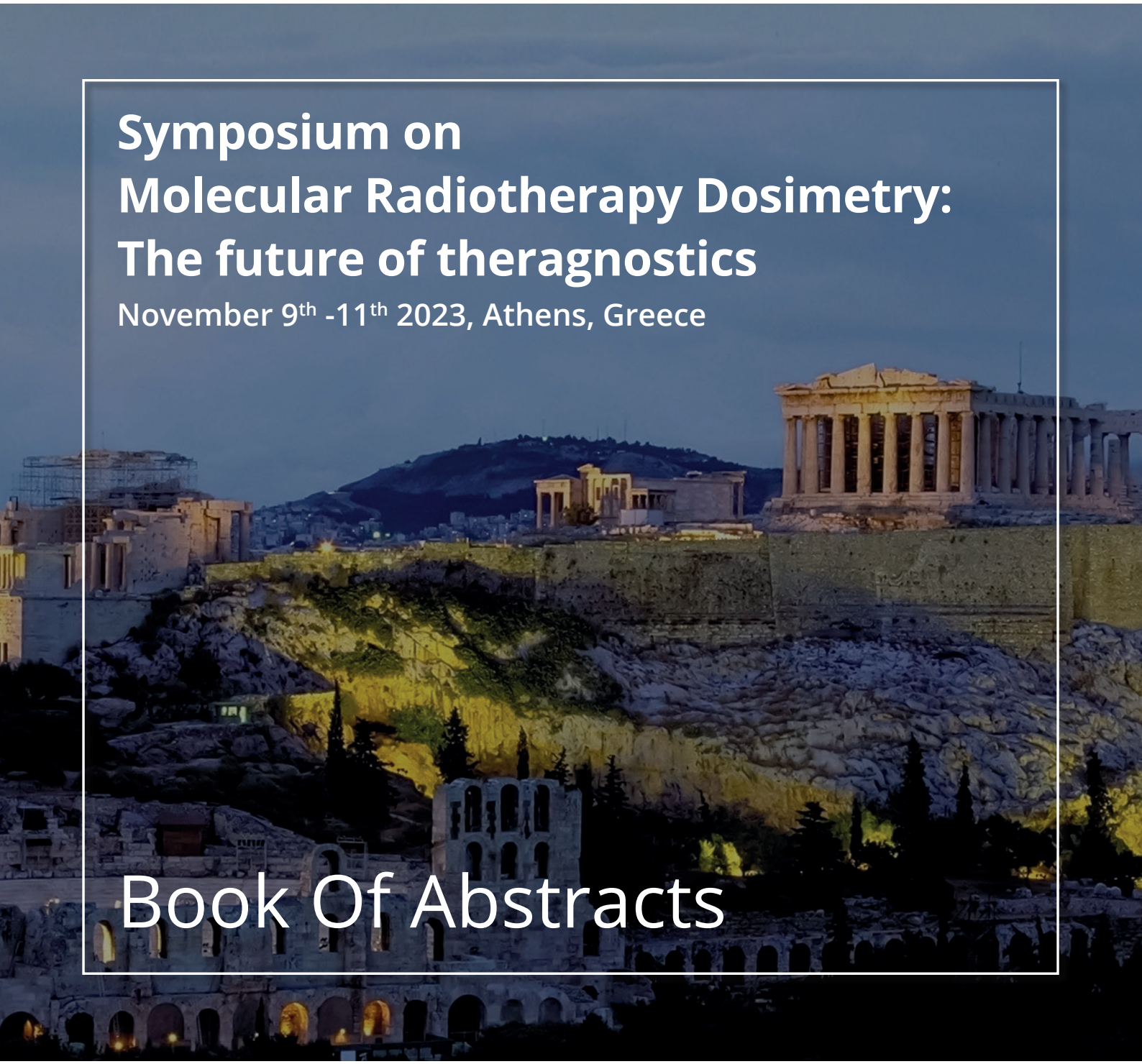

Symposium on Molecular Radiotherapy Dosimetry: The future of theragnostics

November 9th -11th 2023, Athens, Greece

Book Of Abstracts

Organised by

EFOMP
EUROPEAN FEDERATION OF ORGANISATIONS FOR MEDICAL PHYSICS

SIG
RADIONUCLIDE INTERNAL DOSIMETRY

Hosted by

THE HELLENIC ASSOCIATION OF MEDICAL PHYSICISTS (HAMP)

NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS
MEDICAL SCHOOL
"ATTIKON" UNIVERSITY HOSPITAL
2ND DEPARTMENT OF RADIOLOGY
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Organized by EFOMP Special Interest Group for Radionuclide Internal Dosimetry

Introduction

The European Federation of Organisations for Medical Physics (EFOMP)[1] is an umbrella organization for 36 National Member Organisations which together represent around 10000 medical physicists and clinical engineers working in the field of medical physics. Supporting bodies of EFOMP are its 6 advisory committees, the European School for Medical Physics Experts (ESMPE), the European Journal of Medical Physics (EJMP), Working Groups and Special Interest Groups (SIGs).

The first EFOMP SIG (Radionuclide Internal Dosimetry / SIG_FRID) was officially created in February 2021. The SIG_FRID is a permanent structure with an objective to create a network of medical physicists working in radionuclide dosimetry and fulfil the need for networking, education, research and professional exchanges in this field.

EFOMP SIG_FRID organised the 1st EFOMP Symposium on Molecular Radiotherapy Dosimetry in Athens, Greece from November 9th to November 11th 2023.
The Symposium gave the opportunity:

- to review and share ongoing developments in radionuclide imaging and dosimetry;
- to consider how personalised treatments may improve effectiveness at a time of rapid expansion of theragnostics and molecular radiotherapy
- to discuss networking and synergies within a multi-disciplinary community at a time of challenge and opportunity.

This event brought together, for the first time, 180 physicists and clinicians with a strong interest in molecular radiotherapy. Scientific aspects concerning imaging, internal dosimetry and radiation protection was discussed in addition to clinical practice. A main aim of the meeting was to share experience and resources. It has been an opportunity for stakeholders to build networks, to discuss how to move forward and to establish close working relationships between academia, the clinic and industry.

The Symposium was hosted by the Hellenic Association of Medical Physicists and the National and Kapodistrian University of Athens. Its structure was composed of an Organising and Scientific Committee and within the programme there were 8 regular sessions , 3 ePoster sessions, 2 Continuous Professional Development (CPD) sessions, a Round table and a Sponsor Session. EFOMP policy statement NO. 19: Dosimetry in nuclear medicine therapy – Molecular radiotherapy[2] was officially presented here.

This abstract book contains the abstracts of the 1st Symposium on Molecular Radiotherapy Dosimetry. All studies were presented as oral communications during the event and were also available during the meeting.

This event has been accredited by the European Board for Accreditation in Medical Physics (EBAMP) as a CPD event for Medical Physicists at EQF Level 7” and has been judged to have 19 hours of educational experience, which, according to the EBAMP protocol is equivalent to 27 CPD points (Accreditation Code for the event is: APP00249).

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1. EFOMP Structure www.efomp.org
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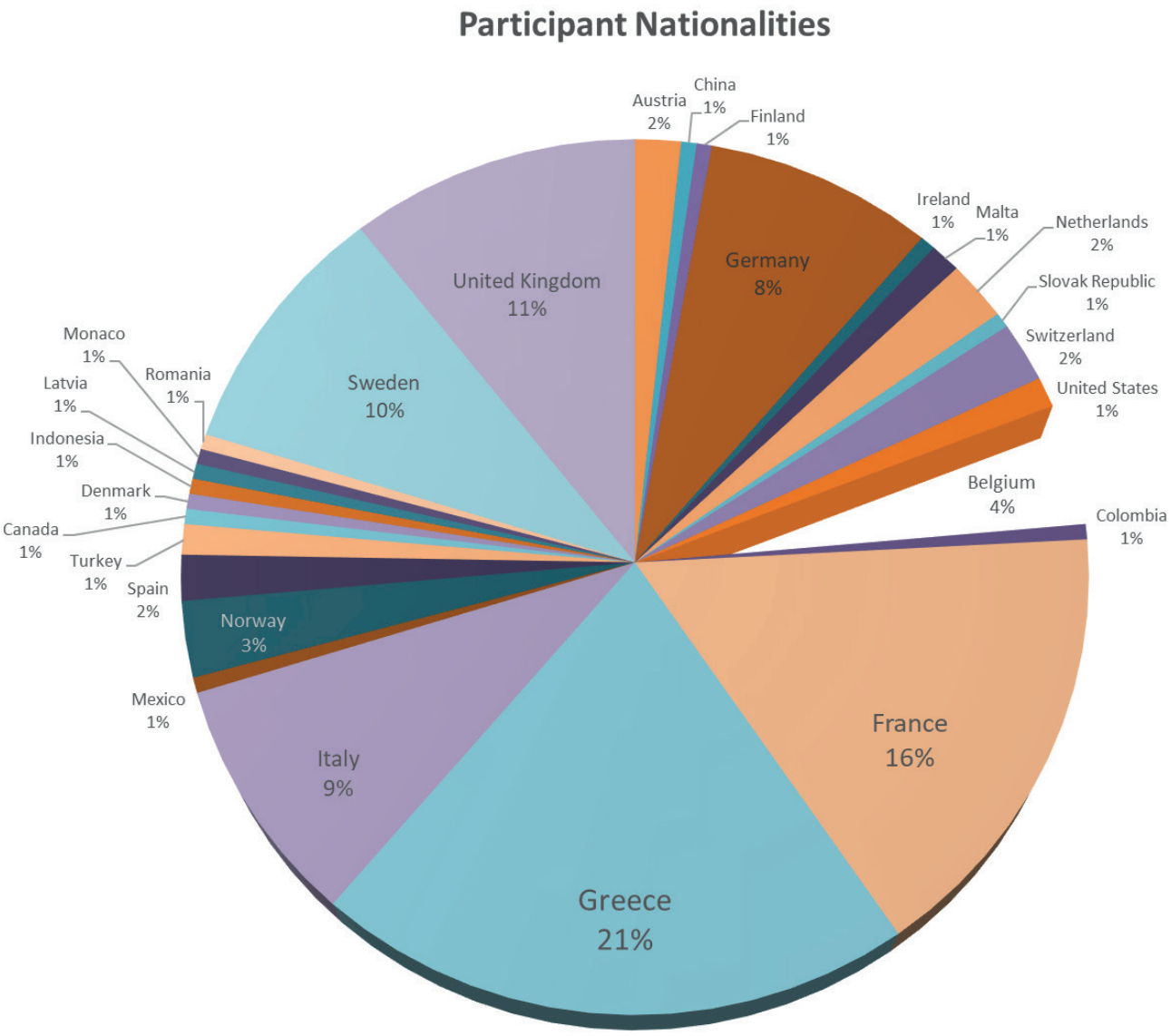
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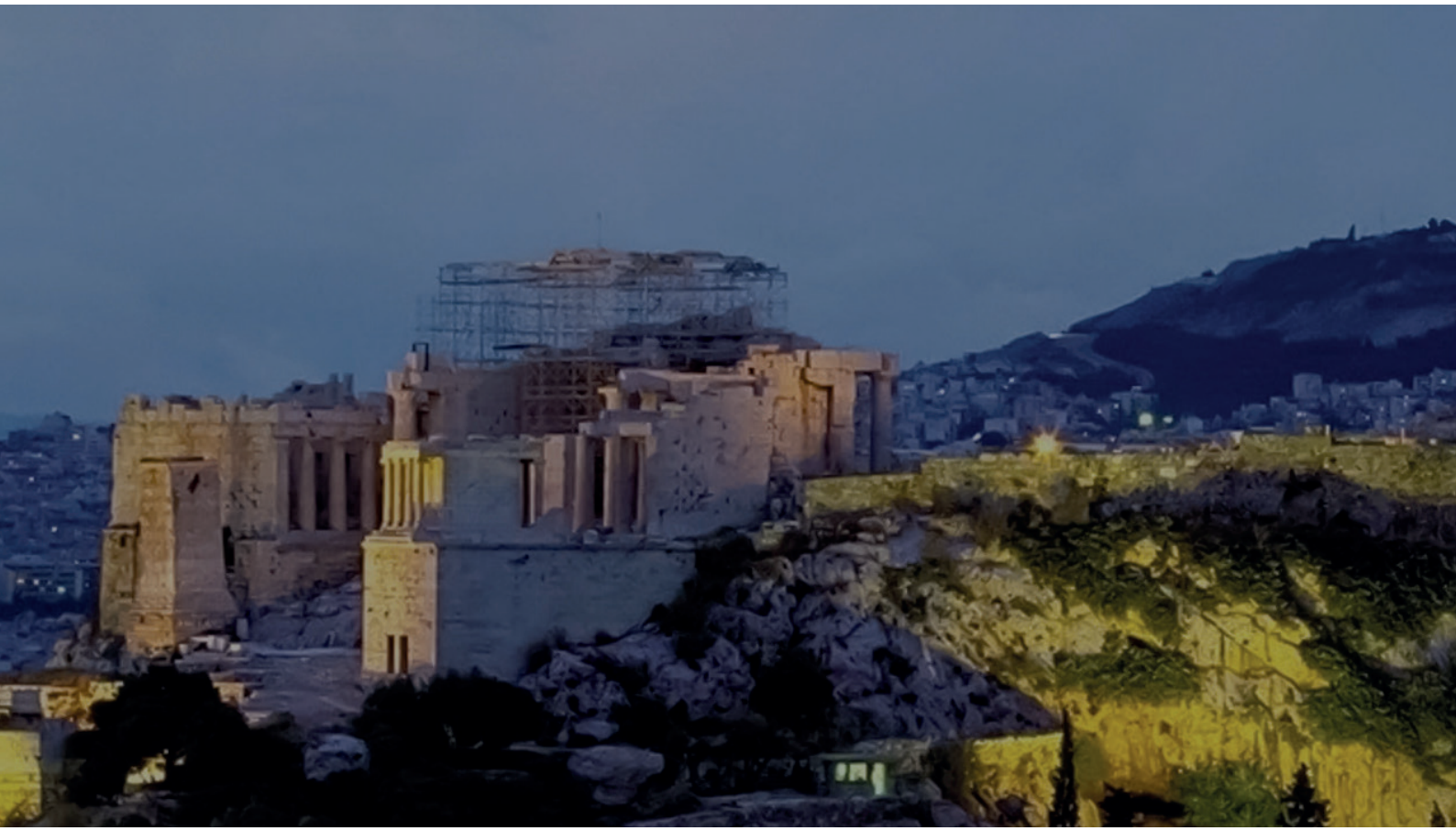

Contents

Invited Speakers

Invited speaker 1

Title
Implementation of dosimetry for molecular radiotherapy; results from a European survey

Authors
S. Peters, J. Tran-Gia, S. Agius, O. V. Ivashchenko, J. N.l Badel, M. Cremonesi, J. Kurth, P. Mínguez Gabiña, E. Richetta, K. Sjögreen Gleisner, J. Tipping, M. Bardiès, C. Stokke

Abstract
Purpose: The use of molecular radiotherapy (MRT) has been rapidly evolving over the last years. The aim of this study was to assess the current implementation of dosimetry for MRTs in Europe.

Methods: A web-based questionnaire was open for treating centres between April and June 2022, and focused on the years 2020-2022. Questions addressed the application of 16 different MRTs, the availability and involvement of medical physicists, software used, quality assurance, as well as the target regions for dosimetry, whether treatment planning and/or verification were performed, and the dosimetric methods used.

Results: A total of 173 responses suitable for analysis was received from centres performing MRT, geographically distributed over 27 European countries. Of these, 146 centres (84%) indicated to perform some form of dosimetry, and 97% of these centres had a medical physicist available and almost always involved in dosimetry. The most common MRTs were 131I-based treatments for thyroid diseases and thyroid cancer, and [223Ra]RaCl2 for bone metastases. The implementation of dosimetry varied widely between therapies, from almost all centres performing dosimetry-based planning for microsphere treatments to none for some of the less common treatments (like 32P sodium-phosphate for myeloproliferative disease and [89Sr]SrCl2 for bone metastases).

Conclusions: Over the last years, implementation of dosimetry, both for pre-therapeutic treatment planning and post-therapy absorbed dose verification, has increased for several treatments, especially for microsphere treatments. For other treatments that have moved from research to clinical routine, the extent to which dosimetry is used decreased in recent years. However, there are still large differences both across and within countries.

Invited speaker 2

Title
Quantitative imaging and dosimetry of radioiodine in multi-centre clinical trials

Authors
J. Taprogge

Abstract
Radioactive iodine (131I-NaI) has long been used as a treatment for differentiated thyroid cancer. Many patients respond well to the initial therapy but approximately 15% of patients have local recurrence, develop distant metastases or become radioiodine refractory. Outcome should ultimately be dependent on radiation doses delivered to targets and not administered activities. Multi-centre clinical trials are necessary to address these questions but challenges such as the lack of standardised quantification and absorbed dose calculations must be addressed.

