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EDITORIAL

European Association of Nuclear Medicine (EANM) response to the proposed ASTRO's framework for radiopharmaceutical therapy curriculum development for trainees

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The American Society for Radiation Oncology (ASTRO) and the ASTRO board of directors approved in the fall of 2021 a new framework for radiopharmaceutical therapy curriculum development for trainees, which was published by Ana P. Kiess et al. [1]. Being members of the European Association of Nuclear Medicine (EANM) Board, we want to comment officially on behalf of the EANM.

Although the paper by Kiess et al. may have its merits at trying to fill in a gap in workforce and related expertise appearing in a North American context in nuclear medicine, we think that this proposal may not be the ideal solution. In this regard, it may be worthwhile to describe the history and framework of radiopharmaceutical therapy in more detail, to better understand which pitfalls for radiation oncologists and radiotherapists, as well as for the patients, may linger in a simplified proposition not taking into account all ins and outs.

Kiess et al. start by stating that in 2017, the ASTRO board of directors prioritized radiopharmaceutical therapy as a leading area for new therapeutic development. However, radiopharmaceutical therapy in the context of the specialty of nuclear medicine is not so recent as it actually has already a history of more than 70 years [2].

Starting with iodine-131 therapies for hyperthyroidism and thyroid cancer as early as in the 1940's, a lot of therapies using radionuclides and radiopharmaceuticals have been introduced in nuclear medicine:

- Radiation synovectomy using Erbium-169, Rhenium-186, or Yttrium-90;
- [^{131}I]mIBG therapy for children suffering from neuroblastoma;
- Therapies for liver cancer using at first [^{131}I]NaI, then ^{188}Re-labelled lipiodol and finally commercially available ^{90}Y- or ^{166}Ho- labelled microspheres;
- Radioimmunotherapy with Bexxar (([^{131}I]Tositumomab) or Zevalin ([^{90}Y]Y-Ibritumomab tiuxetan);
- Bone palliation using [^{153}Sm]Sm-EDTMP, [^{177}Lu]Lu-EDTMP, [$^{186/188}$Re]Re-HEDP, [^{89}Sr]$SrCl_2$, and [^{223}Ra]$RaCl_2$;
- ^{177}Lu-labelled somatostatin analogues for neuro-endocrine tumours (e.g. [^{177}Lu]Lu-DOTATATE).

These (and more) are all examples that go back for decades already. As illustrated, both oncological and non-oncological indications are considered, using different radiopharmaceuticals and radionuclides, in addition to "classical" beta-emitters nowadays also including alpha-emitters [3–5].

Over all these years, research development both in terms of the radiopharmaceuticals and the radionuclides used was boosted and clinical care using radiopharmaceutical therapies in general was accommodated primarily by nuclear

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medicine physicians and their colleagues as radiochemists, radiopharmacists, radiobiologists, medical physicists, and others, mostly in close collaboration with the referring physicians such as endocrinologists, paediatricians, rheumatologists, urologists, and medical oncologists. In particular, highly interdisciplinary research such as, e.g. with urology was the key to successful development of novel radiopharmaceuticals and their clinical application to patient treatment.

The therapy stratification, follow-up, and prediction are performed by nuclear medicine physicians within the framework of theranostics using the twin radiopharmaceuticals tailored for imaging. To optimize the metabolic information obtained using dedicated SPECT or PET systems, hybrid imaging nowadays allows for a one-stop shop for the patient by adding CT or MRI capabilities, often in close collaboration with radiologists for the anatomical reporting. Major steps and progress in detection technology, software analysis, and quantification methodology in the last decades and especially in the last years all had a major impact on the quality, accuracy, and understanding of the results of imaging in the stetting of diagnosis and therapy using radiopharmaceuticals.

What Kiess et al. [1] rightfully have detected is a breakthrough over the last decade in terms of a better understanding of molecular pathways in oncology, with a translation by pharmaceutical companies into new precision therapies such as immuno-therapy and, because of growing clinical evidence, progressively being better reimbursed by health authorities, resulting in a boost for improved patient treatment. In its slipstream, a growth in commercial availability and dissemination of radiopharmaceuticals helps to answer the rapidly growing clinical needs for precision medicine by offering added value imaging and related therapy.

