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REVIEW ARTICLE

Highlights of the 32th Annual Congress of the EANM, Barcelona 2019: the nucleolympic games of nuclear medicine—a global competition for excellence

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Abstract
The 32th Annual Congress of the European Association of Nuclear Medicine (EANM) returned to Barcelona, Spain, from the 12th to the 16th of October 2019, under the chairmanship of Professor Francesco Giammarile. With a total number of 6833 participants from all over the world, the EANM congress was the year's most important meeting in nuclear medicine worldwide. The congress was an unprecedented success, with more than 1800 submitted abstracts presented in scientific sessions and a variety of lectures including CME sessions from all fields of nuclear medicine and multidisciplinary joint symposia with clinical societies. Innovative research was presented in all fields, showing important developments in radiopharmacy and preclinical oncology, PET and non-PET diagnostic strategies, new therapeutic approaches and molecular imaging-based prediction of prognosis and treatment response. In the field of physics and instrumentation, technological progresses, radiomics and artificial intelligence were highlighted as most relevant areas of innovation. This review gives a summary of our personal choice among the most notable developments of this year's contributions as presented in the Highlights session of the Annual congress of the EANM 2019. EANM 2019 outlines a bright future for nuclear medicine, with groups competing all over the world to bring innovation across all fields of medicine, through increased standardization, progressively lower radiation dose and increasingly high clinical impact.

Keywords EANM 2019 · Annual Congress · Abstracts · Highlights · Nuclear medicine · Novel developments

Introduction

In 2019, the 32th Annual Congress of the European Association of Nuclear Medicine (EANM) took place in Barcelona, Spain, from 12 to 16 October 2019 under the chairmanship of Professor Francesco Giammarile. With a total number of 6833 participants, and among these 1971 attendees from non-European countries, the EANM congress was the year's most important meeting in nuclear medicine not only in Europe but worldwide. Looking at the development over the last 10 years, we could compare EANM 2019 with EANM 2009, which also took place in Barcelona. There was a tremendous 20% increase in number of participants, from 5485 in 2009 to 6833 in 2019, and contributions coming from 19 additional countries. These changes were paralleled by similar developments regarding submitted and accepted abstracts, with 1982 submitted abstracts in 2009 and 2268 in 2019, and contributions from 20 additional countries, again reflecting that the EANM Congress is the world's leading meeting in nuclear medicine. The acceptance rate of submitted abstracts slightly decreased from 85 to 81% resulting in 1883 accepted abstracts in 2019 (Fig. 1).

The Congress program offered scientific sessions and a variety of lectures such as plenary lectures, symposia and CME sessions, covering all relevant fields of nuclear medicine with multidisciplinary innovative research in radiopharmacy and preclinical oncology, PET and non-PET diagnostics, novel treatment approaches with radioligand therapy, molecular imaging-based prediction of prognosis as well as therapy response assessment. In the field of physics and instrumentation, the major innovations concerned imaging technology and dosimetry, as well as the use of radiomics and artificial

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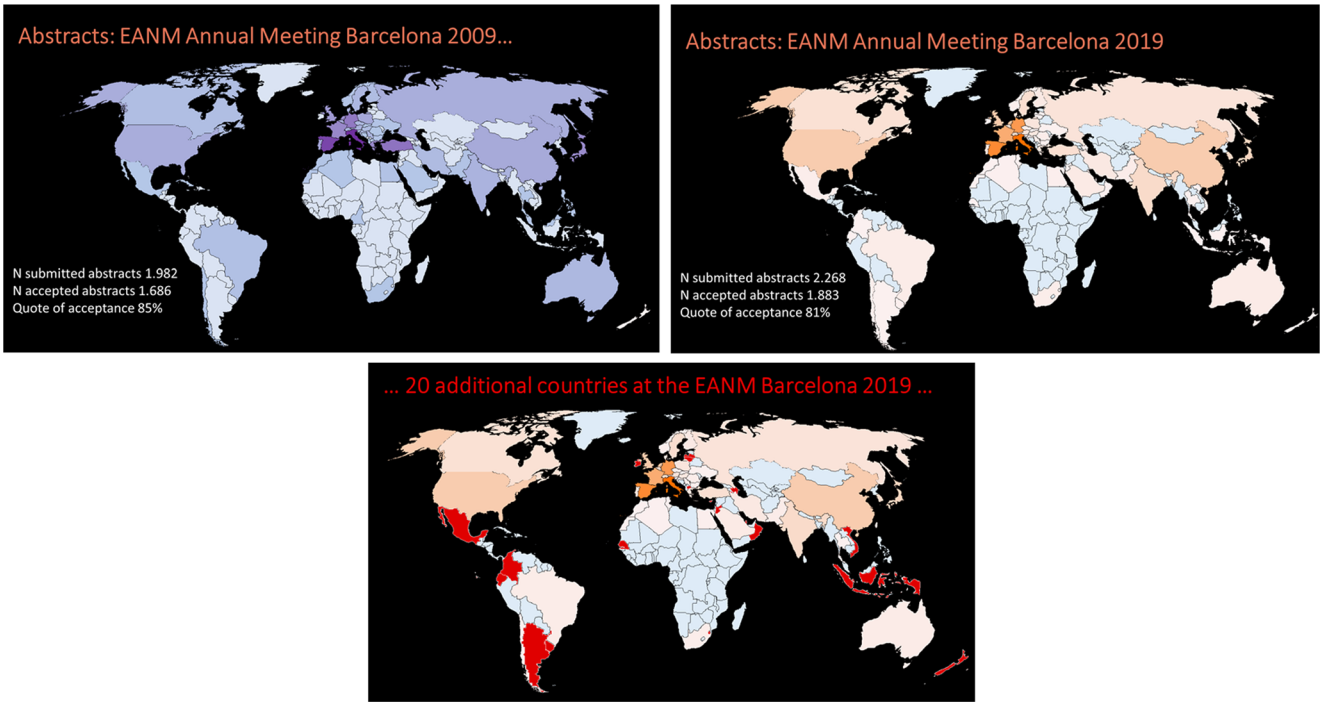

