (and hence for the ratio of cumulated/injected activity) and percentage of tracer uptake for an arbitrary tissue. Calculated estimates from these analytic solutions for the whole grey and white matter are in very good agreement with human literature data: 7.55 versus 6.57 (± 1.51) MBq.h (per unit of administered activity of 37 MBq), .204 versus .220 (± .090) h, and 6.25 versus 6.90%, respectively. We conclude that the proposed kinetic model analysis has proven effective in assessing absorbed dose to human brain in [¹⁸F]-FDG PET imaging, under physiological conditions. It is suggested that it could be applied to other tissues and other PET tracers.

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Relevance of antibody immunoreactivity in modelling radioimmunotherapy with anti-CD66 antibody

P. Kletting, S. N. Reske, G. Glatting; Universität Ulm, Ulm, GERMANY.

Aim: Radioimmunotherapy (RIT) with anti-CD66 antibody is used in the conditioning before stem cell transplantation. The modelling of RIT with anti-CD66 antibody might be further improved taking into account that during the labelling procedure DTPA is bound to the complementarity determining regions (CDR) of the antibody. The implementation of a reduced immunoreactivity might help to estimate other parameters more accurately such as the binding rates or the number of antigens and might therefore allow a better prediction of the therapeutic biodistribution. **Methods:** Two different physiologically based pharmacokinetic (PBPK) models were fitted to biodistribution data of 4 AML and 1 ALL patients (gamma camera images of liver, spleen, red marrow and total body plus pretherapeutic and therapeutic serum measurements). Model A included immunoreactivities for In-111 and Y-90 labelled antibody which were calculated based on the average number of DTPA (fragments) per antibody (93±1%). For model B an optimal immunoreactivity of 100% was assumed. The model fits were compared using the corrected Akaike information criterion (AICc). To test the prediction accuracy, both models were fitted solely to the data obtained during pretherapeutic measurements. Thereafter, the simulated prediction of the therapeutic time activity curve in serum of the models was compared to the corresponding measured data. **Results:** For 4 out of 5 patients model A is most supported by the data according to the AICc. Visual inspection showed excellent fits for both models. The difference of the determined organ residence times using model A (red marrow 38±2.6 h; liver 4.9±0.9 h; spleen 2.4±0.8 h and total body 68.9±1.6) and B were <1%. The predictions of the therapeutic serum concentration were also similar. The average relative error of predicted and measured data points for model A and B were (20±17)% and (22±21)%, respectively. **Conclusions:** The results indicate that the implementation of the immunoreactivity is stronger supported by the data than assuming 100% fully intact antibodies. In addition, the prediction accuracy of the model is increased. However, the improvement is not substantial. More patient data must be investigated to draw a final conclusion. **Research support:** German research foundation (DFG GL 236/7-2)