The validation of [^{177}Lu]Lu-PSMA compounds for prostate cancer therapy, for example, follows and connects with the related imaging using, e.g. [^{68} Ga]Ga-PSMA-11 and [^{18}F]PSMA-1007 heralding the appearance of the new kid on the block in terms of a new clinical indication. The results of VISION trials established a new clinical standard [6]. Accordingly, the latest EU and ASCO GU update guidelines strongly recommend offering [^{177}Lu]Lu-PSMA treatment to pre-treated mCRPC patients with one or more metastatic lesions, highly expressing PSMA (exceeding the uptake in the liver) on the PET/CT scan using diagnostically radiolabelled PSMA compounds [7].

In this regard, the EANM organizes a multidisciplinary, so-called, FOCUS 5 meeting in 2023 — 'by the expert for the expert'. The aim is to critically assess the latest developments in molecular hybrid imaging and now especially related systemic radiopharmaceutical therapy in prostate cancer, to reach a multidisciplinary consensus on the current state-of-the-art and to generate expert recommendations on how to guide the field towards establishing clinical impact in line with the theranostics concept.

The specialty of nuclear medicine uses unsealed radioactive sources of for diagnosis and therapy, whereas radiotherapy makes use of sealed sources or external irradiation. Both modalities are a completely different ballgame, especially taking into account the dynamics and kinetics of the systemically administered radiopharmaceuticals and the related theranostic imaging. Particularly, since in radiopharmaceutical therapy, most treatments are administered systemically and because radiobiology of EBRT cannot be extrapolated to RPT, there is a need for specific radiobiology of radiopharmaceutical therapy [8, 9].

Not surprisingly, the training of nuclear medicine in Europe encompasses in general 5 years, similar to the present training in radiation oncology. Considering the existing training program in radiation oncology and time already devoted to radiopharmaceutical therapy in the classical nuclear medicine training program, it may be a major challenge for the radiation oncology program to accommodate the time necessary for the training in radiopharmaceutical therapies, even omitting teaching and training on the related imaging.

It provides some hope for the future that Kiess et al. [1] — on behalf of ASTRO — reflect in their conclusions that collaboration with other specialties, especially the ones at the core of radiopharmaceutical therapies, i.e. nuclear medicine, represented by the SNMMI in the USA, should be considered [10]. Especially since what primarily is at stake is the quality and safety of radiopharmaceutical therapy for the patient.

In Europe, the EANM, representing 40 member states, has the advantage of a sufficient and expert dedicated and specifically trained workforce to accommodate the medical breakthroughs and growing clinical needs for radiopharmaceutical therapy and its related imaging. We think that this may have been due to a fundamentally different choice in Europe in general as compared to the USA for keeping nuclear medicine an independent specialty, rather than transforming the imaging branch into an additional certification within the radiology curriculum, leaving the intrinsically related radiopharmaceutical therapy orphanage.

This different position is fully reflected by the European Training Requirements published by the NM section of the UEMS (https://uems.eanm.org/commitees/education-syllabus/syllabus/). Radiology as a specialty focuses more on highly specialized regional morphological examinations and anatomically image-guided interventions, rather than on a holistic approach of molecular pathways and related theranostics. It is a long way for radiology from thinking in terms of molecular pathways, physiopathology, and radiopharmaceutical therapies, while the same accounts for radiation oncology in terms of the theranostics concept, related

molecular imaging, and the use of unsealed sources of radioactivity, especially in a dynamic perspective.

This does not mean that radiology and radiation therapy do not share much in common with nuclear medicine, reflected in previous times by the common denominator of organizational clusters on radiation sciences. On the other hand, it also implies that convergence needs much communication, reflection, and understanding. In this regard, the interest of the patient and the quality of the clinical service provided is at the core of what every medical professional society needs to focus on and offer.

Hence, in Europe, the EANM wants to secure the quality of the growing molecular imaging and therapy needs through quality standards, teaching, and accreditation. In order to achieve these goals, the EANM aims at establishing EU wide collaborations with the respective European scientific organization such as EAU, ESMO, and, last but not least, ESTRO. While the US context provides its own challenges, we hope — as intended — that this letter adds to the discussion also in the USA for multidisciplinary collaboration and the right and necessary competences in addition to qualification.

Declarations

Research involving human participants and/or animals This manuscript does not contain proprietary research involving neither humans nor animals.

Informed consent This manuscript does not contain proprietary human data, accordingly an informed consent is not applicable.

Ethical statement This editorial falls outside of the scope of ethical concerns regarding experimentation with humans or animals.

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