Fig. 1 The number and origin of abstracts submitted and accepted at the Annual Congress of Nuclear Medicine of the EANM in 2019 compared to 2009. A clear increase in numbers is seen as well as in the international coverage of the congress, as contributions from 20 additional countries were received in 2019 compared to 2019, reflecting that the EANM Congress is the world's leading meeting in nuclear medicine

intelligence, the newest trends. In the closing session of the congress, the Highlights lecture, a choice of the most innovative and interesting contributions were presented. Abstract reviewers nominated 384 of all submitted abstracts for possible inclusion in the Highlights lecture. As presenters of the Highlights lecture, we had the privilege and the responsibility to select the 49 contributions that in our opinion represented the most relevant progresses. More than 75% of these selected 49 abstracts resulted from multinational collaborations, including in 25% of cases three or more countries and proving that the EANM is really a worldwide phenomenon. This brought to the idea of this year's theme of the Highlights lecture: Nucleolympics—worldwide attendance, successful collaboration, team spirit longing to accomplish ambitious goals together, seeking to rise to "new heights". This review gives an overview of the selection presented in the highlights lecture of the EANM 2019. All contributions of the entire Congress can be found in the Congress book being published in the European Journal of Nuclear Medicine and Molecular Imaging, Volume 46, Supplement 1, October 2019.

New developments in radiopharmacy—preclinical oncology

We received a great number of high-quality abstracts on the development and use of innovative radiopharmaceuticals in preclinical oncology, addressing new targets with a great potential of clinical translation.

In a collaboration among groups from the UK and the Netherlands, O' Neill et al. performed a proof of principle study of [^{111}In]-anti γH2AX-TAT, a cell-penetrating antibody allowing for imaging of double-strand DNA damage repair, therefore serving as an in vivo non-invasive biodosimeter in a model of pancreatic neuroendocrine cancer. The authors found an intense uptake in [^{177}Lu]DOTATATE-treated mice, which was significantly higher compared to the uptake observed in non-treated mice. [^{111}In]-anti-γH2AX-TAT allows monitoring of DNA damage following [^{177}Lu]DOTATATE therapy and revealed heterogeneous damage responses, as confirmed in ex vivo analyses [1, 2] (Fig. 2).

Abouzayed et al. from Uppsala, Sweden, presented data on the synthesis and preclinical evaluation of GRPR/PSMA bispecific heterodimers for theranostics application in prostate cancer. The bispecific heterodimer BO530 was radiolabelled with iodine-125 with high radiochemical yields. A biodistribution study in mice bearing GRPR+/PSMA+ xenografts revealed a high tumour uptake over several days, while uptake in normal organs rapidly decreased. These results were confirmed in vivo by SPECT/CT imaging. The heterodimer BO530 can be radiolabelled with iodine-123 for SPECT, iodine-124 for PET or iodine-131 for therapy and therefore is a promising theranostic agent in prostate cancer [3].

Data on a new approach for theranostic application in medullary thyroid cancer were reported by von Guggenberg et al.

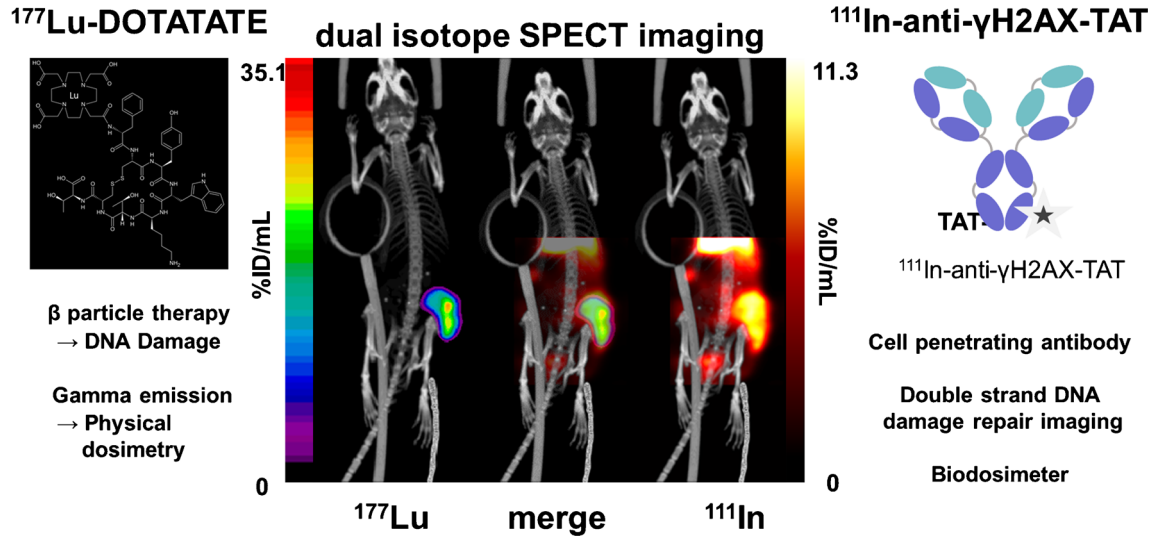

Fig. 2 As shown in this figure, the DNA damage generated by [^{177}Lu]DOTATATE therapy can be visualized in vivo using a modified radiolabelled antibody [^{111}In]-anti-γH2AX-TAT. The application of dual isotope SPECT imaging revealed a heterogenous DNA damage response to beta particle therapy in a xenograft mouse model that could not be accounted for by image-based dosimetry methods. Figure published under a Creative Commons license [2]

from Austria, in collaboration with Poland. The newly developed Ga-68-labelled minigastrin analogue DOTA-MGS5, targeting cholecystokinin-2 receptor (CCK2R) expressing tumours, showed clearly improved metabolic stability and targeting properties compared to the unmodified peptide derivative, resulting in higher tumour uptake and tumour to kidney ratios of the peptide labelled with different radiometals. In a first PET/CT study performed in a medullary thyroid cancer patient, a significant uptake was observed in liver metastases, together with physiological uptake in the stomach. These results are highly promising for the improvement of the diagnosis and therapy of CCK2R expressing tumours [4].