A wide range of absorbed doses to normal organs and targets was observed as part of the MEDIRAD, SELIMETRY and INSPIRE multi-centre prospective clinical trials. For example, absorbed doses to metastatic lesions were found to range from 1 to 1170 Gy from a fixed administration of 5.5 GBq in the SELIMETRY study. In addition, a variation in outcome was found across all studies. Results of these clinical trials have shown that treatment planning using diagnostic pre-therapy imaging with 123I-NaI is feasible and that treatment response in differentiated thyroid cancer patients can be predicted when taking the radiation dose into account.

The results of these multi-centre clinical trials suggest that a personalized approach to treatment is feasible and required. Furthermore, quantitative imaging plays an important role in the accurate assessment of effects of treatments to enhance RAI uptake. Dosimetry and quantitative imaging can be set up for multi-centre clinical studies with little effort and requirements and examples will be discussed here.

Invited speaker 3

Title
AI: a game changer in quantitative molecular imaging and clinical dosimetry

Authors
I. Buvat

Abstract
Artificial Intelligence (AI) is currently invading the medical field, and molecular imaging and clinical dosimetry are no exception. AI can first enhance SPECT and PET image accuracy, which will impact any subsequent use of these images for dose calculation. Second, AI can automate tedious and user-dependent tasks currently needed for personalized dose estimates. Third, AI has the potential to greatly simplify the complicated acquisition and processing protocols that are still currently required for reliable dosimetry. Last, preliminary results suggest that dose estimation could be accurately predicted using AI models without going through an extensive computational pipeline involving error propagation. By combining all these advances, AI should soon contribute to the deployment of clinical dosimetry to achieve the holy grail of personalized radionuclide therapy.

Invited speaker 4

Title
EFOMP policy statement NO. 19: Dosimetry in Nuclear Medicine Therapy – Molecular Radiotherapy

Authors
K. Sjögreen-Gleisner, G. Flux, K. Bacher, C. Chiesa, R. de Nijs, G. C. Kagadis, Thiago Lima, M. Lyra Georgosopoulou, P. Minguez Gabiña, S. Nekolla, S. Peters, J. Santos, B. Sattler, C. Stokke, J. Tran-Gia, P. Gilligan, M. Bardiès

Abstract
The European Council Directive 2013/59/Euratom (BSS Directive) includes optimisation of treatment with radiotherapeutic procedures based on patient dosimetry and verification of the absorbed doses delivered. The present policy statement summarises aspects of three directives relating to the therapeutic use of radiopharmaceuticals and medical devices, and outlines the steps needed for implementation of patient dosimetry for radioactive drugs. To support the transition from administrations of fixed activities to personalised treatments based on patient-specific dosimetry, EFOMP presents a number of recommendations including: increased networking between centres and disciplines to support data collection and development of codes-of-practice; resourcing to support an infrastructure that permits routine patient dosimetry; research funding to support investigation into individualised treatments; inter-disciplinary training and education programmes; and support for investigator led clinical trials. Close collaborations between the medical physicist and responsible practitioner are encouraged to develop a similar pathway as is routine for external beam radiotherapy and brachytherapy. EFOMP's policy is to promote the roles and responsibilities of medical physics throughout Europe in the development of molecular radiotherapy to ensure patient benefit. As the BSS directive is adopted throughout Europe, unprecedented opportunities arise to develop informed treatments that will mitigate the risks of under- or over-treatments.

Invited speaker 5

Title
Therapeutic Radiopharmaceuticals in a changing regulatory landscape

Authors
A. Sundlöv

Abstract
There is a lot going on around radiopharmaceuticals lately, and the European regulatory sphere is no exception. There are several ongoing projects and initiatives by different parts of the European Commission and the European Medicines Agency, among others. The Clinical Trials Regulation is now fully implemented since the beginning of the year, and there is a proposal for a new directive governing the approval of new medicinal products on the table for negotiation in the coming years. Different interest groups are trying to make their voice heard regarding the current and future legislation affecting the development and use of this class of drugs.

Dr Sundlöv is a clinical assessor at the Swedish Medical Products Agency, but also part of several of the ongoing projects and initiatives. Prior to joining the Agency she has many years of clinical experience of radionuclide therapy and can therefore hopefully give an interesting overview of what is going on in the field.

Invited speaker 6

Title
Can dosimetry improve the outcome of molecular radiotherapy for neuroblastoma?

Authors
M. Gaze

Abstract
Neuroblastoma is a predominantly childhood cancer with a variable prognosis. While low risk disease is typically cured, the current survival rate for the majority of patients who have high-risk neuroblastoma is poor. Only about 50% of high-risk patients survive at least five years, despite intensive treatment with chemotherapy surgery, external beam radiotherapy and immunotherapy. Molecular radiotherapy is an attractive treatment with potential for improving outcome, as neuroblastoma is recognised as a radiosensitive tumour type, but multiple metastatic deposits, some to small to be demonstrated by imaging, make conventional radiotherapy unsuitable to combat widespread dissemination, and a systemic treatment is necessary.

131-I mIBG, targeting the noradrenaline transporter expressed by most neuroblastomas, has been the principal form of molecular radiotherapy in clinical use for over 30 years. It can be very effective in some cases, but its use has not been optimised. More recently, 177-Lu DOTATATE, which targets the somatostatin receptor expressed in a proportion of neuroblastoma patients has been investigated, but it remains experimental and does not yet have an established role.

Administered activity is not a guide to radiation absorbed dose in tumours. there is a wide variation about a mean. Treatment with a single fixed administered activity, as is the case in a number of clinical trials, while it may result in a certain response rate, risks underdoing a significant proportion of patients. Dosimetrically guided administration might improve response rates appreciably beyond the average 30% typically reported. The European practice has been to measure and prescribe treatment to a desired cumulative whole-body radiation absorbed dose over two fractions. This standardisation, while better than the use of an arbitrary administered activity, still results in a significant variation in tumour dose. Pre-therapy dosimetry based on 124-I mIBG PET CT may offer a way to prescribe a desired tumour radiation absorbed dose, and improve outcomes, and is the subject of an innovative clinical trial.

Dosimetry is also the basis of a new trial in 177-Lu DOTATATE therapy, which seeks to give dose intense therapy tailored on not exceeding renal tolerance, and is anticipated to achieve a better response rate than an earlier study.

Invited speaker 7

Title
Dosimetry and clinical outcome in radioembolization: light and shadow

Authors
C. Chiesa

Abstract
The talk summarises failures, success and open dosimetric questions in radioembolization with 90Y microspheres. In 2012 the main guideline for staging and treating liver cancer by the European Association for the Study of Liver (EASL), named the Barcelona Clinic Liver Cancer (BCLC) staging system, did not mention Trans Arterial Radio Embolization (TARE), despite 90Y microspheres were used in clinics for more than 10 years. Two large prospective randomised trials (SARAH [1], SIR-veNIB [2]), planned with the Body Surface Area method, in 2017 failed to demonstrate an improvement in overall survival (OS) after resin microsphere TARE with respect to systemic sorafenib. That was the only treatment available at that time for hepato-cellular carcinoma (HCC) advanced patients with portal vein thrombosis (BCLC C). Interestingly, an a-posteriori analysis by the same SARAH group [3] demonstrated that OS was significantly associated (14.1 m vs 6.1 m, $p<0.001$) with the absorbed dose to lesion (cut-off 100 Gy). The same analysis deduced a perfect dependence of disease control on the tumour absorbed dose. In parallel, the large resin sphere studies on progression free survival (PFS) of colorectal metastases met exactly the same negative fate, followed by a-posteriori analyses showing the importance of dosimetry [4].

The absence of dosimetric planning then was advocated as a possible cause of such failures [5,6]. Seen these results, in 2019 TARE was strongly contra-indicated by EASL, and weakly indicated for intermediate patients (BCLC B).

The retrospective trial LEGACY with glass microspheres [7] was the first able to introduce radioembolization in EASL guidelines, but in the early stage of HCC: solitary nodules less than 8 cm in diameter (BCLC 0 & A). Dosimetry however was performed on the bulky injected region (mono-compartment). Moreover, treated patients received a median absorbed dose of 410 Gy, with a large interquartile dispersion ([200 Gy, 800 Gy]). Interesting the remark by Authors about the “successful collaboration among investigators, industry, and regulatory bodies to advance the field of HCC”. A similar collaboration never happened in systemic therapies, despite asked by medical physicists.

The retrospective multicentric TARGET study [8] reported a debatable absence of correlation between non-tumoural liver dose and toxicity after glass microspheres. A timeline cut-off of only 3 months was assumed, while Chiesa et al [9] data demonstrated that treatment related liver decompensation may occur until 6 months after TARE. Moreover, a threshold for the frequency of toxicity was fixed at 15%. Since toxicity occurred in 4.8% of patients, it did not met the threshold to reach the end-point.

The prospective randomized phase II trial DOSISPHERE-01 on lesion larger than 7 cm in diameter is the first high level evidence of the advantage of two-compartment dosimetry (tumour, non-tumour) versus the mono-compartment dosimetry. The arm planned aiming at more than 205 Gy to tumour reached a median OS of 26.7 m vs 10.7 months of the mono-compartment dosimetry arm [10].

The first evidence of advantage of voxel dosimetry over the mean dose approach is reported by Watanabe et al [11] with a toxicity analysis based on non-tumoural liver dose-volume histogram. Proposed safety threshold cannot however be adopted as such, since the work did not differentiate between liver decompensation due to treatment or due to tumour progression, did not stratify on basal bilirubin (which is a major risk factor for decompensation [9]), and Normal Tissue Ccomplication Probability (NTCP) analysis was not performed [12].

Preliminary data of the study NumberDose in TARE [13], ongoing in Milan with glass microspheres, showed an anomalous behaviour of the Tumour Control Probability (TCP) curves, confirmed in the TARGET study, and a totally unexpected lower biological efficacy administering patient with a higher number of glass microspheres per/GBq (second-week administration). This observation, limited to glass microspheres, is opposite to all previously published hypotheses and simulations [14, 15, 16]. After a careful examination of data by Pasciak et al [15], the Milan group made the hypothesis of mega-cluster formation, which happens above a threshold of 15 microspheres/mm3 [13], reducing the uniformity of the absorbed dose distribution on microscopic scale.

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Oral presentation

Invited speaker 8

Title
Absorbed dose-effects in Molecular Radiotherapy: Lutetium-labelled radiopharmaceuticals

Authors
M. Cremonesi

Abstract
The increasing application and development of Molecular Radiotherapy (MRT) together with a rising practice of dosimetry allows to derive crucial information towards therapy optimisation. A variety of therapies have provided evidence of correlations between dosimetry quantities vs. response and toxicity.

The nuclear medicine and oncology community has recognised the most beneficial impact of dosimetry perhaps in the radioembolization of liver lesions. Certainly, the relatively simple dosimetry protocol has been facilitating a wide acceptance in clinical practice, with the promotion by the medical device producers, and formal recommendations/guidelines.

Overall, these achievements have contributed to melt scepticism and open the clinicians to the dosimetry potential. In the last two decades, even before radioembolization, 177Lu-radiolabelled molecules have provided excellent clinical results with increasing diffusion of 177Lu-DOTATATE to treat neuroendocrine tumours. Thereafter, 177Lu-PSMA for metastatic prostate cancer has emerged, and, more recently 177Lu-Lilotomab provided new options for Non-Hodgkin Lymphomas (NHL). These radiopharmaceuticals requiring more complex dosimetry (at least in a first phase experience), because of the systemic approach, specific metabolism, biological decay, did not facilitate wide application. However, dosimetry is more demanded in specialised centres, with relevant results found means of both, key indications for future optimization setting, need of radiobiological deepening, and dose-effect relationships.

177Lu-DOTATATE: the correlation between tumour response and absorbed dose has been demonstrated, as well as a dose-response dependence on tumour grade. The constraint for renal toxicity by means of absorbed dose or BED has not been found yet, indicating a conservative setting. However, comparisons with 90Y-peptide therapy and different number of cycles suggest space for limits higher than those considered (cumulative absorbed dose BED of of 23 Gy or 28 Gy, respectively), and possible better rationales based on dosimetry avoiding a high number of cycles. Most importantly, clinical studies with dosimetry-personalized approaches have shown improved outcomes in terms of higher progression free survival and overall survival.

177Lu-PSMA: interesting studies investigated the concept of theragnostic in patients with prostate cancer, comparing diagnostic and therapeutic agents (68Ga-PSMA vs. 177Lu-PSMA), analysing the possibility to extrapolate dosimetry and provide predictive models. The literature is not well aligned on results / conclusions, providing nice matter of discussion and further perspectives to deep.

177Lu-Lilotomab: the predictivity of toxicity by bone marrow dosimetry has often led to unsuccessful or minor results, indicating insufficient information in relation to the very complex bone marrow exchange with the radiopharmaceutical, inadequate dosimetry blood-based methods in absence ot more specific clinical data, etc. Imaging investigation has offered cues for improvement, such as sources for dosimetry inaccuracies, need of more specific clinical data, and/or information on individual active marrow reserve/ distribution. 177Lu-Lilotomab dosimetry studies based on SPECT reached the difficult goal of predicting myelosuppression.

The presentation will summarise the literature on this topic.

ID9 (oral presentation)

Title
Experimental dosimetry of in vitro irradiation of tumor cells with 212Pb

Authors
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Abstract
Introduction: Targeted alpha therapy (TAT) is a promising internal radiotherapy for the treatment of small and disseminated targets, such as brain metastases [1][2]. Research on this therapy based on alpha-emitting radionuclides is gaining a lot of practicality thanks to recent developments in heavy ions production [3]. Developments of new TAT treatments include in vitro assays, where their biological effectiveness on tumor cells is compared to other reference treatments through imaging and dosimetry. However, while the short and dense ionization tracks in biological matter of alpha-emissions constitute the main interest of TAT, this property makes in vitro dosimetry heavily dependent on the spatial distribution of the radionuclides in the culture medium [4].

Materials & Methods: We developed an in vitro dosimetry system, which can be placed just below custom-made culture wells with a 2.5 µm mylar bottom, within a cell culture incubator. The system is based on silicon semiconductor detectors recording energy spectra of the alpha-particles emitted within the culture wells and passing through the cell layer and the culture well bottom. An innovative spectral deconvolution method of the recorded energy spectra was developed and enables recovery of the spatial and time distributions of the radionuclides during the experiment and a calculation of the dose delivered to the cells [5].

This new dosimetry system was used for the first time in cell culture incubator to perform experimental dosimetry in an in vitro study of tumor cells irradiated with 212Pb with different oxygenation conditions. H2030Br tumor cells were grown in 4-wells plates. Six plates were prepared: 3 were used the first day for normoxic irradiations (i.e 21%of O2), and 3 remaining the second experiment day for hypoxic irradiations (1% of O2). For each plate, different activities of 15, 50, 150 and 300 kBq were injected into the cell medium in the wells. After injection, the plates were kept in an incubator for a 4-hour irradiation, on the dosimeter recording the energy spectra of the 4 wells during the whole irradiation. Spectra were deconvolved and dose delivered to cells was calculated for each well.

Results and discussion: Energy spectra measured for the 24 culture wells showed very different profiles and temporal behaviors, even within those which received the same activity. The deconvolution of these spectra and the dose computation led to average doses and standard deviation (over the 6 samples of each tested activity) of (1.08 ± 0.16) Gy, (3.76 ± 1.02) Gy, (14.98 ± 8.25) Gy and (30.35 ± 28.51) Gy for the 15, 50, 150 and 300 kBq activities respectively. The average doses are linearly related to the injected activities. Nevertheless, the dispersion is high (up to 94 % for the 300 kBq activity).

Conclusion: This experiment is the first experimental in vitro dosimetry carried out in cell incubator. It confirms the complexity and variability of isotopes kinetics in in vitro experiments, leading to significant dose variations between samples receiving the same activity. Immunostaining of the cells is currently under completion to establish a dose-effect relationship on Double-Strand-Break occurrence. These results consequently support the need of experimental dosimetry to improve the analysis of radiobiology studies and propose a new method to do it.

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ID10 (oral presentation)

Title

The retina as an organ at risk in molecular radiotherapy in a phase I clinical trial of [131I]ICF01012 in metastatic melanoma: a proposed methodology for calculating patient-specific retinal S-values for dosimetry.

Authors

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Abstract

Background

[131I]ICF01012 is being used for the treatment of pigmented metastatic melanoma. This molecule targets melanin, which is present both in melanoma cells and in the retinal pigment epithelium (RPE) making the retina an unconventional organ at risk (OAR) for which the calculation of absorbed dose becomes a priority. This study aims to calculate patient-specific S-factors by taking into account the micrometric dimension of the retina.

Materials and methods

Patient-specific S-values (S(retina<-RPE)) were calculated with the GATE Monte Carlo platform v9.1 using the emstandard_opt3 physics list and compared to the S-value obtained from manual segmentation on CT images. Patient-specific eye conformations were modelled based on computed tomography (CT) and optical coherence tomography (OCT) images for eye diameter and retinal thickness, respectively, while a single RPE thickness was used. All the voxel material was set to water. The dose actor was used to extract the energy deposited in the retina.

Results

Patient-specific S(retina<-RPE)-values were calculated for the first time using Monte Carlo simulation with a realistic eye model.

There were higher (approximately 1.10E-05 Gy/MBq.s of magnitude) than those obtained from CT-based manual eye segmentation (approximately 1.10E-06 Gy/MBq.s of magnitude).