Watabe et al. from Osaka, Japan, and Heidelberg, Germany, reported on a promising theranostic approach targeting fibroblast activation protein in tumour stroma by [^{64}Cu]- and [^{225}Ac]FAPI-04 in pancreatic cancer xenograft mice. PET imaging of [^{64}Cu]FAPI-04 showed mild uptake in the tumours and relatively high uptake in the liver and intestine. Immunohistochemical staining revealed FAP expression in the stroma of both xenografts. Treatment with [^{225}Ac]FAPI-04 showed significant tumour growth suppression in the PANC-1 xenograft mice compared to the control mice. This study showed the feasibility of theranostics using [^{64}Cu]FAPI-04 and [^{225}Ac]FAPI-04 for the treatment of FAP-expressing pancreatic cancer [5].

Two very interesting contributions from the US were presented by Grudzinski et al., who reported on NM600, a theranostic alkylphosphocholine, with [^{86}Y]NM600 PET showing consistent tumour accumulation and retention across all tumour models, highest in breast and oral cancer models. No signs of acute toxicity were observed [6, 7] (Fig. 3). A combination therapy with molecular targeted radiotherapy, in situ vaccine and immune checkpoint inhibition (ICI) showed the best results, with all mice surviving and 83% of them being tumour-free. Low-dose [^{90}Y]NM600 can improve response to both local and systemic immunotherapy treatments in "cold" tumours that normally do not respond to ICI alone [8].

Regarding innovative treatment options in disseminated ovarian cancer, a collaboration between groups from Gothenburg, Sweden, and Copenhagen, Denmark, showed promising results on the biodistribution and therapeutic efficacy of [^{211}At]Farletuzumab. Palm et al. showed that the tumour-free fraction of three control groups of mice was significantly lower compared to [^{211}At]Farletuzumab-treated mice (being as high as 91%) in a disseminated ovarian cancer mouse model. The authors demonstrated that cell and animal experiments, together with modelling and dosimetry, allowed to optimize clinical therapy. Similar absorbed doses to microtumours are expected in patients from i.p. delivery of 200 MBq/L [^{211}At]Farletuzumab [9].

Besides new treatments of solid tumours, interesting data were also presented on novel therapeutic options in hematological entities.

Quelven et al. from France demonstrated that [^{212}Pb]Rituximab as an alpha-radioimmunotherapy (RIT) induced a significant survival increase compared to control groups in B-non-Hodgkin's lymphoma (B-NHL) models. Survival increase was more marked in early tumour stages compared to advanced tumour stages. In advanced stages, the best survival was effectively obtained with two treatments. These results show the efficacy of [^{212}Pb]Rituximab in this lymphoma model with significant tumour regression and

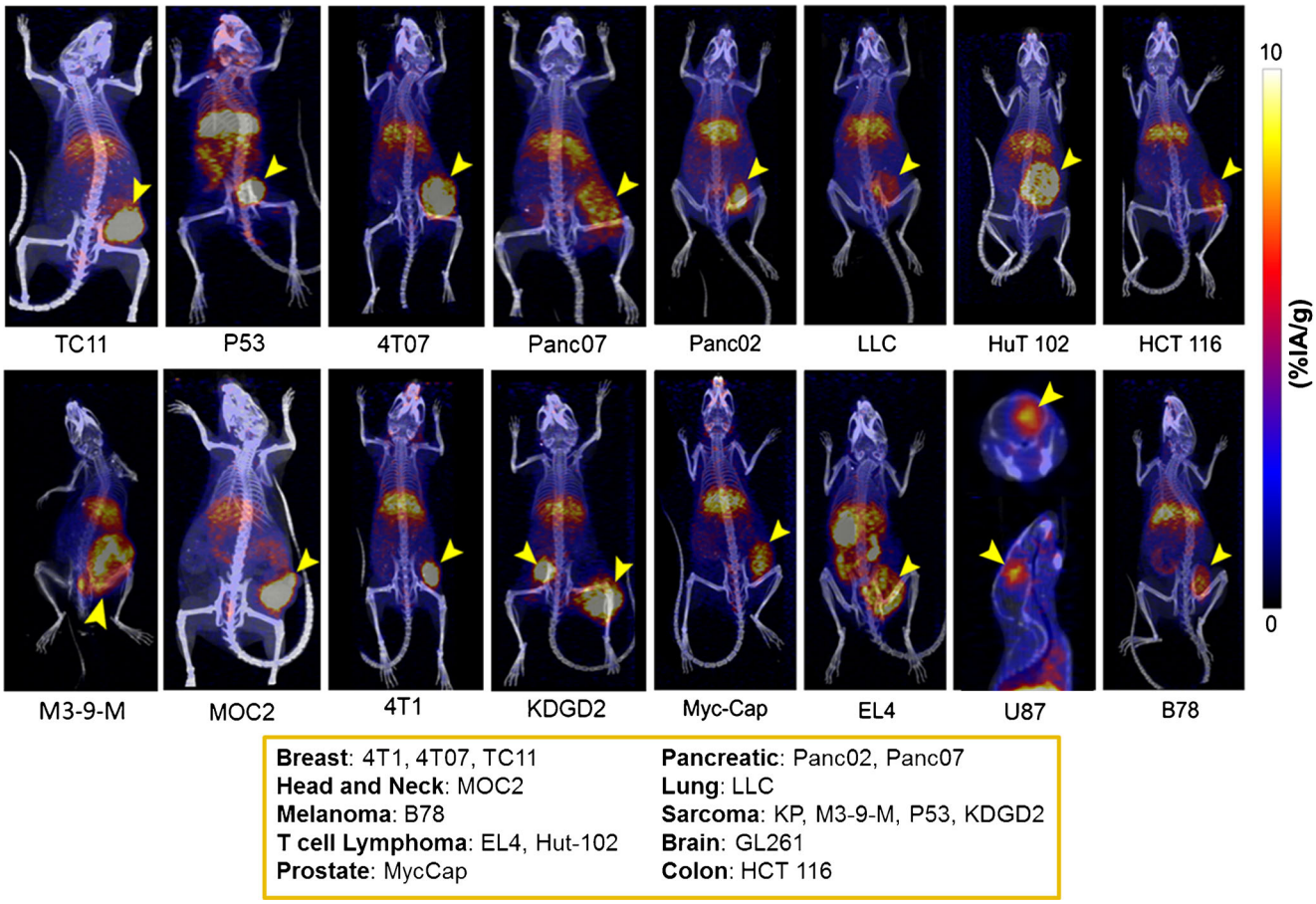

Fig. 3 Mice bearing flank tumours (breast, head and neck, melanoma, T cell lymphoma, prostate, pancreatic, lung, sarcoma, brain or colon) were injected intravenously with [^{86}Y]-NM600 and imaged using microPET/CT. Volume renderings of decay-corrected PET activity are overlaid on CT volumes for each tumour model. Selective tumour uptake in a variety of tumour models illustrates the broad tumour targeting ability of NM600. This research was originally published in the Journal of Nuclear Medicine (JNM). Grudzinski JJ, Hernandez R, Marsh I, Patel RB, Aluicio-Sarduy E, Engle J, Morris Z, Bednarz B, Weichert J. Preclinical Characterization of 86/90Y-NM600 in a Variety of Murine and Human Cancer Tumor Models. J Nucl Med. 2019;60(11):1622–1628. © SNMMI [7]

increased survival highlighting the potential of alpha-RIT in B-NHL treatment [10].

In preclinical CD37-positive chronic lymphocytic leukaemia (CLL) and NHL models, a single injection of [^{212}Pb]NNV003 was safe and effective with promising efficacy in an ibrutinib-resistant CLL model as presented by Saidi et al. [^{212}Pb]NNV003 showed a significantly prolonged survival compared to ibrutinib and controls ($p < 0.0001$). Survival in [^{212}Pb]NNV003-treated mice was 15 weeks compared to only 4 weeks in ibrutinib-treated mice, which was comparable to the survival of the control group [11].

Tracer development and testing in non-oncological applications

New tracers are currently under development for a number of relevant targets in a variety of non-oncological conditions, spanning from neurodegenerative processes to infections and cell grafting.

Yousefi and colleagues in a collaboration across Germany, Sweden and Switzerland have developed and tested a tracer, [^{18}F]FS3-1, targeting alpha-synuclein deposits. These are the molecular component of pathological aggregates, called Lewy bodies, occurring in Parkinson's disease and dementia with Lewy bodies. This translational study has evaluated tracer specificity in vitro and ex vivo and has subsequently tested it in a first-in-human application [12]. Kramer and colleagues from Chile, Germany and Denmark have characterized a PET tracer selective for serotonin 2A receptors, namely (R)-[^{18}F]MH.MZ, in healthy volunteers. They observed a brain distribution consistent with the known target density, namely high levels in the cortical gray matter and the hippocampus, as well as the ability to block binding using a specific antagonist, ketanserine. This tracer has also favorable properties for quantification, given the absence of radioactive metabolites and the good correlation between compartment models

and reference tissue models. Serotonin 2A receptors have been implicated in the pathophysiology of depression, Alzheimer's disease and schizophrenia and are thus relevant drug targets [13]. In a collaboration including colleagues from Germany, United States and Israel Barthel and colleagues have used [^{18}F]F-flusipidine, a sigma-1 receptor antagonist, to measure the effect on these receptors of pridopidine, a drug under development to provide functional benefit in patients with Huntington disease. Using simultaneous PET/MRI, they could show differential changes in perfusion (using arterial spin labelling), glial cell metabolism (with MR spectroscopy), network activation (using functional MRI) and sigma-1 receptor availability with PET in patients and controls, suggesting that the drug could have a specific mechanism of action in patients and validating the use of PET/MR as comprehensive tool for the investigation of pharmacological modulation [14].

Important progresses were also made in developing and validating tracers targeting tau pathology, one of the defining pathological hallmarks of Alzheimer's disease and other neurodegenerative tauopathies such as progressive supranuclear palsy. Mueller et al. reported the results of a multinational collaboration leading to the discovery and preclinical characterization of a promising second-generation tracer, [^{18}F]F-PI2620, with high affinity for the specific target in brain samples, high brain uptake, fast wash-out and low off target binding [15]. Lowe et al. in a study conducted in the United States reported a good correlation between in vivo imaging and post-mortem assessment of tau pathology using one first-generation tracer for tau, namely [^{18}F]Flortaucipir [16].

Hugenberger and colleagues, from Germany, tested [^{18}F]-GP1, a tracer targeting the glycoprotein IIb/IIIa receptor on activated platelets, for its ability to detect thrombi in left ventricle assisting device in a first cohort of five patients. The good match observed between image analysis and presence/absence of a glycoprotein IIb/IIIa thrombus is an important tool to evaluate the necessity of replacement and management strategies in these patients [17]. Lee et al. in a collaborative study among researchers from Korea and Germany have used (S)-4-(3-[18F]Fluoropropyl)-L-glutamic acid ([^{18}F]F-FSPG) for the assessment of patients with inflammatory bowel disease, showing in a phase 2 study including 20 patients that tracer binding was associated with disease activity both in ulcerative colitis and Crohn's disease and could be a promising non-invasive diagnostic marker for active disease [18]. A collaboration between The Netherlands and Sweden, directed by Jansen, has used [^{68}Ga]-NODAGA-exendin-4, a tracer targeting glucagon-like peptide-1 receptor (GLP-1R), to show viability of intrahepatic transplantation of islet of Langerhans grafts in patients with type 1 diabetes, promising as tool to monitor graft functioning in recipients [19].

Finally, [^{18}F]F-Fluorodeoxysorbitol, a patogen-specific agent for Enterobacteriaceae, was used by Granados et al. in the United States and Colombia to evaluate patients with pneumonia and monitor the effect of antibiotics in a first-in-human study, opening new perspectives for bacteria-class specific imaging [20].

Diagnostics: oncology

As in former years, considerable advances were made in clinical oncology and this was reflected by the high number of interesting contributions in this field.

Regarding pediatric oncology, Marner et al. from Denmark presented a large dataset of [^{18}F]FET PET scans in a broad spectrum of pediatric tumour types, including 97 patients and a total of 169 [^{18}F]FET PET/MRI scans. [^{18}F]FET PET combined with MRI showed a significantly higher accuracy for tumour detection compared to MRI alone. In the group of clinically indicated [^{18}F]FET (e.g. due to equivocal MRI), clinical management was influenced in 30% of scans. In conclusion, [^{18}F]FET PET is useful in cases of pediatric brain tumours with difficult clinical decision making [21].