Conclusion

In conclusion, a proposed methodology based on Monte Carlo simulations using a patient-specific eye model was used to calculate the retinal S-values for [131I]ICF01012 in patients with pigmented metastatic melanoma. This methodology provides a first step for future dosimetric approaches in this patient population and highlights the importance of considering variations in retinal thickness when assessing organs of this size.

ID11 (oral presentation)

Title

Bone marrow dosimetry model for somatostatin receptor-based radionuclide therapies; comparison between lutetium-177 and terbium-161

Authors

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Abstract

Introduction

After somatostatin receptor-targeted radionuclide therapy using [177Lu]Lu-DOTATATE, hematological toxicities are a frequent adverse effect. Estimates from bone marrow dosimetry models cannot foresee these toxicities occurring well below the established threshold of 2 Gy. Hematological toxicities are concerning as terbium-161 clinical trials, a potential alternative for lutetium-177, are planned. In order to compare the energy deposits from lutetium-177 and terbium-161 on somatostatin receptor positive CD34+ stem and progenitor cells, we created a theoretical model of a bone marrow cavity.

Methods

According to a predetermined proportion and spatial distribution in reference to the nearest trabecular bone surface, red marrow cells were randomly selected as CD34+. All CD34+ cells were used to represent cellular uptake associated with somatostatin receptor expression, and deposited energy from lutetium-177 or terbium-161 was tallied in these cells. The activity in the extracellular volume represented a non-specific contribution to the energy deposition.

Results

The spatial energy deposition was highest close to the trabecular bone for both radionuclides since this region has the highest concentration of CD34+ cells. The average energy deposition to CD34+ cell nuclei from terbium-161 and receptor-related uptake was twice as high for activity in the cytoplasm compared to lutetium-177, at 2.45 keV/decay as opposed to 1.26 keV/decay. Terbium-161 deposited 25% more energy to the cell nucleus for the non-specific activity at 10.94 keV/decay compared to 8.62 keV/decay for lutetium-177.

Conclusion
Our findings suggest that somatostatin analogue radionuclide therapy of neuroendocrine tumors may result in a greater absorbed dose from terbium-161 than has been previously seen for lutetium-177. The absorbed dose heterogeneities observed in the bone marrow cavities are not large enough to limit the potentially harmful effects of the low-energy electrons co-emitted by terbium-161.

ID13 (oral presentation)

Title
Quantitative Bremsstrahlung SPECT in post Y-90 Radioembolization Therapy

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Abstract
Y-90 Radioembolization therapy involves the directed injection of 90Y-labelled microspheres administered through the hepatic artery to target a lobe or section of the liver in patients with liver metastasis mainly from colorectal cancer and hepatocellular cancer in cirrhotic liver. Y-90 SPECT imaging is currently performed in post Y-90 radio-embolization therapy procedures to qualitatively assess in vivo the microsphere deposition, confirm the treatment plan and to evaluate for unintended extra-hepatic deposition. SPECT imaging of Y-90 is made possible through the detection of Bremsstrahlung radiation generated by the energetic□□- electrons. In such procedures, the photon flux is high but is characterized by a wide spectrum of energies which lends to imaging with a medium or high energy collimator. Bremsstrahlung SPECT imaging is complicated due to a large amount of septal penetration and energy dependent scatter and attenuation correction. For these reasons, clinical image reconstruction is performed through a scatter-septal penetration compensation technique that employs a main emission window from [100-200] keV and a scatter-septal penetration window between [300-400] keV. Methods are available to convert images from this traditional reconstruction into a quantitative form where each voxel has units of Bq/mL but the results are dependent on the field of view chosen for activity normalization, making this option less reliable and consistent across users and institutions. As a result, a widely applicable SPECT reconstruction algorithm for Y-90 with reliable quantitation is currently lacking.

In this work, we evaluate a novel MonteCarlo-based image reconstruction technique for both its visual qualitative performance and its quantitative accuracy for applicable dosimetry calculations in Y90 therapy. The MonteCarlo technique aims at estimating the true activity through MonteCarlo simulations of the scatter within the patient (and attenuation) septal penetration, in addition to detector response in an iterative process. We assessed the quantitative image reconstruction performance through imaging a solid water+fillable insert phantom prepared with a calibrated activity concentration of Y90-chloride. The performance of both image reconstruction algorithms was then evaluated with a 90Y filled NEMA-IEC phantom and clinical patient scan data. Qualitatively, patient images reconstructed with the Monte Carlo-based reconstruction were evaluated with respect to overall quality of image, noise, smoothness, artefact and extrahepatic uptake. In 10 patients, the two methods were compared with each other on a scale of 1-4, four being the best and 1 worst.

Absolute scanner calibration for Y90 was established at 2.1 cps/MBq for GE and 3.5 cps/MBq for Siemens SPECT cameras, equipped with medium energy collimators. NEMA phantom image quality and quantitative SPECT evalua-

tion led to similar sphere activity recovery with the two reconstruction techniques. However, the Monte Carlo-based method had much lower noise and thus higher SNR. Image quality and smoothness of the image contour were rated higher for MonteCarlo method. Interestingly, there were lesser artefacts on MonteCarlo based image reconstruction. We quantitatively measured the total activity in the liver and treated lobe using the images from both reconstruction methods. The total activity collected in the liver was within 94%, on average, of the clinically administered activity when implementing the MonteCarlo method. Consequently, treatment volume absorbed doses were observed to be in good general agreement with dose calculations from the MIRD single compartment model. Absorbed dose calculations from the traditional SPECT reconstruction method were dependent on the field of view used for activity normalization, generally producing lower dose estimates.
This abstract will discuss the difficulties encountered in Y-90 SPECT imaging for both qualitative and quantitative estimation and the current progress toward fully quantitative Bremsstrahlung imaging. This work will also discuss the Bremsstrahlung emission yield from microspheres being either made of glass (Therasphere) or resin (Sir-Spheres) and the limitation of this study to establish absolute calibration from Y-90 chloride. This work indicates the potential benefit of advanced modeled based Bremsstrahlung image reconstruction and points toward potential benefit of more quantitative imaging for radiation dosimetry evaluation.

ID14 (oral presentation)

Title
Use of artificial intelligence for the reduction of the time footprint on dosimetry procedures in molecular radiotherapy using the radiopharmaceutical 177Lu-PSMA

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Abstract
Introduction
Reducing the temporal footprint of dosimetric procedures is a major challenge for their widespread adoption in molecular radiotherapy (MRT)[[1]]. To address this challenge, we used a neural network to reduce the projections' duration and the number of projections.

Materials & Methods
Fifteen and four patients treated with 177Lu-PSMA and 177Lu-DOTATATE respectively were used as training and validation datasets for a generative adversarial neural network (GAN). Tomographic list-mode images were acquired on DISCOVERY-NM/CT-670 with 60 30-second projections. List-modes allowed us to obtain 6-second projections to train our GAN to estimate 30-second images. Subsequently, we trained a second GAN to estimate 60 projections from a set of 20. We tested our approach on four patients who had undergone post-treatment imaging with four time-point images. We compared the cumulative activities in their organs and tumours estimated from the actual 30-second images, with those obtained from the 6-second and the GAN-generated (30s-GAN) images. The maximum relative deviations of cumulative activities in organs and tumours were calculated between the acquired 30-second images and the 6-second images and those estimated by the 2-piped GANs.

Results

The maximum relative deviations in cumulative activity were 4.32% [resp. 16.09%] for OARs and 8.87% [resp. 7.24%] for tumours between reconstructed images from the 30s projections and generated by the 30s-GAN [resp. 6s projections].

Conclusion

The dosimetry temporal footprint in MRT can be reduced by shortening projections' duration and their numbers. We achieved a reduction factor of 15 while preserving similar quantitative results as compared to our standard acquisition procedure.

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ID15 (oral presentation)

Title

68Ga-PSMA PET/CT Imaging Features with PSA Variation for Castration-Resistant Prostate Cancer Patients

Authors

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Abstract

Introduction: Prostate cancer is a global health concern, and treating advanced cases remains challenging. Radiopharmaceutical therapy using 177Lu-PSMA shows promise. PET/CT imaging helps assess disease extent, and correlating imaging features with serum PSA levels can predict treatment outcomes [1]. This study analyzes correlations between imaging features and PSA levels to highlight PET/CT's predictive value for 177Lu-PSMA therapy.

Methods: We retrospectively analyzed 45 male patients who received 177Lu-PSMA treatment and underwent 68Ga-PSMA PET/CT imaging. Images were pre-processed using deep learning segmentation (TotalSegmentator [2]). Physiological organ uptake was removed, creating a whole-body tumor region (WBTR) without normal uptake. Biological PSA values (initial and final) were obtained. Spearman's rank correlation, a Multi-Layer Perceptron (MLP), and Random Forest were used to assess correlations between PET radiomics and PSA values. Results were compared to a standard approach using the kidney's mean SUV threshold to obtain the WBTR.

Results: A weak but significant correlation existed between WBTR volume and PSA variation (correlation coefficient: -0.41, p-value: 0.01), slightly better than the standard approach (coefficient: -0.34, p-value: 0.02). MLP and Random Forest models predicted PSA variation with mean absolute errors of 163% and 563%, respectively. The standard approach showed errors of 149% (MLP) and 558% (Random Forest).

Conclusion: This preliminary study revealed a weak correlation between WBTR volume and PSA variation. Simple

statistics did not significantly improve predictions. Further research utilizing advanced machine learning techniques is needed to explore this method's potential for predicting response to 177Lu-PSMA therapy.

ID16 (oral presentation)

Title
Predicting initial iodine avidity in thyroid cancer

Authors
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Abstract
Introduction: Prostate cancer is a global health concern, and treating advanced cases remains challenging. Radiopharmaceutical therapy using 177Lu-PSMA shows promise. PET/CT imaging helps assess disease extent, and correlating imaging features with serum PSA levels can predict treatment outcomes [1]. This study analyzes correlations between imaging features and PSA levels to highlight PET/CT's predictive value for 177Lu-PSMA therapy.

Successful radioiodine treatment of thyroid cancer depends heavily on the iodine avidity of the target cancer tissue. As only some 5-15% of patients have tumour burden that would be visible on pre-therapeutic imaging, and as any initial imaging can be confounded by thyroid remnant tissue uptake, other approaches to adapting post-surgical treatment are needed. Adaptation is limited by lack of comprehensive data on which factors can robustly predict avidity.

Materials and Methods
Quantitative measurements of iodine concentration, as a proxy for iodine avidity, in representative surgical specimen from 28 patients were performed. The patients had papillary, differentiated high-grade or poorly differentiated thyroid cancer. The representative samples (primary tumour and lymph node metastases) were then analysed for BRAF V600E and TERT promoter mutations. Immunohistochemical analysis of NIS, TPO, TSH-receptor, Tg, Ki-67 and pendrin expression was performed. Furthermore, data on histological subtyping, tumour size, number of metastases, extra-thyroidal extention, patient age and sex was collected. Multivariate regression modelling was used to find predictors of iodine avidity.

Results
Iodine avidity differed more than thousandfold between patients. Multivariate regression analysis showed 68% of the observed variation could be explained by tumour tissue localisation (primary tumour vs lymph node metastasis), histological subtype, TPO and NIS expression, and TERT promoter mutation. Tumour size and TNM-stage was not significantly correlated to iodine avidity. The model had low variance inflation factors (all below 1.6), normally distributed residuals and no heteroscedasticity - implying low risk of overfitting and bias.

Conclusions
Some two-thirds of the variance in iodine avidity between patients can be explained by genetic and immunohistochemical analysis of surgical specimen. This greatly outperforms TNM-staging, which is currently the basis in most guidelines to determine initial radioiodine dosage. These factors, some of which may require further validation, can be used to guide any adaptive treatment scheme.

ID17 (oral presentation)

Title

Renal dosimetry in [177Lu]Lu-DOTA-TATE therapy based on multiple small VOIs as an alternative to whole-kidney delineation

Authors

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Abstract

Aim: To investigate the use of multiple small VOIs for renal dosimetry in [177Lu]Lu-DOTA-TATE therapy as an alternative to more time-consuming whole-kidney(WK) delineation.

Method: All SPECT images were reconstructed on two OS-EM software with and without resolution recovery(RR): LundaDose and a commercial system (Hermes Medical Solutions). Attenuation and scatter compensation were applied. The study was based on patient and simulated SPECT/CT images and consisted of three steps:

(i)Examining activity-concentration(AC) convergence over iterations on simulated images of three anthropomorphic phantoms with activity distributions representing 24h, 96h and 168h.
(ii)Determining the recovery coefficient (RC) for 2-mL-VOIs, with ten separate XCAT-phantom simulations and activity distribution representing 96h.
(iii)Assessing operator dependence using a) simulated images (i) and b) patient images (n=10). Five operators placed five 2-mL-VOIs in each kidney, guided by different images: with SPECT with RR/CT, SPECT without RR/CT, and CT only. Results were evaluated with respect to: time integrated ACs (TIAC) compared with reference TIACs (simulated images) and deviation between ACs from small VOIs and WK delineation (patient images).

Results:

(i)Eight iterations and ten subsets were found sufficient with and without RR, for both reconstruction software.
(ii)Mean RCs with RR were 1.03±0.04(LundaDose) and 1.1±0.05(Hermes), and without RR 0.91±0.05(LundaDose) and 0.94±0.05(Hermes).
(iii)Most stable and accurate results were obtained by placing five 2-mL-VOIs guided by images with RR/CT, and then applying them for quantification on images without RR and including an explicit RC.

Conclusion: The small-VOI method, using five 2-mL-VOIs, enables a fast and acceptable alternative to WK delineation.

ID18 (oral presentation)

Title
Evaluation of quantitative SPECT using 3D printed anthropomorphic phantoms with non-uniform activity distributions

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Abstract
Aims: SPECT-based activity quantification of 177Lu is challenging for small, non-uniform, and irregularly shaped objects. Our aims were to 3D-print phantom inserts and to assess activity-concentration estimation accuracy based on experimental measurements and Monte Carlo simulations.

Background and Method:
Two kidneys and 5 tumours were 3D-printed. For kidneys, non-uniform activity distributions were constructed with a grid-based technique that utilized the limited spatial resolution of SPECT to lower the mean-activity concentration (Ac) in a region. Kidneys were designed based on XCAT phantoms, and tumours on patient 68Ga-PET-images. Kidneys encompassed cortex, medulla and renal pelvis where medulla was printed using the grid technique, while tumours were hollow.

Phantoms were filled with 177Lu and imaged with a SPECT/CT. Ac in each insert was determined by manual delineation of the whole objects in SPECT. Estimated Ac was compared with the reference Ac and presented as recovery. Monte Carlo simulations of the targeted activity distribution in kidneys were performed and SPECT images compared with physical measurements both qualitatively and quantitatively.

Results: Recovery was 89% and 95% for the kidneys and 61%, 65%, 68%, 69% and 77% for the 5 tumours. Measured and simulated SPECT showed agreement in activity distribution and quantitative profiles, confirming the grid-based technique for mimicking non-uniform activity distributions.

Conclusion: 3D-printed grid-based techniques facilitate production of non-uniform anthropomorphic phantoms that are easy to use as they can be filled from a single stock-solution. The phantoms provide clinically relevant images and are currently used for method comparison and validation in a clinical multicentre study.

ID20 (oral presentation)

Title
Anatomy-based correction of kidney PVE on 177Lu SPECT images

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Abstract

Introduction

In peptide receptor radionuclide therapy (PRRT), accurate quantification of kidney activity on post-treatment SPECT images paves the way for patient-specific treatment. Due to the poor spatial resolution of SPECT images, partial volume effect (PVE) is one of the most important quantitative biases. In this study, we aimed to evaluate and compare the performance and robustness of anatomy-based PVC algorithms for recovering the accurate activity concentration of realistic kidney geometries on 177Lu SPECT images recorded under clinical conditions.

Materials and Methods

Based on the patient's CT scan data, three pairs of fillable kidneys with surface to volume ratio ranging from 1.5 to 2.8 cm-1, were 3D printed and successively mounted in the IEC phantom with a dedicated fixation system. Fully quantitative 177Lu SPECT/CT recordings were performed for the three modified IEC phantoms and for 6 different Target-To-Background ratios (TBRs: 2, 4, 6, 8, 10, 12). Two VOI-based [Geometric Transfert Matrix (GTM) and LABBE] and five voxel-based [GTM + Multi-Target Correction (MTC), LABBE + MTC, GTM + Region-Based Voxel-wise correction (RBV), LABBE + RBV and iterative Yang (IY)] methods were evaluated on this data set. Kidney recovery coefficients (RCs) were determined from anatomical CT-based segmentations and background RC was determined for voxel-based method by using a region eroded of 3 cm with respect to the initial background segmentation. In addition, the robustness of PVC methods to Point Spread Function (PSF) inadequacy, segmentation mismatch and background heterogeneity were evaluated.

Results

For all recordings, accurate background quantification was achieved with RCs ranged from 1.03 to 1.06 (1.05 ± 0.01). Without PV-correction, the average kidney RCs over all TBRs ranged from 0.66 ± 0.05 to 0.82 ± 0.02. For a TBR of 12, all anatomy-based method were able to recover the kidneys activity concentration with an error < 6 \%. The LABBE method offers the highest robustness to PSF and registration mismatches, but is also the most sensitive to background heterogeneity. Among voxel-based methods, MTC images were less uniform than RGB-based images (RBV, LABBE-RBV, IY) at the outer edge of hyperfixing areas (kidneys and spheres).