A collaboration between eight European centres reported the final results of a phase I clinical trial using a novel CCK2 receptor-localizing radiolabelled peptide probe for personalized diagnosis and therapy of patients with progressive or metastatic medullary thyroid carcinoma. The positive results on stability, radiolabelling and toxicity of [^{111}In]CP04 enabled the development of a clinically useful formulation. Safety of ^{111}In-CP04 intravenous injection was confirmed. The dosimetry data with vs. without gelofusine co-injection showed promising results justifying the start of clinical trials with Lu-177-labelled CP04 [22] (Fig. 4). Non-invasive imaging of tumour -associated fibroblasts by [^{68}Ga]FAPI-PET/CT is increasingly being used in different tumour entities showing promising results.

Serfling et al. (Würzburg and Heidelberg, Germany) reported on their first experience in head and neck cancer diagnostics using [^{68}Ga]FAPI PET/CT compared to [^{18}F]FDG PET/CT, including six patients with primary tonsil carcinoma. In all patients, [^{68}Ga]FAPI-PET/CT detected the primary lesion and FAPI uptake in the tumours was confirmed by immuno-histochemistry. There was no significant FAPI uptake in the contralateral tonsil in contrast to [^{18}F]FDG PET/CT, which was positive also in the contralateral tonsil due to inflammatory tissue. To conclude, in comparison to [^{18}F]FDG, [^{68}Ga]FAPI allows for a better differentiation between tumour tissue and inflammatory changes [23].

Regarding imaging of prostate cancer, Farolfi et al. conducted a multicenter retrospective study (several European and one US centre) on the performance of [^{68}Ga]PSMA-11 PET in patients with PSA persistence after radical prostatectomy for the detection of residual prostate cancer. In this study on 210 high-risk patients, [^{68}Ga]PSMA-11 PET detected disease in more than two thirds of patients with PSA persistence

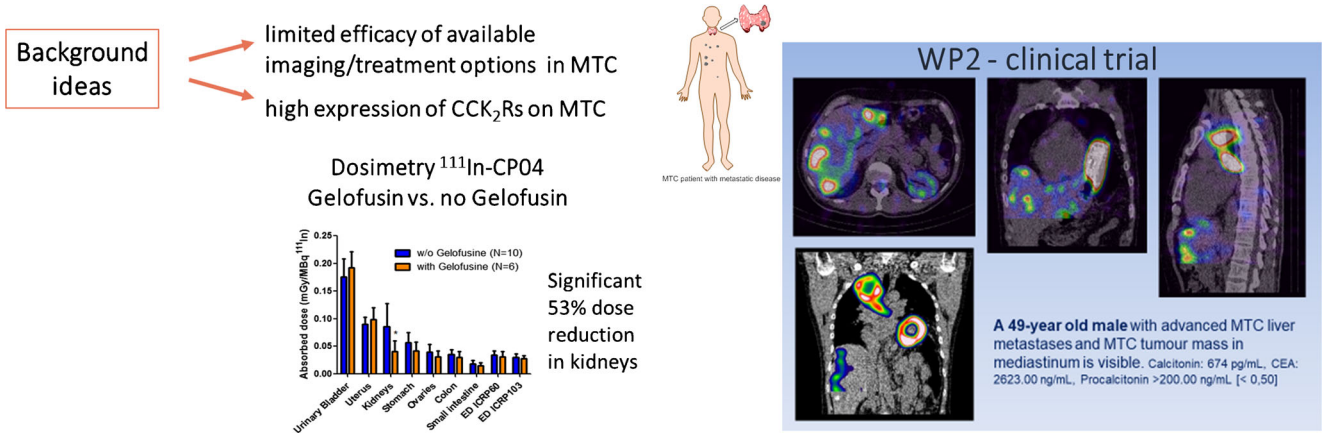

Fig. 4 In an attempt to produce therapeutic options with CCK2/gastrin receptor-binding radiolabelled analogues, it has been observed that DOTA-DGlu-DGlu-DGlu-DGlu-DGlu-Ala-Tyr-Gly-Trp-Met-Asp-Phe-NH2 (CP04) shows the most promising characteristics: high metabolic stability and receptor affinity with a high and prolonged tumour uptake against low renal retention, and was therefore selected for clinical evaluation. Receptor targeting was achieved to some extent in CCK2/gastrin receptor expressing tissues and, most importantly, in tumour tissue with a high tumour-to-background ratio

after radical prostatectomy. Thirty-six percent of patients had disease limited to the pelvis with the obturator region being the most commonly involved region. In a subgroup with both pre- and post-prostatectomy PET, 45% of patients had at least one lesion already detected at baseline scan suggesting PET persistence. These data support a role for [^{68}Ga]PSMA-11 PET to identify residual disease in high-risk patients [24].

Physics

This year, EANM congress has seen also a high number of contributions on technical development of the technology used for nuclear medicine imaging. Multiple groups are working on modifying the design of PET scanners in order to obtain an extended field of view at costs comparable to commercially available systems, using either a sparse detector module confirmation, as in a study conducted in the United States by Zein and colleagues [25] or axial ring splitting with/without radial compression, as proposed by Vandenberghe and colleagues from Belgium, United Kingdom and the United States [26] (Fig. 5). Other relevant developments concern the production of 68 Ga, increasingly used in high impact tracers, from a biomedical cyclotron, as tested by researchers from Canada and Denmark [27], or the refinement of drop-in gamma probes to be used during robot-assisted laparoscopic surgery, in a clinical study conducted across Germany, The Netherlands and Belgium [28]. Finally, the development of new technologies evolves in parallel with adapted quality assurance strategies. Valladares et al. have reported on the consensus recommendations from a European network for quality controls of the most recent hybrid tool which has entered the clinical nuclear medicine arena, namely PET/MRI hybrid systems [29].

Radionuclide therapy

Besides innovative research regarding diagnostics, interesting therapeutic approaches in oncology are tested, either against new target structures or using new radionuclides like alpha-emitters.

A group from Chile presented data on the preliminary evaluation of tumour uptake and laboratory parameters after a single dose of [^{177}Lu]RM2 radioligand therapy (RLT) in metastatic castrate-resistant prostate cancer (mCRPC). Four patients with late-stage mCRPC underwent [^{68}Ga]PSMA-11 and [^{68}Ga]RM2 PET/CT, a tracer targeting the gastrin releasing peptide receptor, both with comparable uptake. All received a single dose of 5.6 GBq [^{177}Lu]RM2 which was well tolerated without relevant side effects.