Conclusion

Anatomy-based PVE correction enable accurate SPECT quantification of the 177Lu activity concentration inside realistic kidney geometries. Combined with recent advances in deep-learning based algorithms for automatic segmentation of whole-body CT, these approaches could be of particular interest in the setting of a fully automated OAR dosimetry pipeline with PVE correction.

ID21 (oral presentation)

Title
Internal Dosimetry Results Reporting Practices for [177Lu]Lu-DOTA-TATE Therapy: where do we stand?

Authors
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Abstract
Aim:
Absorbed dose calculation in radionuclide therapy (RNT) is a complex process. EANM Dosimetry Committee guidance was established in 2010 to standardise reporting of dosimetry results, specifying the minimum details necessary to ensure the reproducibility of published work. EFOMP's SIGFRID workgroup on time-activity data fitting reviewed published papers on [177Lu]Lu-DOTA-TATE therapy to evaluate compliance with EANM guidance and to investigate whether sufficient data are provided to reproduce the methodology.

Methods:
Articles in PubMed published up to December 17, 2022, focused on [177Lu]Lu-DOTA-TATE RNT, including dosimetry, using SPECT imaging, were searched. Articles were refined to include those containing clinical studies with >=5 patients. Results were reviewed and compared to EANM Dosimetry Reporting Guidance.

Results:
A total of 110 articles were extracted, with 46 meeting the refined criteria. Of these, 93% fully complied with reporting guidelines for imaging equipment used, 85% image acquisition, 89% image processing, 85% corrections applied, 56% phantom and calibration measurements, 100% imaging scheme, 82% time-activity fit type, 74% fit integration and extrapolation procedure, 63% reference dosimetry phantom used, 70% reported S-values used, 87% described tumour dosimetry calculation, 76% mentioned dosimetry software, 100% reported absorbed doses, and 14% provided statistical error calculations. Only 21% of papers fully complied with EANM guidance.

Conclusions:
Although EANM Dosimetry Reporting Guidance exists since 2010, these recommendations are insufficiently implemented in articles on RNT. While data collection information is well documented, details on actual dosimetric calculations are scarce. To establish reproducible and comparable RNT dosimetry studies, results reporting quality metrics must be adopted and enforced by the journals in the field.

ID22 (oral presentation)

Title
Time-Activity Data Fitting in Molecular Radiotherapy: background, methodology and pitfalls

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Abstract
Aim:
Absorbed radiation dose calculations require time-integrated activities (TIAs) of tissues estimated by calculating the area under the time-activity curve (TAC). The process can be user-dependent, with users' decisions affecting the accuracy of calculated absorbed doses. Despite the importance of TIA values, there is no consensus on processing time-activity data. To minimise site-dependent variability in dosimetry, this work provides an overview of quality assurance and uncertainty management considerations that can be readily implemented.

Methods:
We review the main requirements of TAC fitting: (1) collection of data required for the fit, (2) definition of the model/function used to model the change of organ activity with time, (3) actual processing of data and definition of underlying uncertainties, (4) selection of data required for presenting the result of the fit.

Results:
We have determined the four major phases of TAC fitting, founded on results from the most up-to-date literature. We provide detailed information on how to implement a robust TAC strategy, together with a mathematical description of relevant fit functions and quality control measures to verify the accuracy of the TAC fit. We illustrate the data pipeline with examples of 4 TAC fitting models using synthetic data for 177Lu-PSMA therapy.

Conclusions:
We present a detailed workflow to be considered within the mathematical framework of fitting TACs to data for dosimetry applications. Each step of the workflow is described, and through examples, the pros and cons of a reduced time point acquisition scheme and the effect of noise in the measurements are demonstrated.

ID24 (oral presentation)

Title
A novel model-based equation for size dependent mean recovery coefficients for spheres and other shapes

Authors
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Abstract
Background: For spheres and cylinders theoretical curves for the recovery coefficient (RC) of the signal maximum are known, but this is not the case for the mean RC and other shapes. Some empirical equations with one or two fit parameters have been utilized on which is improved.

Methods: A novel equation for the recovery coefficient for large spheres is derived and generalized into an equation for arbitrary shapes such as spheres, ellipsoids, cylinders and cubes. It is verified on data from numerical simulations The novel equation is compared to published results with SPECT kidney phantom measurements and with PET measurements with the IEC NEMA PET body phantom with six spheres (EARL).

Results: The signal loss for large spheres is inversely proportional to the radius, where the slope is proportional to the spatial resolution. For non-spherical shapes the generalized radius or sphericity should be used. An empirical equation with one fit-parameter for smaller objects is presented. It is shown that the EANM-guidelines two-parameter logistic function results in a poor fit if inverse proportionality to the radius and the theoretical slope are forced and it gives a suboptimal fit if both parameters are fitted.

Conclusions: A novel model-based equation for the mean RC-curve is derived. It can be used for different shapes as long as the sphericity is taken into account and it is accurate down to RC=10%. One parameter is directly related to the spatial resolution and the other parameter is an empirical fit parameter.

ID28 (oral presentation)

Title
Combined planar and SPECT image methodology for bone marrow dosimetry during treatment with [177Lu]Lu-DOTATATE

Authors

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Abstract

Introduction: A combined planar and SPECT image methodology for bone marrow dosimetry previously published by our research group showed a significant correlation between absorbed bone marrow dose and haematological toxicity. The method divided the body into a low and high uptake compartment in planar images. The kinetics of the low uptake-compartment was adjusted by the activity concentration in the lumbar vertebrae in SPECT to represent the bone marrow. A specific uptake related to somatostatin receptors in the red marrow has been identified and the aim of this study is to update the dosimetry method and use the kinetics of the high-uptake compartment, which includes organs with a specific uptake, to represent the bone marrow. Methods. 49 patients treated with [177Lu] Lu-DOTATATE was included in the study. 4 planar images (2, 24, 48 and 168 h.p.i.) and a SPECT-CT (24 h.p.i.) were collected. The body was divided into a high uptake compartment consisting of liver, spleen, kidneys, and tumours, and low uptake compartment consisting of the rest of the body. The kinetics of the high uptake compartment was adjusted by the activity concentration in the lumbar vertebrae. The absorbed bone marrow dose was calculated as the sum of the cross-doses from the high and low uptake compartments and the selfdose from the bone marrow itself. Results. A longer retention was observed for the bone marrow when the kinetics of the high uptake compartment was utilized instead of the kinetics of the low uptake compartment. The absorbed bone marrow doses were 0.39 and 0.40 Gy/7.4 GBq for treatment fraction one and two. Significant dose-response relationships were established after treatment cycle one and two between decreased platelet counts and absorbed bone marrow dose with r-values at -0.45 and 0.65. Conclusion. Utilizing the high uptake compartment in planar images more closely resembles the kinetics of bone marrow, resulting in longer retention in the red marrow similar to that seen in a recent SPECT-based study. Absorbed bone marrow doses was estimated and its correlation to the level of platelet counts for treatment fraction one and two. The study will continue including dosimetry for treatment fraction three and four.

ID29 (oral presentation)

Title

223Ra alpha-emitter radionuclide pharmaceuticals (RN) and external beam radiotherapy (EBRT): a radiobiological model for the combined treatment

Authors

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Abstract

Purpose: In order to enhance treatment efficacy for metastatic castration-resistant prostate-cancer (mCRPC) patients, a combined treatment approach with 223Ra radionuclide therapy (223Ra-RN) and external beam radiotherapy (EBRT) is used. Neutropenia is a common complication of both therapies, but data reported in literature on safety are not homogeneous[1,2]. This work aimed to assess the dose-dependent relationships predicting the efficacy (two-year overall survival, 2y-OS) and safety (neutropenia, TOX) following 223Ra+EBRT combined treatment.

Material/Methods: A cohort of patients was derived from the literature. Since the dose-limiting factor in toxicity is red marrow irradiation, the absorbed dose of bone metastasis for both therapies was used for both TOX and 2y-OS. For 223Ra-RN, we adapted the linear–quadratic model previously developed and published for high-LET short-range alpha-emitters[1]. The doses delivered using 223Ra and EBRT were both converted into EQD2 for combined treatment(EQD2TOT). Mixed-effect logistic regression models were derived for both the 2y-OS and TOX.

Results: 223Ra injection activity levels vary from placebo to 80 kBq/kg, associated or not with EBRT. Logistic regression models revealed a dose-dependent increase in terms of EQD2TOT for both the 2y-OS (intercept=-1.364; slope=0.006; p-value≤0.05) and TOX (-5.035;0.018;≤0.05). The logistic regression models revealed no significant effect of the EBRT schedule on the TOX (p=0.05), while the EBRT schedule significantly impacted the 2y-OS (p=0.006).

Conclusion: The presented radiobiological model describes a dose-dependent relationships able predict the safety (TOX) and efficacy (2y-OS) following combined treatment 223Ra+EBRT. This development could help both to support a global description of patient outcomes and guide future treatment optimization.

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ID34 (oral presentation)

Title
Salivary glands dosimetry in 18F-PSMA-1007 PET/CT: comparison among different calculation approaches

Authors

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Abstract

Background/Purpose: We compared several methods for salivary glands (SGs) dosimetry in 5 patients undergoing three time-point 18F-PSMA-1007 PET/CT (0.5h, 2h and 4h post-injection). We also calculated the absorbed dose (AD) variation across patients and single SGs [1], and we conducted a preliminary assessment of the impact of activity distribution within the SGs.

Methods Volume and mass of parotid and submandibular glands were derived from CT. PETs were used to derive TIACs. Average ADs to single SGs or to the total SG volume (tSG) were calculated with: (i) GATE/GEANT4 Monte Carlo simulation considering activity in the entire PET field-of- view (MC) or within the SGs only (MCsgo); (ii) spherical model (SM) of OLINDA/EXM_2.1, adopting patient-specific (SMps) or ICRP89 masses (SMstd); (iii) ellipsoidal model [2]; (iv) MIRD approach with organ S-factors from OLINDA/EXM_2.1 and OpenDose collaboration, with and without cross-irradiation contribution from outside the SGs. The maximum percent AD differences across single SGs (δmax) and across patients (Δmax) were also calculated.max) and across patients (Δmax) were also calculated.max) were also calculated. Furthermore, we implemented MC simulations setting homogeneous activity within SGs (MChom), and we computed maximum and minimum dose-rate (DRmax, DRmin) within SGs for each acquisition.

Results Compared to MC, all methods underestimated the ADs to single SGs (average relative differences between −11.9% and −30.5%). δmax) and across patients (Δmax) were also calculated.max was never below 25% (highest value =702% for SMstd). Considering tSG, an average agreement within 10% of MC estimations was obtained only with methods accounting for cross-irradiation from neighbouring regions. Δmax) were also calculated.max ranged between 58% and 78% across patients. We found up to 50% DRmax and DRmin discrepancies between MChom and MC.

Discussion/Conclusions Adopting simplified geometries and neglecting cross-irradiation from neighbouring regions considerably underestimate ADs to SGs compared to MC. Specific masses of single SGs should always be used given their large intra- and inter-patient variability. Assuming activity homogeneity within SGs significantly affects DRmax and DRmin estimations.

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Keywords personalized dosimetry, salivary glands, 18F, PSMA, prostate cancer, Monte Carlo

ID35 (oral presentation)

Title

Discrepancies between PET-measured and vendor-stated 90Y-microspheres vial activities and Monte Carlo investigation of their causes

Authors

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Abstract

Background/Purpose A recent multi-center study [1] reported systematic discrepancies between PET-measured (APET) and vendor-stated activity (AV) for 90Y glass and resin microspheres vials, with mean APET/AV ratios of 0.79 for glass and 1.15 for resin, while 1.00 was found measuring 90Y- chloride liquid solution. We investigated the possible causes of discrepancies by developing Monte Carlo (MC) simulations of activity-meter estimations for the three types of vial configurations.

Methods The geometry of a commonly used activity-meter and of the three vial configurations were implemented in GAMOS/GEANT4. The decays of the 90Y sources were simulated, scoring the energy depositions in the activity-meter sensitive volume and converting them into electric current per unit activity. The contribution of Internal Bremsstrahlung (IB) to the beta decay, recently proven to be relevant for 90Y [2], was included.

Results Comparing the current per unit activity obtained for 90Y glass (Iglass) and resin (Iglass) microspheres vials and for the 90Y-chloride vial (Ichloride), ratios of Ichloride/Iglass = 0.80 and Ichloride/Iresin = 1.18 were found, in excellent agreement with the activity ratios reported in [1].

Discussion/Conclusions The results suggest that the activity discrepancies found in [1] can be attributed to the different vial geometry and source composition of the two commecial 90Y- microspheres vial configurations, beetween each other and with respect to the 90Y-chloride source, and in addition to the metrological approach adopted for activity-meter calibration, plausibly done using 90Y-chloride, in view of the results. In addition, IB showed to give a relevant contribution in accurately estimating the electric current in activity-meters for 90Y sources.

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Keywords 90Y, microspheres, TARE, vials, PET, activity measurements, Monte Carlo, Internal Bremsstrahlung

ID36 (oral presentation)

Title
Bone marrow dose in Lu-177-PSMA therapy: case report and discussion

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Abstract
Background: Lutetium-177-PSMA (prostate-specific membrane antigen) therapy is used for metastatic castration-resistant prostate cancer (mCRPC) in up to six treatment cycles, each with 7.4 GBq administered in six-week intervals. This fixed scheme is considered safe [1,2], but a more personalized treatment could benefit patients. The most critical healthy tissue for acute side effects is bone marrow: increasing the administered activity per cycle could cause myelotoxicity. Thus, evaluating the radiation dose to the bone marrow is essential for personalized dose escalation. Many of the Lu-177-PSMA treated patients have disseminated or diffuse bone involvement, which makes the task to assess the dose to the active bone marrow even more complicated.

Case presentation: A case of Lu-177-PSMA-I&T treated 78-yr-old man with mCRPC and high skeletal tumor burden is presented and discussed from the viewpoint of bone marrow dose evaluation. The patient's treatment is ongoing: three cycles completed so far. The patient received a reduced activity of 5.1 GBq in the cycle 1 due to a contamination event; cycle 2: 7.2 GBq, cycle 3: 7.6 GBq. According to a commercial dosimetry software using artificial intelligence (AI) based segmentation and voxel S-value kernels, the mean dose to bone (all bony structures) were 8.0 Gy, 9.4 Gy, and 7.8 Gy in cycles 1-3, respectively; the mean dose to whole body were 1.2 Gy, 1.6 Gy, and 1.2 Gy; and to the kidneys 1.2 Gy, 2.4 Gy, and 2.5 Gy. A recoverable decrease in haematological parameters has been observed: nadirs -37% white blood cell count (grade 0 to grade 0, CTCAE 5.0), -17% haemoglobin concentration (G1 to G1), and -21% platelet count (G0 to G1). Alkaline phosphatase (AP) first increased but is now decreasing. Prostate-specific antigen (PSA) has decreased by 59% in 12 weeks.

Discussion: Individualized administration of molecular radiotherapy (MRT) is much encouraged yet in its infancy [3]. The bone marrow is the main organ at risk, if administered activity (per cycle) is to be increased. Some myelosuppression can be observed at the current conventional treatment scheme for small molecule Lu-177-PSMA therapy [4,5]: extrapolation from this data can provide insight. The question is, how to determine the dose distribution to the active bone marrow [6]? Traditionally, the bone marrow dosimetry has relied on blood activity measurements and reference anatomies, and a tolerance limit of 2 Gy is generally acknowledged. Osseous tumor burden can significantly affect the location of the active healthy bone marrow [7]: the distribution can be determined using diagnostic tracers [8], and bone sub-segmentation can refine the analysis [9]. AI-based segmentation can considerably enhance the MRT dosimetry workflows and thus take part in enabling personalized treatment planning. We will include the complete dose-volume histograms produced by the voxel dosimetry software for the case presentation in all treatment cycles as well as a comparison to a traditional planar whole-body image-based bone marrow dose calculation method. The case will be compared to other Lu-177-PSMA treated patients with and without extensive bone uptake, and the complexity of the bone marrow dose-response will be elaborated.

Conclusion: The presented mCRPC patient with extensive diffuse bone involvement appears to have relatively high mean dose to bone, which is to be expected with high osseous tumor load. The patient's blood counts indicate mild, recovering myelosuppression, while PSA and AP are decreasing. Evaluation of the dose to healthy bone marrow is a complex task that needs to be further discussed.

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ID37 (oral presentation)

Title

Quality assurance (QA) of the Q-suite® 2.0 software package for absorbed dose calculation for SIRT treatment with 166Ho microspheres

Authors

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Abstract

Purpose: Perform the QA of the software package Q-Suite®2.0 (Terumo) for absorbed dose calculation, designed for treatment planning of SIRT with 166Ho microspheres.

Methods: The dosimetry was performed with Q-suite® 2.0 and was compared to OEDIPE1 using the same input data (SPECT/CT images, DICOM RT-Struct files). This study was conducted on 10 patients who received administration of 166Ho-microspheres, including two patients with a pulmonary shunt. The methods employed for dose calculation were Local Deposition (LD) and Voxel Dose Kernel convolution (DVK) for Q-Suite®2.0, and GATE Monte Carlo simulations for OEDIPE (MC-GATE). The comparison was made on volumes, counts, absorbed dose (AD) and dose volume histogram (DVH) results for different organs, distant or source of 166Ho emission.

Results/discussion: The choice in the method used for calculation had minor influence on AD. Regarding liver regions, relative differences in AD were below 10%, with substantially lower values between DVK and MC-GATE (median of 1.5% for tumor; 3.0 % for perfused liver). These differences were generally higher for structures located further from the source, such as healthy liver and heart.

For the two patients with a pulmonary shunt, deviations between LD and MC-GATE were larger for lungs, with a median relative difference reaching 14% for AD. The median differences on the VDGy (LD vs. MC-GATE) were around 10% for the right lung.

For lesions and perfused liver, they were around 5% with LD and 2% with DVK.

The observed discrepancies on AD could be explained by the differences on the volumes of the VOI [2.9% to 7.7%] and on the number of counts within the VOI [1.3% to 9.2%].

Conclusion: When applying a similar processing approach, results obtained were comparable for the two software packages. DVK gave the closest results compared with MC-GATE.

1 OEDIPE has been developed at IRSN to carry out personalized dosimetry for internal radiotherapy based on MC simulations using the anatomical and functional data of patients.

ID38 (oral presentation)

Title

Initial results of the INSPIRE clinical trial – Radioiodine dosimetry for differentiated thyroid cancer patients

Authors

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Abstract

Introduction: The treatment of differentiated thyroid cancer (DTC) patient after thyroidectomy remains controversial with studies suggesting that radioiodine therapy might not always be required. Nevertheless, approximately 10-15% of patients will at some point during follow-up have a recurrence, metastatic disease or become iodine refractory. Multi-centre clinical studies involving dosimetry are essential to identify personalised treatment strategies.

Methods: The INSPIRE clinical trial (ClinicalTrials.gov Identifier: NCT04391244) is recruiting 150 patients in the UK to investigate dosimetry for DTC patients. The primary aim is to determine the range of absorbed doses delivered to target and non-target tissues. Secondary aims include relationships of absorbed doses with outcome and toxicity.

Results: Initial results of the first 35 patients have shown a large range of absorbed doses for both thyroid remnants and organs-at-risk. Thyroid remnant absorbed doses ranged from <1 to 250 Gy while the median absorbed dose to salivary glands was 0.3 Gy (Range 0.1 to 1.7 Gy).

Discussion: The interim study results help to improve our understanding of absorbed doses to thyroid remnants and normal organs following RAI therapy. These results can help in the development of personalised treatment strategies for these patients. Furthermore, it has been shown that multi-centre dosimetry studies are feasible and the INSPIRE study is encouraging exchange of quantification and dosimetry methodologies across centres.

ID39 (oral presentation)

Title
Lesion dosimetry in treatments of neuroendocrine tumours with [131I]I-mIBG

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Abstract
In treatments of neuroendocrine tumours with [131I]I-mIBG, high activities could be administered. For instance, we have recently treated an adult woman for a neuroendocrine tumour with 14.8 GBq (the maximum activity of 131I permitted in our centre). Those treatments always start on Wednesdays, when the radiopharmaceutical is received, and patients remain as in-patients in isolated wards for several days. As the wards are quite far from the department of nuclear medicine, images are not acquired before the week-end for radiation protection reasons and the first image is not acquired until Monday, with a second image acquired on Wednesday. Therefore, the information about the lesion uptake of the [131I]I-mIBG during the first treatment days is missing.

We usually perform lesion dosimetry assuming a mono-exponential behaviour of the [131I]I-mIBG in the lesions, but it would be of interest to study whether that behaviour can be assumed. This could be better done in centres in which the treatment wards are close enough to the department of nuclear medicine. Moreover, dosimetry based on a single time-point acquisition could be performed as it is being done in treatments with [177Lu]Lu-DOTA-TATE.

For the abovementioned patient, dosimetry of 4 lesions using the MIRD schema were performed, obtaining absorbed doses of 33 Gy, 41 Gy, 18 Gy and 17 Gy, which results in values of 2.2 Gy/GBq, 2.8 Gy/GBq, 1.2 Gy/GBq and 1.1 Gy/GBq. Those values are in the lower part of the range of published results.

In conclusion, lesion dosimetry in treatments of neuroendocrine tumours with [131I]I-mIBG is feasible but for radiation protection reasons the image acquisitions during the first days may be missing. The pharmacokinetics during the first days should be investigated, as well as the possibility of dosimetry based on a single time-point acquisition.

ID39 (oral presentation)

Title

Fully automated deep learning-guided segmentation and lung-shunt fraction calculation on total body planar images

Authors

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Abstract

Introduction: SIRT (Selective Internal Radiation Therapy) with 90Y is efficient for the management of unresectable liver malignancies (1). The simulation study using 99mTc-MAA enables to perform personalized radiation dosimetry and to exclude patients with extrahepatic uptake, usually those presenting with high lung shunt fraction (LSF) values (2, 3). SPECT/CT acquisition is recommended to measure the LSF in the simulation acquisition. However, due to the acquisition time and low signal-to-noise ratio in SPECT images, LSF is commonly calculated on planar images in clinical scenario (4). The lack of anatomical information and the non-quantitative nature of planar images limit the visual ability of physicians in creating the boundaries of the lung and liver to calculate LSF. In this study, we suggest an alternative approach using automatic segmentations from CT images.

Methods: We included 50 patients who underwent 99mTc-MAA simulation scan prior to Y90-SIRT therapy. The acquisition included a single-bed SPECT/CT scan covering the liver and part of the lung, and a total-body planar anterior/posterior image. We segmented the lungs, liver, and bones on co-registered CT using a deep learning model developed by our group. Then, anterior-posterior (AP) projections of SPECT, CT, and segmentation mask were generated by summation along one axis. The posterior planar image was flipped to match the anterior view and summed together. The SPECT AP projection image was registered to the summed planar image by moving the SPECT image in craniocaudal and minimizing the difference between the two images by gradient descent optimizer. The SPECT, CT, and segmentations were co-registered before, so the estimated shift was implemented on CT and segmentation projections. After co-registering all images, the segmentation masks on the planar image were saved.

Results and Discussion: Unfortunately, commercial gamma cameras do not save information regarding the total body table position and image position in physical space. At the same time, the routine LSF measurement on the planar image is prone to inter/intra observer differences due to visualization variations by changing the image display window/level. Besides, radiotracer accumulation in the liver may not cover the whole liver and it makes the lungs/liver boundary and their overlap detection more complicated. Our methodology was successfully implemented in all cases in less than a minute per case. Through our suggested approach, the LSF can be calculated through the automatic segmentation of the liver, lung, and their overlap. Besides, the physician can visualize all anatomical information available on CT, SPECT, and segmentation projections, registered to the planar image, and edit the masks if needed.

Figure 1 shows an example of fused image visualizations.

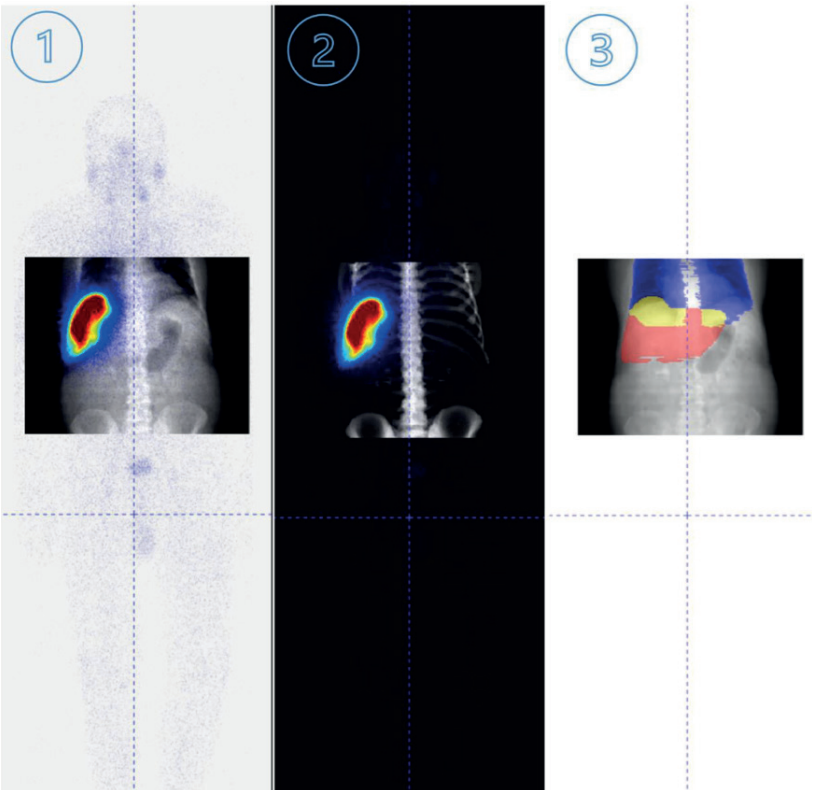

Figure 1. Example of co-registered images and viewing method adopted for the calculation of LSF. (1) TB planar image and the CT projection fused, (2) TB planar image and bone segment projection, (3) CT projection image, lung (blue), liver (red) and their overlaps (yellow) segmentations.

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ID48 (oral presentation)

Title

A realistic multi-region model of a mouse kidney for preclinical dosimetry of beta- and alpha-particle emitting radionuclides

Authors

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Abstract

Introduction: Absorbed dose heterogeneity is a major modifier of tissue response which can confound the analysis and prediction of toxicity in radiopharmaceutical therapy. Preclinical nephrotoxicity studies with detailed dosimetry of kidney tissues are useful to investigate the dose-response relationship of alpha- and beta-particle emitting radioligands with a non-uniform distribution in kidney tissues and provide insight on the translatability of the dose-response relationships of different radiopharmaceuticals. Such analyses are however limited by the scarcity of reference S values available in the literature for various tissues of the mouse kidney.

Materials and methods: A computational multi-region model of a mouse kidney was developed based on high-resolution magnetic resonance imaging data of a healthy mouse kidney [1]. The model was used to calculate S values and energy absorbed fractions for 5 kidney tissue regions (cortex, outer stripe of outer medulla (OSOM), inner stripe of outer medulla (ISOM), inner medulla and papilla and pelvis) for a wide range of beta- and alpha-emitting radionuclides of interest in targeted radionuclide therapy, using Monte Carlo calculations (MCNP6.2). Additionally, the applicability of regional S values was demonstrated for a [131I]-labeled anti-HER2 single-domain antibody (sdAb) fragment with predominant retention in the OSOM. The sub-organ distribution of [131I]-sdAb in mouse kidney tissues was determined with digital autoradiography and gamma counting (for the whole kidney activity).

Results: The considerations of activity distribution in kidney tissues can have a substantial impact on the dose estimations of specific tissues, particularly for alpha emitters and low to medium-energy beta emitters. High-energy beta emitters (e.g. ^{90}Y, ^{188}R, ^{32}P) cross-irradiate surrounding kidney tissues more than low-energy beta emitters (e.g. ^{177}Lu, ^{67}Cu, ^{161}Tb), which cross-irradiate mainly the adjacent tissues (e.g. cortex-OSOM). Instead, the energy emitted by alpha emitters is absorbed mostly within the source region. For the [^{131}I]-sdAb, the OSOM absorbs about 2.0 times more dose than the cortex and the ISOM, and about 2.6 times more dose than inner tissues. Compared with sub-organ regional dosimetry, the assumption of a uniform distribution of activity throughout kidney tissues would result in an underestimation (-57%) of the dose to the OSOM and an overestimation (~30%) of the dose to the other tissues (including the cortex).

Conclusion: The use of regional S values allows a more realistic estimation of the absorbed dose in different kidney tissues from therapeutic radioligands with a non-uniform distribution in kidneys. This constitutes an improvement from the simplistic (less accurate) renal dose estimates assuming a uniform distribution of activity throughout kidney tissues. Such dosimetry improvement is expected to support preclinical studies essential for a better understanding of nephrotoxicity in humans.

References

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ID51 (oral presentation)

Title
Towards single-time-point dosimetry in [^{177}Lu]Lu-PSMA-617 therapy

Authors

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Abstract

Aim: To validate a single-time-point (STP) dosimetry for [177Lu]Lu-PSMA-617 therapy using non-linear mixed-effects modelling (NLMEM) and population-based model selection (PBMS).

Materials and Methods: 63 mCRPC patients receiving 6 GBq of [177Lu]Lu-PSMA-617 were included. SPECT/CT images were taken on days 0-3 and once between days 6-9. Six sum-of-exponentials functions were compared to find the best fit function to determine the kidney time-integrated activity (TIA). The function parameters were fitted to the all-time-point (ATP) data using NLMEM. A PBMS was performed, using the Akaike weight, to select the best function. The parameters from ATP fitting were used to calculate the reference TIAs and absorbed doses (ADs). In STP dosimetry, the selected function's parameters were fitted to the STP data of a specific patient within the NLMEM by simultaneously fitting the ATP data of all other patients with the STP data of that specific patient. The fitted parameters were used to calculate TIAs and ADs. The performance of the STP method was evaluated using relative deviations to the ATP NLMEM approach and root-mean-square errors (RMSEs).

Results: The function, consisting of six parameters, was deemed the best representation of the data (Akaike weight=100%). The STP method utilising a SPECT/CT image on day 2 demonstrated best performance, with a relative deviation of (5±10)%. Compared to other time points, it exhibited the lowest RMSEs (11%) for the relative deviations of the absorbed dose.

Conclusion: The proposed STP dosimetry with a SPECT/CT image at day 2 could potentially personalise renal dosimetry in [177Lu]Lu-PSMA-617 therapy.

ID52 (oral presentation)

Title
QVolumetrix Validation for Lu-177: preliminary results

Authors
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Abstract
Molecular Radiotherapy Dosimetry (MRD) is becoming widely adopted due to regulatory changes, increasing expertise and clinical interest. Quantitative SPECT imaging is the main input to dosimetry calculations; this needs to be accurate for any dosimetry to be clinically useful. As a first step, clinical departments should consider traceable validation of quantitative imaging as part of commissioning MRD procedures, with the aim of establishing traceability in the dosimetry measurements, as is common practice in external beam radiotherapy. This work aims to perform traceable calibration and verification of imaging systems in our centre and compare the accuracy of two different camera sensitivity calibration methods.

Quantitative imaging calibrations were carried out using non-carrier added Lu-177 with a petri dish in planar mode (manufacturer recommendation) and a large-volume cylinder in SPECT/CT (Tran-Gia et al., 2021). Partial volume corrections were determined using hollow spheres and large sphere phantoms. For validation, a 3D printed two-organ phantom was scanned. Acquisitions were performed on three gamma cameras, including two scintillation cameras and one CZT system. All activities were traceable to primary standards at NPL, including uncertainties. Images were reconstructed using the manufacturers' software, and the reconstruction parameters chosen to ensure convergence. All images were analysed using the manufacturer's software tools and independently using ImageJ and Matlab. The manufacturers' reported activities were compared to the measured and known phantom activities in the two-organ phantom.

Results will be presented at the symposium including a comparison between these two calibration methods, uncertainties for the three systems and its implication on MRD.

ID53 (oral presentation)

Title
A review of the role of imaging and dosimetry in clinical trials of Lu-177 for the treatment of cancer

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Abstract
Introduction: Over the last twenty years, nuclear medicine therapy has grown exponentially in terms of both patient numbers and clinical indications.

This is reflected in the growing number of clinical trials registered in the "ClinicalTrials.gov" database. This work presents a tool based on the Python programming language to extract information from the database to analyse the role of imaging and dosimetry.

Methodology: A raw database was set up from "ClinicalTrials.gov" applying the single keyword "lutetium 177".
A script based on Python V3.11 was written, including standard module Pandas aiming to manipulate two-dimensional, size-mutable, heterogeneous tabular data. The Natural Language Toolkit (NLTK) library was implemented as natural language processing (NLP) to analyse text data.

This study focused first on primary outcome measures of greatest importance as specified in the protocol.
Results: Data extraction at the date of 30th of June 2023, yielded 236 clinical trials involving 177Lu, increasing from 1 in 1996 to 42 in 2023.

Inclusion of the terms "imaging" or "dosimetry" in primary outcome measures identified 32 clinical trials, increasing from 1 in 2006 to 6 in 2023.

In the 19 multicentre Phase 3 trials listed, only three included imaging or dosimetry.
NLTK analysis enabled deeper analysis of the inclusion of imaging and dosimetry in outcome measures.

Conclusion: The analysis of a snapshot of nuclear medicine clinical trials involving lutetium-177 was performed using Python scripts. This tool offers the potential to analyse the role played by imaging and dosimetry in clinical trials of radiotherapeutics, based on quantitative and qualitative analysis. Analysis is ongoing and further complementary outcomes will be presented.