Despite stable binding to tumour lesions for at least 7 days, no therapeutic PSA response was observed. Therefore, further evaluation is necessary to define the role of this promising approach in prostate cancer treatment [30].

Besides clinical data on safety and efficacy, dosimetry is crucial for new treatment approaches. Kurth et al. from Rostock, Germany, presented the first in human dosimetry of [^{177}Lu]RM2 RLT in mCRPC patients. Six out of 35 screened patients showed a sufficiently high GRPr expression in ^{68}Ga-RM2 PET justifying [^{177}Lu]RM2 RLT. Therapy procedure was accompanied by dosimetry, based on quantitative SPECT/CT and whole body-imaging. [^{177}Lu]RM2 showed a significant uptake in tumour lesions. The highest exposed organ at risk was the pancreas, which was, however, below the maximum tolerable dose. In metastases, therapeutically relevant tumour doses were reached. Therefore, [^{177}Lu]RM2 is a treatment option for mCRPC patients without sufficient PSMA expression [31].

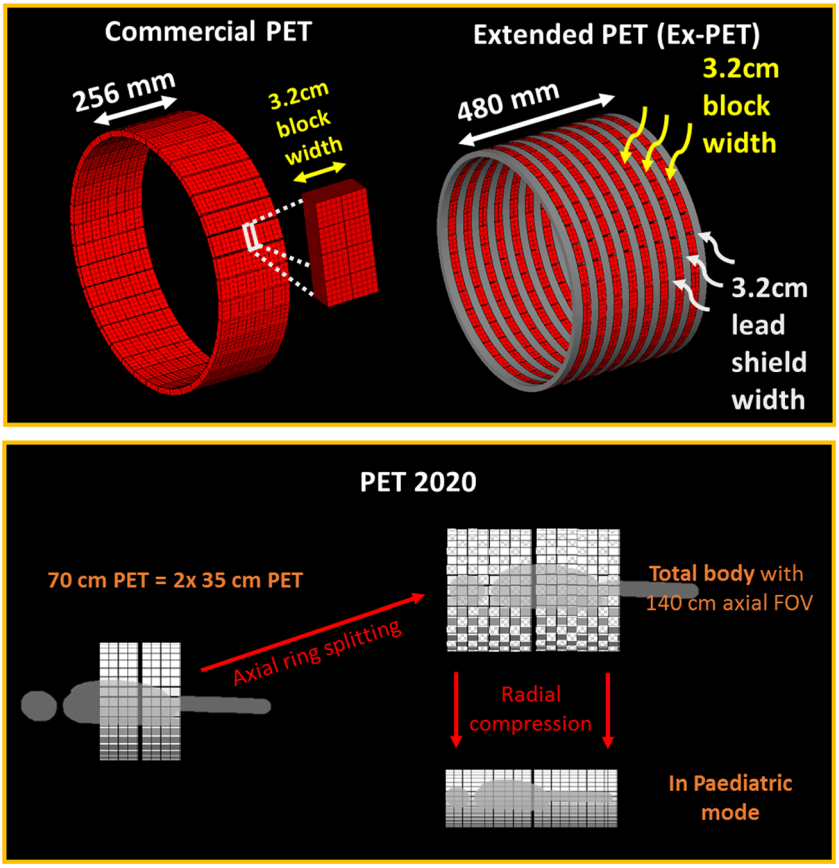

Fig. 5 Upper part: illustration of one concept of an axially extendable PET scanner, scanner geometry simulation. On the right, commercially available system with 8 compact LSO module rings, on the left, Ex-PET with extended AFOV incorporating gaps of equal width as the detector modules. Shielding rings have been inserted in the gaps between the detector module rings to reduce the inter-crystal blocks scattering and parallax effect. Lower part: illustration of an alternative concept of an axially extendable PET scanner. By splitting the rings in the axial direction, the 70-cm system can be extended into a 140-cm total body scanner. The smart organization of the gaps enables to further radially compress this configuration into a system with reduced diameter, which further increases the sensitivity

Besides identifying new targets suitable for therapeutic approaches, the use and combination of different radionuclides for radiolabelling are an interesting concept to increase efficacy and minimize side effects as shown by the group from Bad Berka, Germany. Kulkarni et al. presented data on a tandem PSMA RLT with Acc-225 and Lu-177 in advanced prostate cancer. Forty-three patients were treated with a combination of Ac-225 and Lu-177-labelled PSMA in the same cycle. No severe toxicity was observed. PSA response was reached in 84% of patients and imaging assessed by PSMA PET/CT showed partial or mixed response in 75% of patients. The authors showed that tandem therapy is feasible, safe and effective in end-stage metastatic prostate cancer being refractory to [^{177}Lu]PSMA. The risk of dose-limiting toxicity, namely xerostomia, can be minimized by lowering the activity of [^{225}Ac]PSMA [32].

Besides PSMA, RLT alpha-emitters are also increasingly being used in treatment of neuroendocrine tumours (NET): a group from New Delhi, India, presented their first clinical experience on safety and efficacy of [^{225}Ac]DOTATATE targeted alpha therapy in metastatic gastroenteropancreatic (GEP) NETs. Thirty-five patients with stable or refractory disease after [^{177}Lu]DOTATATE received [^{225}Ac]DOTATATE therapy. None of the patients experienced grade 3 or 4 hematologic and renal toxicities. Regarding response, a Chromogranin A decline higher than 50% was observed in 60% of patients. According to the RECIST-based response criteria, an objective response was reached in nearly 66% of patients. These results indicate that [^{225}Ac]DOTATATE therapy is safe with limited side effects and represents a new option in the treatment of end-stage GEP NET [33].

Besides systemic treatment options for metastasized tumour entities, interesting data on local treatment of lung malignancies were also presented.

Belhadj-Tahar et al. (China, France) reported on five patients suffering from local primary and secondary lung malignancies, not amenable to surgery, who received Rhenium-188-ImDendrim, a new potential anticancer agent administered directly into lung tumours under CT guidance and local anesthesia. The authors showed that Rhenium-188-ImDendrim diffused in all tumour parts and remained 72 h with no significant diffusion out the site of injection, as confirmed by SPECT imaging. No serious adverse events were observed. All targeted tumours were responding at 12 weeks, with two complete responses in [^{18}F]FDG-PET/CT. Percutaneous single and iterative administrations of this novel

Rhenium-188-Imdendrim brachytherapy device into lung cancers are safe and well tolerated [34].

Dosimetry

The developments in radionuclide therapy are accompanied by relevant developments in dosimetric strategies.

Preclinical studies, as the one presented by Tamborino and colleagues conducted in Belgium and The Netherlands, allowed comparing the cellular dosimetry of 177-Lutetium-labelled somatostatin receptor agonists and antagonists, studying a number of parameters linked with DNA damage induction and cell death [35].

In clinical studies, the number of image acquisitions and measurements required might represent a limitation for their routine applicability. Sandstrom et al., from Sweden, have measured the error induced in estimating the absorbed dose to kidneys based on one or two SPECT measurements vs. three measurements in patients with neuroendocrine tumours receiving [^{177}Lu]-DOTATATE therapy, in order to validate the most efficient acquisition protocol [36]. The stability of estimates over reconstructions and vendor was instead the focus of the study of Meyer Viol et al., from The Netherlands, which showed that with standardized reconstruction methods, inter-system variations in quantification were significantly reduced, a required step towards universal dose limits [37].

Finally, the standardization of therapeutic strategies requires also standardized systems for incident reporting. Marengo et al. presented a new IAEA tool to report incidents in therapeutic nuclear medicine, built as an extension of a Web-based system initially developed for radiotherapy [38].

Prediction and therapy response assessment

PET-derived metabolic parameters have been used in various settings for prediction of prognosis and treatment response as well as therapy response assessment of new treatments.

A collaboration between Munich and Heidelberg, Germany, showed that voxel-wise analysis of dynamic [^{18}F]FET PET enables non-invasive prediction of IDH genotype in newly diagnosed glioma. In this study, 322 patients underwent dynamic [^{18}F]FET PET imaging and contrast-enhanced MRI prior to surgery. Voxel-wise time to peak analysis was able to discriminate between IDH wild-type and mutant gliomas: in the overall group, %time to peak (cutoff > 22%) predicted an IDH wild-type status with a PPV of 89%. In the critical subgroup of non contrast-enhancing gliomas, the combination of dynamic time to peak and subsequent tumour to background ratio analysis increased the diagnostic accuracy. Voxel-wise dynamic FET PET thus allows for prediction of the prognostically pivotal IDH mutation status [39].

Regarding relapsed/refractory diffuse large B cell lymphoma, it is known that despite significant clinical benefits, patients treated with CD19 CAR T cells may experience early progression within the first 90 days after infusion. In a study by Vercellino et al. (Paris, Créteil, France), it was shown that after multivariate analysis, only the number of previous lines, total lesion glycolysis (TLG) as well as total metabolic tumour volume (TMTV) were predictive of relapse. High baseline TMTV and TLG were correlated to CAR T cell treatment failure in this entity [40].

Concerning the use of [^{18}F]FDG PET/CT in therapy response assessment, the two following contributions were highlighted.

Lhommel et al. from Brussels, Belgium, presented the results of the REACHIN study on the value of [^{18}F]FDG PET/CT to evaluate the efficacy of regorafenib in locally advanced non-resectable/metastatic biliary tract tumours. Sixty-six patients were included in this double blinded RCT phase II trial. Twenty-nine patients received [^{18}F]FDG PET/CT comparing [^{18}F]FDG tumour metabolism at baseline and after 2 weeks of either placebo or regorafenib treatment. ΔSUVmax, ΔMTV and ΔTLG showed a significant decline between baseline and follow-up scan for the treated group compared to the placebo arm. [^{18}F]FDG PET/CT is able to discriminate early metabolic tumour changes in this setting [41].

Lopci et al. (Milan, Italy) reported the results of a proof-of-concept study on the effect of Sorafenib on tumour glycolytic metabolism at 24 h, 1 week and 8 weeks of therapy in 13 patients with metastatic hepatocellular carcinoma (HCC). Responding tumours showed an increase in SUVmax at 24 h, which was negatively correlated to SUVmax at 1 week, indicating that [^{18}F]FDG PET can evaluate metabolic shift at 24 h. Moreover, as early as after 1 week of therapy, metabolic parameters (SUVmax, MTV, TLG) could predict response according to mRECIST. Additionally, MTV at 1 week was an independent prognostic factor for progression-free survival at multivariate analysis [42].

Radiomics

Radiomic feature extraction is a relevant strategy to identify information hidden in our medical imaging data. A reliable use of radiomic features needs stability across centers and vendors. For this reason, Pfaehler and colleagues from Germany and The Netherlands have developed 3D-printed phantom inserts, based on heterogenous patient tumours, to identify reconstruction settings harmonizing radiomic feature values in a multi-center setting: importantly, features extracted from EARL-compliant images were more reproducible than