ID54 (oral presentation)

Title
Terbium-161 SPECT Imaging: Assessing Quantifiability for a Novel Theragnostic Nuclide

Authors
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Abstract
Introduction: Terbium-161 (^{161}Tb) is a novel theragnostic nuclide, for which the potential for quantitative γ-camera imaging remains relatively unexplored. The aim of this study was to assess the quantitative accuracy of 161Tb SPECT imaging for different collimator design options.

Materials and methods: Measurements were conducted on a GE Discovery NM/CT 670 Pro with a 75 keV±10% photopeak window. Three collimator designs were employed: extended low-energy general-purpose (ELEGP), low-energy high-resolution (LEHR), and medium-energy general-purpose (MEGP). Septal penetration was measured planarly using a petri dish. SPECT calibration factors were determined using a homogenous cylinder phantom, and recovery coefficients (RCs) using a Jaszczak phantom with 6 spherical inserts (0.5–16 mL). An Elliptical LungSpine Phantom with 8 spherical inserts (V = 2, 4, 8, and 16 mL, times two), was measured using three different background activity levels (cold, 1:20, and 1:10). Reconstruction was performed using a Monte Carlo-based OSEM algorithm with 6i10s.

Results: LEHR showed some septal penetration, whereas effects were negligible with ELEGP and MEGP. LEHR produced the highest RCs (0.32–0.70), followed by ELEGP (0.26–0.67) and MEGP (0.27–0.63). In the anthropomorphic study, LEHR displayed the greatest uncertainty (mean relative quantification error±standard deviation; 2.63%±9.04%), while ELEGP (0.18%±6.44%) and MEGP (3.58%±6.41%) had lower uncertainties.

Conclusion: While the complex decay scheme poses some challenges, quantitative SPECT 161Tb imaging appears feasible. Although LEHR produces good visual image quality, using said collimator will result in unwanted contributions from high-energy photons, potentially compromising the quantitative accuracy.

ID55 (oral presentation)

Title

^{124}I PET dosimetry to optimize 131I therapy of Metastatic Differentiated Thyroid Cancer (MDTC): initial results of a phase II trial

Authors

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Abstract

Aim: to optimize 131I therapy of MDTC with dosimetric treatment planning with 124I.

Methods: Preliminary phantoms with hot 124I spheres of volume down to 0.02 mL were used to compare conventional PVE correction versus large VOI approach. Patients were prepared with hormon withdrawal both for dosimetry and therapy. Administration of 124I (100 MBq) was followed by blood sampling and whole body counting at 2, 6, 24, 96 h. PET scans were taken at 24 and 96 h. Response was assessed on 18F FDG PET, contrast-enhanced CT or MRI, 124I PET and thyroglobulin level at 6 months.

Results: PVE correction was abandoned in favour of the large VOI approach. An upper limit to mass was attributed to lesions undetectable on CT. We studied 11 patients. 7/11 were dropped out to standard remnant ablation since lesions were 124I negative. 4 received 5 optimised treatments (3, 4a, 4b, 7, 8). For treatments 3 and 4a, fixed activity for MDTC in our centre (7.4 GBq) was reduced to 5.5 and 3.7 GBq for safety, while in treatments 4b and 8 the presence of bone metastases leaded to deliver 1.5 Gy and 2.0 Gy to blood (20 GBq and 16 GBq, respectively). Patients 3 & 4, previously unsuccessfully treated with external beam, showed complete 124I response after maximized iodine therapy.

Discussion & Conclusion: 124I PET was superior to post-therapy 131I SPECT/CT for staging. Predictive lesion dosimetry was less important than blood dosimetry, since heterogeneity of predicted absorbed dose seldom allowed a true optimisation, leading rather to maximization.

The study is funded by AIRC Foundation (Italian Association for the Research on Cancer)

ID56 (oral presentation)

Title
The EARL Quantitative Lu-177 SPECT-CT accreditation programme

Authors
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Abstract
Introduction: Quantitative SPECT/CT imaging is an important prerequisite for treatment planning and verification in 177Lu-based radiopharmaceutical therapies. However, SPECT/CT imaging protocols for 177Lu at different systems and/or centres can yield varying quantitative outcomes, which hampers scientific progress in this rapidly developing field. To combine the efforts of many years of EU-funded projects between metrological institutes and nuclear medicine research facilities [1] with the longstanding success of the EANM Research Ltd (EARL) accreditation program for FDG-PET [2], a task group was recently formed to define a harmonisation programme for traceable calibration of quantitative 177Lu SPECT/CT systems.

Materials and Methods: After an initial test phase based on a few centres, a larger pilot study is launched: voluntary centres can perform measurements according to a first EARL protocol and submit their data for analysis. The merged data will be used to define manufacturer and/or model specific characteristics for an objective evaluation of harmonisation and criteria for passing/failing accreditation. The aim is to determine balance between efforts and a practical level of harmonisation. The trial period will allow for the incorporation of feedback from participating centres and/or other interested international sites.

Results: At this stage, the accreditation programme requires participating sites to: 1) demonstrate a path to accurate measurement of 177Lu activity (traceability to standards of radioactivity); 2) provide an image calibration factor converting count rate to activity concentration (determined by measurement of a large cylinder phantom filled with a uniform 177Lu solution); 3) provide data from a NEMA IEC PET body phantom SPECT/CT measurement (cold background; 177Lu-filled sphere insert with a 60-mm diameter sphere replacing the smallest one) for a spatially resolved assessment of quantitative accuracy.

Conclusion: After a trial period with an adequate number of participants, the accreditation program is expected to start in 2024.

Literature

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2. Aide N EJNMMI 2017;44(Suppl 1)

ID57 (oral presentation)

Title

Reducing the influence of noise in bone marrow activity concentration estimates by using AI-generated projections in the SPECT reconstruction

Authors

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Abstract

Aim/Introduction

Accurate SPECT-based bone marrow activity quantification is challenging due to noise. AI-generated projections (e.g., synthetic intermediate projections (SIPs) or denoised projections) have an inherently low noise level and could thus improve accuracy. The aim of this study was to assess the quantitative accuracy in SPECT reconstructions performed with and without AI-generated projections at clinically realistic noise levels.

Method & Materials

This study included patients (n=13) treated with ^{177}Lu-DOTATATE. To replicate the noise level in patients, Poisson-distributed noise was added to projections of a Jaszczak phantom. Five noise levels were mimicked, with 100 realizations for each, ranging from highest activity concentration found in the vertebrae 24 h p.i. to 60% of the minimum. Three different reconstruction techniques were explored (6i10s); 30 projections, 30 projections + 90 SIPs, and 30 AI-denoised projections. Recovery coefficients (RCs) and the coefficients of variation (COVs) of the RCs were calculated. All images were reconstructed with a MC-based OSEM with 200 updates.

Results

The vertebral cavity's concentration decreased during the first 50 updates for most patients, showing increased variation with more updates. AI-generated projections reduced uncertainties (COVs) compared to conventional ones. However, using true projections resulted in higher RCs. AI-denoised projections had less RC-reduction than SIPs.

Conclusion

The dramatic increase in noise, and subsequent variation in activity concentration, observed at higher updates illustrates the challenge with SPECT-based bone marrow dosimetry. AI-based methods offer more stable estimates, making them promising for dosimetry applications.

ID59 (oral presentation)

Title

A 6 years 'experience of dosimetry in clinical routine for patients treated with ^{177}Lu-DOTATATE: Absorbed dose-effect relationship exploration

Authors

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Abstract

Purpose

Clinical dosimetry was implemented in our nuclear medicine department as part of the first [^{177}Lu]Lu-DOTA-TATE treatment for neuroendocrine tumours. This work presents (1) our clinical dosimetry workflow and its implementation, and (2) the associations between mean absorbed doses to lesions and organs at risk (OAR) and clinical outcomes.

Material and Methods

Different phantoms filled with ^{177}Lu were acquired on both SPECT/CT Discovery NM/CT 670 and 870 CZT systems (GE) to determine calibration factor (CF), recovery coefficients (RC) and for the final validation process. Similar acquisition and reconstruction protocols were used for phantoms and patients. Post-therapeutic SPECT-CT dosimetry considering OAR (healthy liver, kidneys, bone marrow, spleen) and tumours was performed on 34 patients using PLANET® Dose. Lesions were selected and measured on the baseline CT and at 3 months after the end of treatment. Clinical data including tumour volume variation, progression free survival (PSF) and overall survival (OS) were assessed and associated with absorbed doses to lesions and OAR.

Results

SPECT/CT calibration factors of 56 and 64.2 Bq.counts−1 were obtained with both systems respectively, and uploaded on PLANET® Dose. Logarithm fitting curves were established for partial volume effect correction. For each patient, a dosimetric report was supplied. For dosimetry studies, 146 lesions were analysed. The average of the cumulative mean absorbed dose to tumours was 101.3 ± 54.6 Gy. We found a significant reduction of 21.9% in lesion volume when the cumulative absorbed dose to lesions increased from 55.8 Gy to 130.7 Gy ($p<0.001$).

At patient's level, both the average and the lowest of cumulated absorbed dose to lesions were predictive of PFS ($p=0.03$, $p=0.01$), whereas only the lowest cumulated absorbed dose to a lesion was predictive of OS ($p=0.01$). Linear mixed-effect models revealed some significant associations between the lymphocytes, haemoglobin or platelets's levels and the mean absorbed doses to the spleen or bone marrow.

Conclusion

A post ^{177}Lu-DOTATATE dosimetric analysis may predict tumour response to treatment and toxicity outcomes. Dosimetric reports provide a reliable database for further explorations.

ID60 (oral presentation)

Title

Comparison between deep learning-based partial volume correction and iterative Yang technique for 177Lu SPECT/CT imaging

Authors

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Abstract

Purpose:

This work presents a deep learning-based method for partial volume correction (PVC) in quantitative 177Lu SPECT/CT imaging (DL-PVC), which is compared with the iterative Yang method.

Methods:

A dataset of 10,000 activity distributions was generated by randomly placing random voxelized shapes inside anthropomorphic XCAT phantoms [1]. Using the SIMIND MC program [2], SPECT projection sets were simulated for a Siemens Intevo Bold SPECT/CT system. Reconstructions were performed using standard OSEM with PSF modeling (STIR, [3]). Based on these reconstructions, a u-net was trained (input: SPECT reconstructions, output: original activity distributions). The dataset was divided into 9000/500/500 for training/validation/testing. For benchmarking against state-of-the-art PVC methodology, PETPVC ([4], iterative Yang) was applied to all test data. SSIM and NRMSE between original activity distributions, and SPECT reconstructions without/with PVC were calculated for all test data for quantitative performance analysis. Validation for real SPECT/CT data (3D-printed models of a sphere, an ellipsoid, and a renal cortex) was performed based on the recovery coefficient without/with PVC.

Results:

Simulations: DL-PVC resulted in significant improvements (paired Wilcoxon test, $p<0.01$) in the quality parameters in comparison to PETPVC and without PVC (no PVC: 0.89/10.4%, PETPVC: 0.93/8.6%, DL-PVC: 0.95/7.8%, [SSIM/NRMSE]). Phantom measurements: For sphere (recovery coefficients of 0.73/0.84/0.89 [no PVC/IY/DL-PVC]) and ellipsoid (0.67/0.87/0.96), DL-PVC resulted in the highest recovery. For the renal cortex, PETPVC yielded the highest recovery (0.48/0.80/0.77).

Conclusion:

This work presents the enormous potential of deep-learning based PVC for quantitative SPECT. The method can alleviate the well-known problem of poor spatial resolution in SPECT/CT imaging.

Results

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ID61 (oral presentation)

Title
Evaluation of n.c.a. Lu-177-Dotatoc in Inoperable Neuroendocrine Liver Metastases of Gastro-Entero-Pancreatic (GEP) Tumors

Authors
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Abstract
Aim:
To evaluate the effectiveness of n.c.a. ^{177}Lu-DOTATOC in inoperable liver metastases, positive for sst2 receptor due to NET-GEP tumours. ^{177}Lu-DOTATOC has been infused trans-hepatically ('ARETAIEION' PROTOCOL), minimising the toxicity of non-target tissues.

Materials and Methods:
The average activity/session/ patient was 7.3±2.3 GBq. Repetitions did not exceed 6-fold, with treatment intervals of 8-11 weeks. Absorbed doses delivered to metastases, kidneys and red marrow were calculated according to MIRD scheme (OLINDA 1.1 software). The derived values were correlated to RECIST1.1 criteria. CT/ MRI scans were performed during the treatment and monthly US for follow-up. Toxicity (WHO criteria) was measured using blood and urine tests.

Results:
None of the patients resulted in complete response; partial response was assessed in 6 (66.0%) and disease stabilization in 3 (34.0%). An 8-month median survival time was estimated for all patients. 6/9 (66.0%) showed a mean target diameter shrinkage, ranging from 32%-46%. The organ average radiation dose was found as follows: (a) Liver-Tumour 23.2±0.9mGy/MBq, (b) Liver 0.11±0.02 mGy / MBq, (c) Kidneys 0.4±0.09 mGy / MBq, (d) Spleen 1.2±0.02 mGy / MBq and (f) Bone marrow 0.023±0.004 mGy/MBq. WHO toxicity grade 2 erythro-, leuko- and thrombo-cytopenia occurred in 2 (22.0%) cases after the 3rd session.

Conclusion:
In unresectable metastatic liver lesions positive for sst2 receptors, repeated, trans-hepatic high doses of n.c.a. ^{177}Lu-DOTATOC resulted as a promising therapeutic outcome with a partial response in approx 66% of the treated patients. Given the locoregional modality character of the administration technique, no nephrotoxicity has been observed.

ID68 (oral presentation)

Title
AlphaMet: A European project on metrology for emerging targeted alpha therapies

Authors
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Abstract
Targeted alpha therapy (TAT) is a rapidly growing cancer treatment modality. Presently, only 223RaCl2 has regulatory approval, but its success resulted in unprecedented levels of interest and investment in TAT for a variety of cancers.

As a result of the short penetration range and high linear energy transfer of alpha particles, which can cause more DNA damage than beta particles, TAT is showing promising efficacies and increased survival in early phase clinical trials. However, these advantages bring several unmet and unique measurement challenges which remain a barrier to enable their safe and optimised implementation. These include the lack of validated primary (secondary) activity standards, the time-dependent in-growth of the decay progeny, the separation of the decay products, and the low administered activity levels and the microscopic uptake distribution that result in poor quantification of the activities and absorbed doses in-vivo. The best approach to deliver TAT is still under debate and good practice guides are not available, with treatments currently administered with administration regimens more akin to chemotherapy, with fixed or weighted-scaled activities and not guided by dosimetry. This contrasts with external beam radiotherapy, where treatments are traceable to primary standards and accuracy in dose delivery to patients is below 5%. The accuracy, reproducibility, and uncertainties in the delivery of TAT are presently unknown, with a recent ICRU Report 96 highlighting the need to address the lack of traceability and standardisation/harmonisation.

The AlphaMet project brings together experts from National Metrology Institutes, hospitals, academia, and industry to support end-to-end traceability before wide routine adoption of TAT. The project will start in September 2023 and this

presentation will provide an overview of the consortium and research aims, as well provide information about ways in which other end-users and stakeholders can get involved.

Acknowledgements

Additional AlphaMet co-authors: Bailat C.[10], Collins S.M.[1], Fenwick A.J.[1], Frederic J.[10], Kellett M.[2], Lassmann M.[5], Robinson A.P.[1], Salas Ramirez M.[5], Sochorova J.[17], Solc J.[17], Struelens L.[15], Ziegler S.[8,9], Ziemek T.[6]

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ID71 (oral presentation)

Title
Flexible actuated lung phantom for the assessment of nuclear imaging systems

Authors

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Abstract

Physical phantoms are commonly used to evaluate diagnostic imaging systems as they are tools for quality control measurements, assessing image quality or characterizing nuclear imaging equipment required to get information about physiological processes to diagnose pathologies such as cancer [1,2].

Recently, innovative processes have been used to produce anthropomorphic phantoms and assess materials with mechanical and radiological features that enable them to be considered as potential options in phantom manufacturing. Nevertheless, there is still a lack of actuated phantoms with the capacity to simulate inherent processes in patients, such as breathing, peristaltic movements, blood irrigation, etc [3,4].

This work presents the development of an actuated soft robotic lung phantom to characterize and evaluate radiopharmaceuticals on nuclear imaging systems. The proposed design contemplates both lungs, the trachea and two hollow spherical inserts which simulate tumors. The trachea and tumors were obtained by 3D printing with polylactic acid (PLA) filament and were coated with epoxy resin [5]. The lungs were obtained with the rubber silicone Eco-FlexTM 00-33 AF [6], following a casting process with 3D printed molds. Phantom actuation was obtained through instrumentation and control stages which included an air bomb, an air flow sensor, electronics, and an Arduino Uno microcontroller. The proposed control was volume-based on a healthy adult. The volumes were analyzed with the air flow sensor and the

graphical system of Arduino IDE.

The developed phantom is expected to be used for assessing the performance of position and motion-correction algorithms, that could impact quantification processes of lung malignancies [7].

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ID72 (oral presentation)

Title
Application of priors in EARL Lu-177 SPECT accreditation with an Open-Source reconstruction software

Authors
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Abstract
Aim/Introduction:
The EARL Lu-177 SPECT methodology enables assessment of the quality of quantitation by characterizing the recovery coefficient in different sized volumes. The aim of this project is to investigate the effect of priors in quantification using an open-source reconstruction platform (STIR [1]).