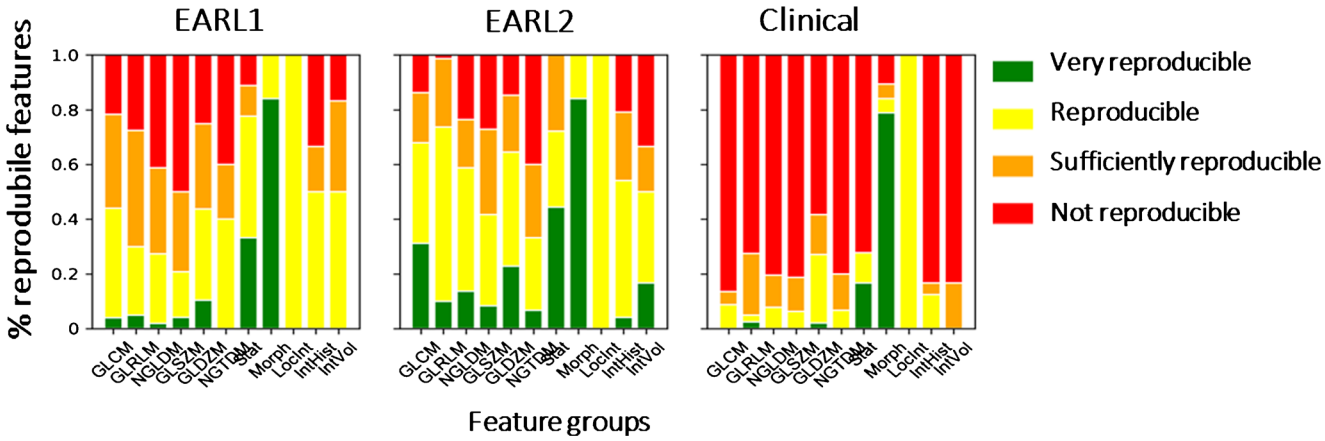

Fig. 6 A large number of radiomic features are harmonized using EARL-compliant reconstructions. The use of EARL2 is beneficial when compared with EARL1. When using clinical preferred settings, only a small number of features are found to be reproducible. This research was originally published in the Journal of Nuclear Medicine (JNM). Pfaehler E, van Sluis J, Merema BBJ, van Ooijen P, Berendsen RCM, van Velden FHP, Boellaard R. Experimental Multicenter and Multivendor Evaluation of the Performance of PET Radiomic Features Using 3-Dimensionally Printed Phantom Inserts. J Nucl Med. 2020;61(3):469–476. © SNMMI [44]

features extracted from clinical preferred reconstruction, highlighting the important added value of standardization [43, 44] (Fig. 6).

Texture feature analysis was tested this year in a wide range of applications, in particular the detection of infective endocarditis in a study conducted in Italy and The Netherlands [45], the prediction of lesion grade in patients with prostate cancer combining PET and MRI parameters, as studied in Vienna, Austria, by Papp and colleagues [46] and the prediction of treatment response to anti-programmed death 1 (PD-1) antibody treatment in refractory Hodgkin lymphoma patients [47], evaluated in a multicentric Italian project.

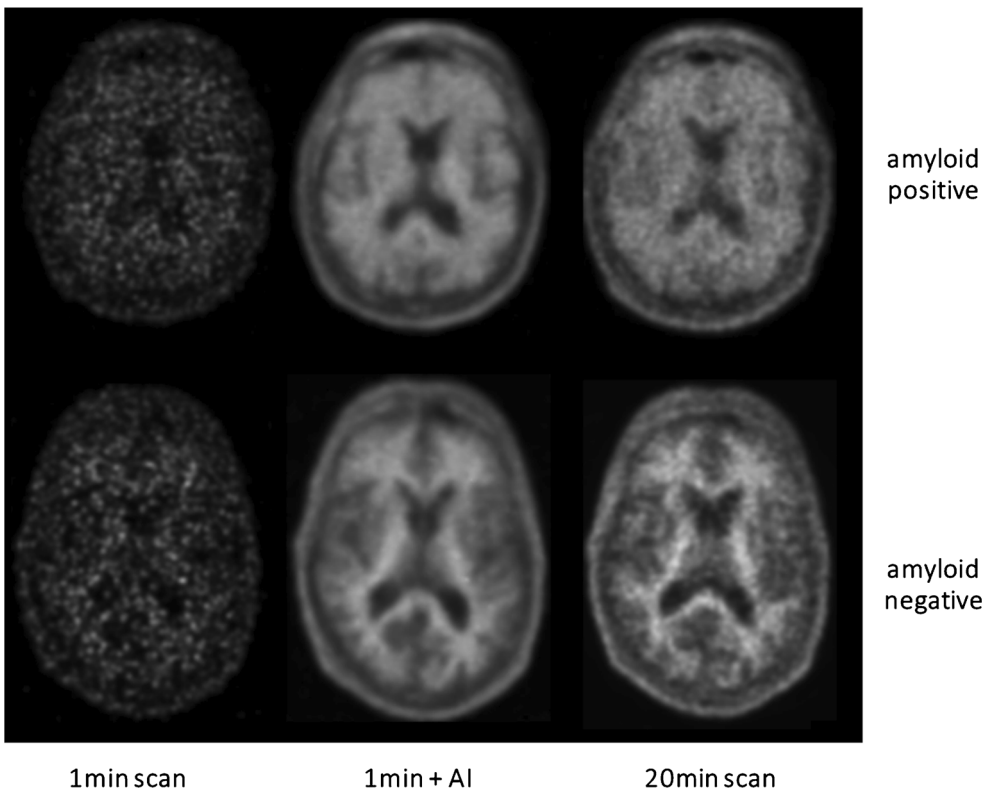

Fig. 7 The figure above illustrates the improvement of image quality and readability by using a trained neural network on a 1-min Florbetaben-PET/MRI-scan, comparable to the standard 20-min acquisition

Artificial intelligence

Artificial intelligence (AI) is exploding in all fields of medicine, including nuclear medicine. We received a high number of very interesting contributions using AI to either improve image quality or extract additional information from our images. In particular, deep learning approaches were used to reconstruct high-quality images from low-count acquisitions in various applications, in PET and SPECT. Gaede et al., in Denmark, worked on 2-[^{18}F]FDG PET images acquired during breath hold in patients with Hodgkin lymphoma, reducing by more than 80% the time needed [48], Schurer and colleagues, from Germany and the United States, processed amyloid images, obtaining and adequate performance with images acquired reducing tracer dosage or scan duration by 95% [49] [Fig. 7] and Reymann et al., in a study conducted in Germany, performed denoising in bone SPECT using deep learning, obtaining the best results by a modified U-Net architecture [50]. The group of Shi and colleagues, in Switzerland and Germany, used instead machine learning to predict post-therapy dosimetry for 177Lu-PSMA I&T treatment from pre-treatment PET imaging, obtaining accurate predictions with relevant improvements as compared with other approaches, such as population-based estimates [51].

Conclusions

Overall, the Highlights of EANM 2019 outline a bright future for nuclear medicine, with specific applications across all fields of medicine, namely increased standardization, progressively lower radiation dose and increasingly high clinical impact. The global and fair "competition" among all groups contributing to this world-leading event and striving for excellence exemplifies perfectly what we consider the "nucleolympic" spirit.

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Compliance with ethical standards

Conflict of interest Sarah Schwarzenböck (first author) declares that she has no conflict of interest. Valentina Garibotto (second author) has received research grants from Roche, Merck, Siemens, GE and Cerveau.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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