Materials and Methods:
Two Lu-177 phantoms were prepared according to EARL [2] requirements. The projections were reconstructed in STIR with 2 subset OSEM, saving every 5 sub-iterations, correcting for attenuation and scatter. Permutations with and without PSF modelling (in 2D) were investigated with and without incorporating a log-cosh prior and two different penalty strengths. Recovery coefficients (RC) were estimated for the 60mm sphere for all the tested algorithms, while noise was

estimated by the standard deviation in a 40 mm region within the largest sphere. The algorithms were compared for noise and quality of convergence at 100 sub-iterations.

Results:
In the PSF reconstructions, ringing artefacts were visible. Application of the prior eliminated the artefact after 100 sub-iterations. Compared to OSEM applying PSF decreased the standard deviation from 6.22 to 3.54, while RC (60mm) was improved from 0.814±0.035 to 0.880±0.037. Applying the prior without PSF with penalty weighting of 0.1, standard deviation was 1.07 with the RC (60mm) hardly affected at 0.803±0.03. The combination of PSF and prior provided the best results with standard deviation at 1.02 while preserving the RC (60mm) at 0.871±0.037 with penalty strength of 0.1.

Conclusion:
Appropriate use of priors in image quantification using an open-source reconstruction platform (STIR [1]) improves dosimetry.

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ID74 (oral presentation)

Title
Comparison and evaluation of n.c.a. and c.a. 177Lu-[DOTA0, Tyr3] OCTREOTATE in (GEP-NETs) treated patients

Authors
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Abstract
Aim: To evaluate and compare the dose uptake profile of non carrier added (n.c.a.) and carrier-added (c.a.) 177Lu-DOTA-TATE in inoperable GEP-NET liver metastases pts, with sst2 receptor over-expression. 177Lu-DOTA-TATE (n.c.a.) was i.a. infused, after catheterization of the hepatic artery, whereas (c.a.). 177Lu-DOTA-TATE was infused intravenously [antecubitally].

Materials and Methods: The average of n.c.a. (Group A) and c.a. (Group B) 177Lu-DOTA-TATE activity/patient/session, (Group A: 12 cases, Group B: 4 cases) was the same, i.e.7.3±2.3 GBq. For both groups session-repetitions did not exceed 6-fold with treatment intervals of 5–8 weeks. Blood samples were collected 2, 4, 8, 24 hrs p.i. in parallel with a 24 hrs urine collection. Dosimetry was performed using the OLINDA 1.1 code.

Results: The dose uptake profiles of these radiopeptides are markedly different, due to their administration route (i.a. vs. i.v.) and their different specific activities (~80 Gy/mg vs. ~ 30 Gy/mg of the theoretically 110 Gy/mg, expected. The organ average radiation dose of n.c.a./c.a. ^{177}Lu-[DOTA0,Tyr3]octreotate ratios were found as follows: (a) Liver tumour of 20 gr spherical mass was estimated to be 8.3/0.96 mGy/MBq, (b) Liver 0.82 /1.03 mGy/MBq, (c) Kidneys 0.41/1.48 mGy/MBq, (d) Spleen 1.4/2.3 mGy/MBq and (e) Bone marrow 0.0025 /0.06 mGy/MBq.

Conclusion: Using n.c.a. ^{177}Lu-octreotate (a) 8.6 fold higher tumour absorbed doses as compared to c.a one was found, (b) 0.3 fold lower absorbed doses to kidneys was observed advocating that higher doses might be reached to tumours minimising the dose to critical organs (kidneys, bone marrow).

ID75 (oral presentation)

Title
Parametric modelling study of intracellular radionuclide distribution impact in Targeted Alpha Therapy

Authors

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Abstract

In the context of predicting biological effects in Targeted Alpha Therapy (TAT), nano/micro-dosimetry are essential to consider the very heterogeneous dose deposition at cell level. The objective of this study is to evaluate theoretically the importance of radionuclide cell internalization in microtumors treated with TAT on physical and biological endpoints.

We used Monte Carlo simulations to track alpha particles in complex in silico3D cell populations using the CPOP/Geant4 code [1], which allows deformable cell membrane to mimic tissue compaction. The code was adapted to generate radionuclide source distributions in various internalization cases that may be encountered in targeted therapy [2] and collect specific energies, alpha kinetic energies and cross-fire contribution in each cell nucleus. The biophysical model NanOx (Nanodosimetry and Oxidative stress) [3] was used to calculate therapeutic indexes from the simulation such as Tumor Control Probability (TCP). We also studied the influence of the cell packing, tumor size, cell line, alpha's energy and 211At radionuclide daughter diffusion after fixation.

When regarding the specific energies, a low impact of radionuclide internalization was found, of less than 5% and 30% in cytoplasm and nucleus source distribution, respectively, compared to membrane adsorption only. The maximum was obtained for small tumors (30 µm radius) because of lower cross-fire contribution. The TCP calculations highlighted larger impact of radionuclide distribution for activity per cell below 30 mBq. For example, a factor up to 18 on TCP was obtained from membrane-to-nucleus distribution in a microtumour of 95 µm radius treated with 211At. An RBE µ of 6.9 was calculated in the membrane distribution case.

This study highlights the need for considering biological endpoints in the evaluation of intracellular radionuclide distribution impact in TAT response.

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ID76 (oral presentation)

Title
Predicting radioiodine ablation therapy outcome using machine learning

Authors
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Abstract
To date, 106 differentiated thyroid cancer patients treated with either 1.1 or 3.7 GBq of radioiodine under TSH stimulation have been recruited to the multi-centre Medirad project [1]. The main aim of this project was to establish the range of absorbed doses and associated uncertainties received by the thyroid remnant as well as normal organs. A secondary aim was to explore any association between routine biochemistry data as well as thyroid remnant radiation dosimetry and treatment success (defined as thyroglobulin < 2.0 ng ml-1 at 6-9 months post-treatment). The aim of this study is to apply machine learning techniques to predict radioiodine ablation therapy outcomes.

Out of the 106 patients, 84 achieved complete response, and 5 and 14 patients had incomplete and indeterminant response at follow-up, respectively. 3 patients were lost to follow-up. The data from the Medirad project has been curated in preparation for statistical analysis (univariate and multivariate logistical regression) and the application of machine learning methods.

Results will be presented for a variety of supervised data classification algorithms including logistical regression, k-nearest neighbours, and decision trees. The performance of each algorithm will be assessed in terms of the accuracy with which successful ablation can be predicted.

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ID78 (oral presentation)

Title

Comparing implementations of a PBPK model for PRRT with [177Lu]Lu-DOTA-TATE in SAAM II and MATLAB/SimBiology

Authors

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Abstract

Aim/Introduction

A physiologically-based pharmacokinetic (PBPK) model for peptide receptor radionuclide therapy (PRRT) with [177Lu]Lu-DOTA-TATE may enable individualisation and is therefore implemented and analysed in SAAM II (version 2.3) and Simbiology (MATLAB version 2021a). This study investigates the concordance of the results to establish the performance of the model implemented in MATLAB.

Materials And Methods

[68Ga]Ga-DOTA-TATE PET/CT and [177Lu]Lu-DOTA-TATE hybrid planar SPECT/CT biokinetic data of 12 neuroendocrine tumour patients were investigated [1,2]. A whole-body PBPK model was implemented in SAAM II and SimBiology/MATLAB, and its model parameters were fitted to the biokinetic data. Time-integrated activities (TIAs) were calculated using both software and compared for (a) identical pharmacokinetic and (b) fitted parameters. The absorbed doses (ADs) for kidney, spleen, liver and lesions were calculated.

Results

Simulations with the same parameters gave absorbed dose-difference (ΔADs) for kidneys, spleen, liver, and tumours of -14mGy (0.25%), 23mGy (0.17%), 5mGy (0.12%), and 74mGy (0.17%), respectively. The fitted parameters were equal within the 95% confidence level. The Akaike Information Criterion (AIC) of the Simbiology/MATLAB fit was lower than that of the SAAM II fit. After fitting, the maximum ΔAD in kidneys, spleen, liver, and tumours were −0.17Gy (3.4%), −0.29Gy (4.0%), −0.07Gy (1.9%), −1.84Gy (17%), respectively.

Conclusion

A model implemented in Simbiology/MATLAB is now available. Differences observed after fitting are attributed to using different minimisation algorithms. The fit achieved with the sbiofit function of MATLAB is deemed superior to the Rosenbrock fit of SAAM II, based on the AIC evaluation.

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ID80 (oral presentation)

Title

Clinical phase 0 trial of 212Pb-PSMA therapy AB001: activity concentrations of 212Pb and 212Bi in whole blood, plasma, and red blood cells

Authors

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Abstract

Introduction: A phase 0 clinical trial of alpha radiotherapeutic AB001, a prostate-specific membrane antigen (PSMA)-targeted small molecule radiolabelled with 212Pb, was conducted at Oslo University Hospital. Blood activity concentrations of 212Pb and 212Bi were investigated. Methods: Three patients with metastatic castration resistant prostate cancer were injected with 9.4±0.3 MBq AB001. Blood was drawn 0.5±0.1, 1.6±0.2, 4.6±0.3, and 18±1 hours post– injection. From each sample, 1 mL of whole blood, 1 mL of plasma, and 1 mL of red blood cells (RBC) were measured on a gamma counter. Two energy windows were used for estimation of activity concentration: 55–300 keV (efficiency factor 0.826) for 212Pb (measured for 40 minutes 12–28 hours post-collection) and 470–810 keV (efficiency factor 0.111) for 212Bi (measured for 10 minutes 0.6–1.7 hours post-collection). Time integrated activities were calculated using trapezoidal integration and a tail with physical decay.

Results: At all measured time points, activity per gram of 212Pb was 11±1 (minimum 8.9, maximum 12.6) times higher for plasma than the RBC fraction. At time of sampling, 212Bi was not in equilibrium with 212Pb. The time integrated activity coefficients per gram for the whole blood, plasma, and RBC fractions were 642±120, 1126±178, and 104±22 Bq×hours/g/MBq for 212Pb and 430±88, 747±134, and 73±22 Bq×hours/g/MBq for 212Bi, respectively.

Conclusions: The activity per gram of the plasma fraction was consistently approximately ten times higher than for the RBC fraction. This indicates in vivo stability of AB001, since free lead naturally accumulates in RBC. Further work will focus on comparisons with published pharmacokinetic models for other PSMA targeting therapies.

ID82 (oral presentation)

Title
In vitro dosimetric analysis of Alpha therapy using ^{223}Ra for prostate cancer cells

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Abstract
Objective: Accurate dosimetry is essential to comprehend the relationship between absorbed dose and its effects, involving targeted effects on irradiated cells and non-targeted bystander effects on nearby non-irradiated cells. Therefore, the primary objective of this study was to introduce a new approach for conducting in vitro dosimetric analysis in alpha therapy using 223Ra for prostate cancer cell lines. Through this approach, the study aimed to explore the presence of bystander effects and their potential contribution to the overall cell killing and the absorbed dose-effect relationship.

Methods: Dosimetric scenarios were evaluated, considering cell sizes and activity distribution patterns. Experimental results indicated minimal cellular uptake of Xofigo, focusing on activity in the medium as the primary irradiation source. Two scenarios were studied: (1) homogeneous activity distribution throughout the medium and (2) homogeneous deposition at the bottom of the well. S-values from GATE 9.0 and MIRDcell13.3 were used for estimations. In biological experiments, DU145 and C4-2 prostate cancer cells were exposed to varying XofigoTM (223RaCl2) concentrations for 90 minutes (donor cells). Bystander effect investigation involved treating DU145 and C4-2 recipient cells with conditioned medium from the donor cells.

Results: Dosimetric findings indicate that the activity deposited at the bottom of the well plays a substantial role in the total absorbed dose received by the cells, surpassing the impact of evenly distributed activity in the medium. Biological measurements demonstrated 80% cell killing at 9.25 kBq/mL induced by targeted effects, accompanied with about 30% cell killing through bystander effect in recipient cells. The real contribution of the nontargeted effect in irradiated cells, using the Bliss theory, were around 10% or less in all administered activities. The survival fraction results displayed a linear correlation with the absorbed dose for both cell lines. The bystander effect showed a dose-dependent trend in recipient cells, with no significant difference between the two cell lines.

Conclusion: This study provides valuable insights into the dosimetric analysis in alpha therapy using XofigoTM for prostate cancer cell lines. The findings highlight the importance of considering localized activity deposition and cell size when estimating absorbed doses. Additionally, a bystander effect was observed, indicating radiation-induced damage beyond the directly irradiated cells.

Keywords

Radionuclide sedimentation, alpha therapy, absorbed dose-effect, bystander effect

ID84 (oral presentation)

Title

Absorbed dose rate algorithm comparison in ^{177}Lu-based molecular radiotherapy dosimetry.

Authors

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Abstract

Introduction: Calculation of absorbed dose rate (ADR) is an important step in the Clinical Dosimetry Workflow (CDW). Local energy deposition (LED) and voxel S value (VSV) convolution are the most common algorithms used in current commercial software. Monte Carlo (MC) simulations are not as widely used due to their long calculation times but represent the ground truth for ADR calculation benchmarking.

Methods: This work compares LED and DVK convolution against MC simulation. Data was collected during 3D dosimetry of the first two cycles of a group of five patients who received Lutathera® treatment at ICM (10 clinical dosimetry studies with four time points each). ADR calculations were carried out with and without density correction. Dosimetry was performed using the open-source software OpenDose3D. For each clinical dosimetry study, ADR calculation was performed using the Monte Carlo code GATE, in homogeneous medium or based on CT-derived density maps. To ensure a more comprehensive assessment, the study incorporated 3D gamma index maps for ADR comparisons (Fig 1), going beyond mean value comparisons.

Results: Results in homogeneous soft tissue show that LED underestimates ADR due to cross-irradiation. Furthermore, these results allowed verifying convolution approach with VSV. To assess the impact of heterogeneities on energy deposition, an analysis was conducted using MC results in homogeneous and heterogeneous media. Results with density correction in soft tissue show 3%-5% of LED underestimation, whereas convolution showed a better agreement, with slight differences less than 1% (Fig 2). However, the ADR comparisons for bone marrow demonstrated higher underestimation from 6%-25%.

Keywords

Absorbed dose rate algorithms, OpenDose3D, ^{177}Lu-DOTATATE therapy.

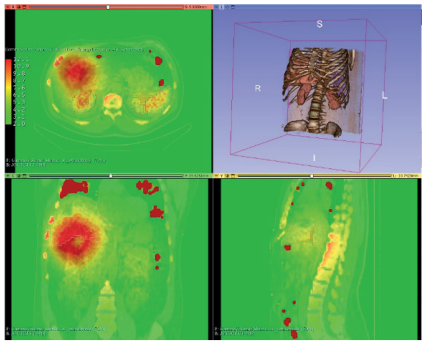

Figure 1: 3D gamma index map computed between Monte Carlo and LED ADR images. 2% of absorbed dose difference criteria and 5 mm of distance to agreement was used as criteria. Values were scaled by 100 for better representation.

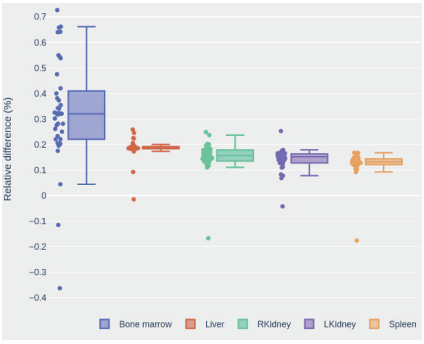

Figure 2: Comparison between VSV convolution and Monte Carlo simulation for OAR in homogeneous soft tissue. 10 clinical dosimetry studies with four time points each = 40 ADR per OAR.

ID85 (oral presentation)

Title
Clinical Dosimetry Workflow comparison with OpenDose3D in molecular radiotherapy

Authors
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Abstract
Background: The aim of this study was to compare three different Clinical Dosimetry Workflows (CDWs) within one software, OpenDose3D, to explore the impact of specific methodologies and workflow variations on absorbed dose (AD) calculations during PRRT with ^{177}Lu.

Methods: Images from 5 patients (4 SPECT/CT time-points per patient) from the first cycle of Lutathera® treatment were used. The dataset included five organs at risk (segmented automatically on the CT [Wasserthal et al. 2023]) and 14 tumours (segmented on the SPECT images, keeping each tumour volume constant between time points).
Three CDWs were compared:

- Activity CDW (ACT): Segmentation at the first time-point and rigid registration (on the whole field of view – FOV) are performed, keeping the VOI constant. Cumulated activity in VOI is calculated, then the absorbed dose is computed using the Local Energy Deposition (LED) assumption on the average mass of the VOI.
- Absorbed Dose Rate (ADR): Segmentation and registration are performed as in ACT. Absorbed dose rates are calculated first at the voxel level using LED, averaged on the VOI and integrated to provide the absorbed dose.
- Automatic (AUTO): no registration is performed, and segmentation is done at each time point. The rest of the CDW is identical to ADR.

ACT is the most conventional approach, ADR is seen in some clinical dosimetry workstations, and AUTO is an attempt to simplify the CDW and decrease operator dependent sources of variation.

Results: Box plots were used to visualize the spread of absorbed dose values across patients and CDW. Initial results showed good agreement between ADR and ACT for OAR and tumours (between -4% and 4%) (Figure 1). ACT consistently reported lower AD, possibly due to slightly different ways of computing AD.

ADR and AUTO presented significant differences in AD values (Figure 2). ADR consistently reported lower ADs, attributed to registration and VOI propagation issues. Aligning small tumours in the ADR CDW proved very challenging.

Conclusion: Results highlighted the impact of registration and VOI propagation on the resulting absorbed doses. They suggest performing registration on each VOI rather than on the whole FOV. However, not knowing the ground truth limits the value of these comparative studies.

Keywords
Clinical dosimetry workflow, OpenDose3D, 177Lu-DOTATATE therapy.

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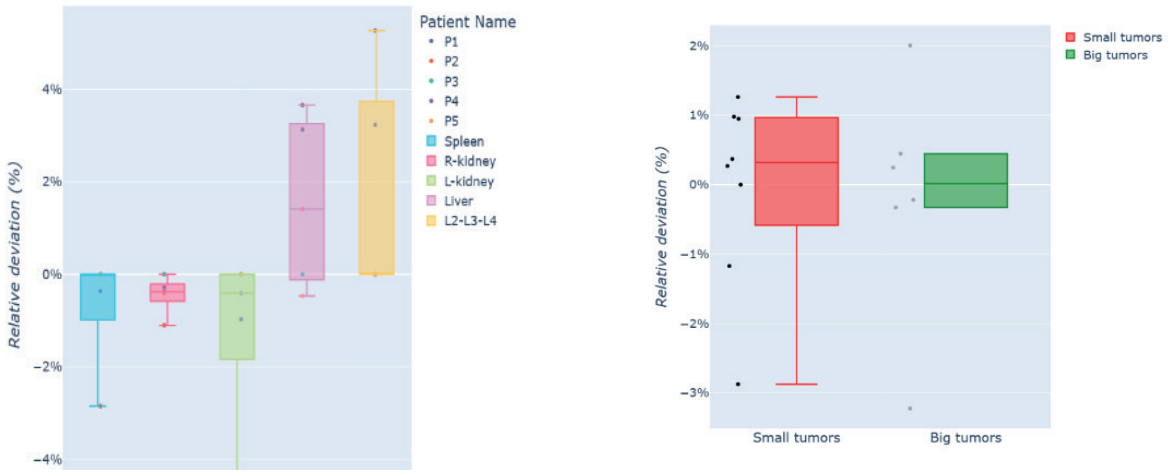

Figure 1: Relative deviation between ACT and ADR for OAR (a) and tumours (b)

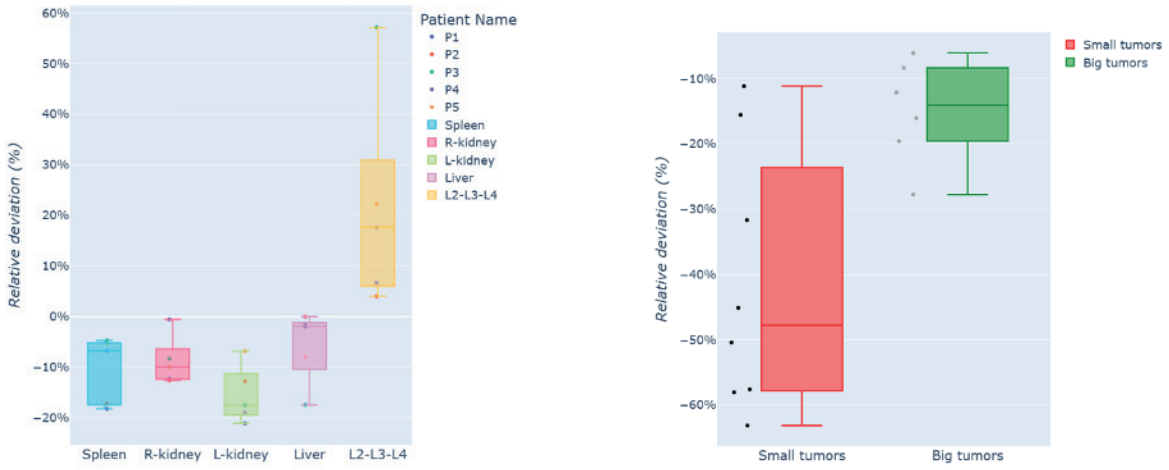

Figure 2: Relative deviation between ADR and AUTO for OAR (a) and tumours (b)

ID86 (oral presentation)

Title

OpenDose3D, an open-source software for advancing clinical molecular radiotherapy dosimetry

Authors

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Abstract

Introduction: The increasing adoption of molecular radiotherapy (MRT) calls for robust and accurate tools to perform clinical dosimetry. Several software solutions have emerged, including commercial FDA-cleared or CE-marked, and in-house academic software. In this context, we present OpenDose3D (V1), a freely available and open-source software intended for both clinical dosimetry research purposes and benchmarking of clinical dosimetry software.

Methods: OD3D is a module within the 3D Slicer software (Fedorov et al. 2012), accessible through the radiotherapy extensions section. Being a part of 3D Slicer, OD3D benefits from advanced tools for 3D image manipulation and segmentation.

Essential steps of the clinical dosimetry workflow (CWD) are included in OD3D.

- A specific SPECT sensitivity calibration and recovery coefficient module was created (Fig 1).
- Two different Clinical Dosimetry Workflows (CDWs) are available in the software, depending on how time-dependent variable are dealt with: (1) activity, cumulated activity and absorbed dose or (2) activity – absorbed dose rates and absorbed dose.
- In addition, an attempt to automatize most steps is currently tested.

Sanity checks verify that patient images and calibrations were acquired and reconstructed using the same protocol. Registration can be carried out in Rigid or Elastic mode. Organs at risk contouring is performed manually or automatically (Wasserthal et al. 2023). Absorbed dose rate images are calculated assuming Local Energy Deposition or by convolution of Voxel S Values. Additionally, Monte Carlo (GATE) macros can be automatic created, and results can be imported after the simulation. Different models of time activity/ADR curve fitting are available, and automatic selection of the best-fit is also an option.

Results: OD3D proposes a wide range of features, including automatic segmentation, absorbed dose calculation for an extensive list of radioisotopes (Fig 2), and Monte Carlo simulations. The software offers different CDW and attempts to decrease operator dependent sources of variation. Furthermore, unlike traditional "black box" solutions, OD3D generates intermediate results, which improve traceability and represent a valuable tool for benchmarking.

Conclusion: OD3D contributes to the advancement of personalized MRT and facilitates the standardization and improvement of clinical dosimetry practice.

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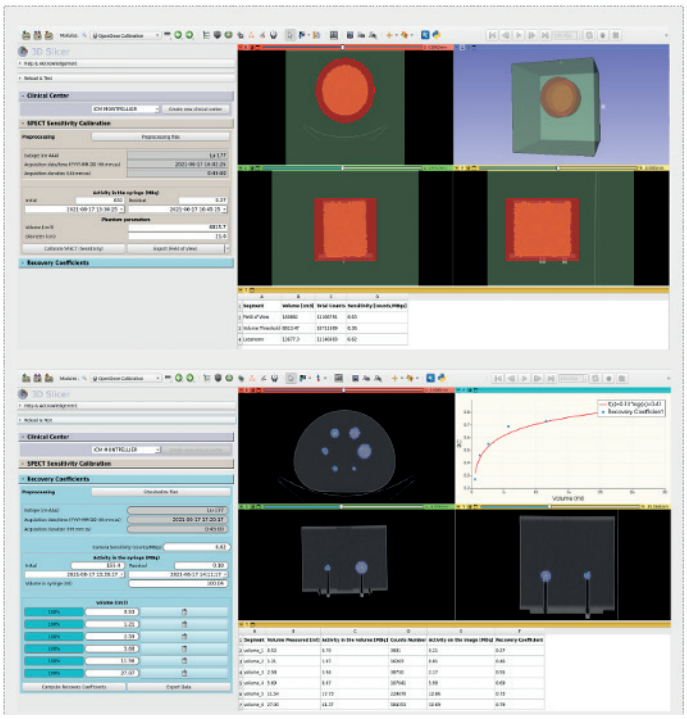

Fig 1: OD3D Calibration module includes SPECT sensitivity calibration and recovery coefficients determination.

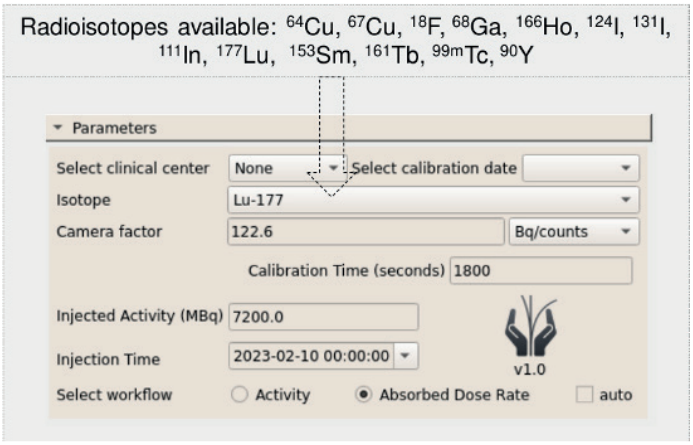

Fig 2: OD3D parameters selection. List of radioisotopes available.

ID88 (oral presentation)

Title

Deep learning-assisted prediction of ^{90}Y SIRT post-therapy dose distribution from pretreatment ^{99}mTc-MAA dose maps

Authors

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Abstract

Background: Radioembolization, known as SIRT with 90Y microspheres, is a well-established treatment modality for unresectable liver cancer (1, 2). Treatment planning and simulation of 90Y microspheres therapy is implemented by injecting 99mTc-MAA as a theranostic pair. A number of studies have shown discrepancies between the simulation and post-therapy dose distributions (3, 4, 5, 6). The aim of this study was to use deep learning (DL) for accurate prediction of post-therapy 90Y dose distribution from pre-treatment 99mTc-MAA dose maps.

Material and methods: Clinical data of 134 patients who underwent 99mTc-MAA simulation and treated with 90Y glass microspheres were included in this study. The tumors (T) and whole liver (WL) were delineated by an experienced nuclear medicine physician and a previously developed automated segmentation model in our lab, respectively. Afterwards, the whole normal liver (WNL) was derived by subtracting T from WL. CT of 99mTcMAA and 90Y were co-registered. Dose maps were calculated from SPECT images using local energy deposition method for both 90Y and 99mTc-MAA. The dose maps were cropped to a bounding box with a size of 80 × 80 × 64 voxels covering the WL. The dataset was randomly split into 70 % train and 30 % test. A modified UNETR architecture (7) implemented in MONAI platform was trained by feeding 99mTc-MAA dose maps as input and 90Y dose maps as reference for 200 epochs and learning rate of 1e-4. Quantitative metrics including SSIM (%),ME (Gy), MAE (Gy), RE (%), RAE (%) and pass rates (%) from gamma evaluation (DTA of 4.79 mm and DD of 1%) were calculated between 99mTc-MAA and DL results with regard to 90Y.

Results: The voxel-wise quantitative metrics summarized in Table 1 demonstrates a significant improvement when using the DL approach. Our model significantly improved accuracy as the voxel-wise RE decreased from 259% to 30%. The metrics calculated for organ-level dosimetry are provided in Table 2. The RE of WNL and lesion decreased from 104.23% to 9.28% and from 112.54 % to 11.13%, respectively.

Conclusion: 99mTc-MAA simulation dose images are different from Y90-SIRT treatment. This discrepancy may result in over/under estimation of the mean doses and dose distributions, thus leading to over/under treatment of patients. This problem was tackled through deep learning, which achieved significant improvement in both voxelwise and organ-wise metrics.

Keywords

Radioembolization, SIRT, Deep learning, Voxel dose maps.

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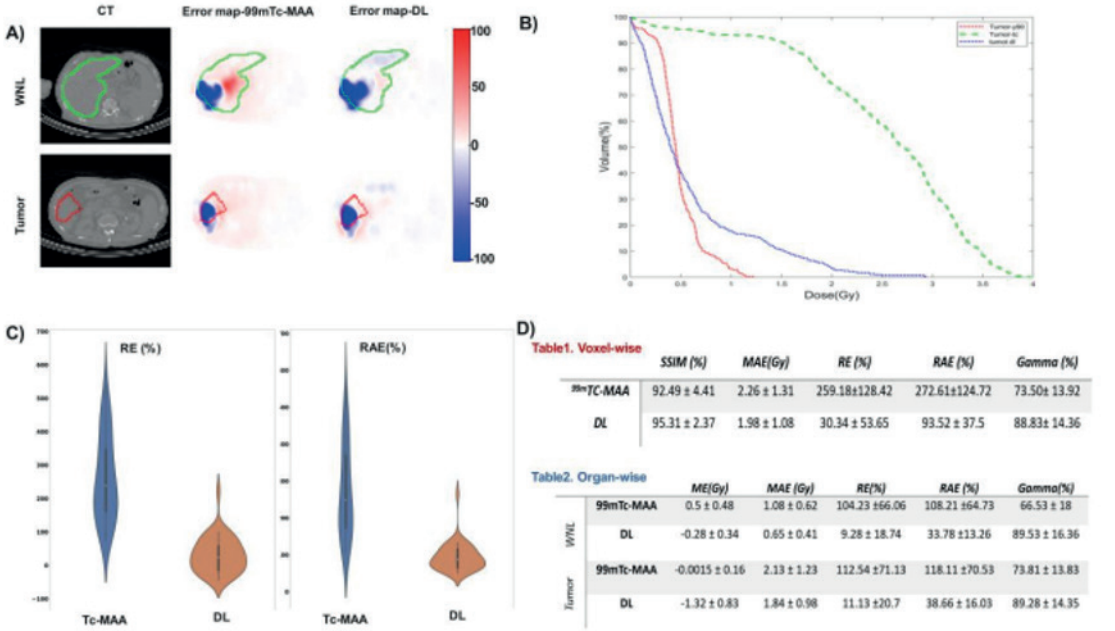

Figure. A) the error maps for 99mTc-MAA and DL result in WNL and Tumor segmentations, B) DVH demonstrates a significant improvement in Tumor dose values when using our DL model C) Violon plots of relative errors (RE(%)) and relative absolute errors (RAE(%)) D) summerized quantitative metrics for voxel-wise evaluation (Table1) and organ-wise evaluations (Table2).

Abbreviations:

- SSIM: structral similarity index
- ME: mean error
- RE : relative error
- RAE: relative absolute error
- DTA: distance to agreement
- DD: dose difference
- MAE: mean absolute error

ID89 (oral presentation)

Title
Evidence of dose response relationships in Y90-DOTATATE therapy

Authors
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Abstract

Aims: The aim of this work is to examine correlations in the absorbed doses delivered to lesions and normal organs following 90Y Radiopeptide therapy and determine potential applications for treatment optimisation.

Methods: Patients underwent 90Y DOTATATE therapy in combination with 111In DOTATATE for imaging. 90Y administered activities ranged from 1811 to 4888 MBq with 111In given at a ratio of 1:25 of the therapeutic activity. Dosimetry results have been analysed for 69 patients treated with multiple cycles, n = 3.2±1.7, (mean±SD). Sequential 111In SPECT acquisitions were performed at 24 h, 48 h and 75 h post administration. Data were acquired on a Siemens Symbia Intevo SPECT/CT system for 72 projections in a 256 matrix for 40 to 60s per view, OSEM reconstruction with 3D detector modelling applying TEW scatter and CT attenuation corrections. Volumes of interest were delineated using the CT data (when available) or manual thresholding on SPECT. Mean counts in each VOI were converted to activity using a pre-acquired calibration dataset. The cumulated activity was determined by taking the integral of a single exponential function fitted to the time activity data, extrapolated from administration to infinity. An S-factor for each VOI was calculated based on the published RADAR S-factors scaled to account for the mass difference between the model and patient anatomy. Lesion S-factors were determined by interpolating between spherical models to match the measured mass. Absorbed doses were calculated according to the MIRD schema (Loevinger & Berman 1968). Trends in population data were analysed using the Graph Pad Prism software to determine population averages in lesion and normal organ absorbed doses. Correlations between dosimetric parameters were measured and trends examined at different treatment cycles. Dose response data was analysed for all patients who received baseline and follow-up DOTATATE imaging (68Ga or 111In). Patients were categorised into either “good/partial response” or “stable/progressive disease” based on the post therapeutic follow-up report.

Results: No correlation between absorbed dose and administered activity was observed for lesions or normal organs. A significant decrease in the lesion absorbed dose with increasing treatment number was observed (Two-tailed Spearman correlation coefficient, r = -0.97, P=0.0002) whilst an increase in kidney absorbed dose was evident (r = 0.98, P=0.015) . A Mann-Whitney non-parametric un-paired T-test indicated significantly different lesions absorbed doses between patients categorised as “good/partial response” and “stable/progressive disease” (P = 0.0003).

Conclusions: Initial results indicate strong evidence of a dose response relationship. Changes in absorbed doses to normal organs and lesions with treatment cycles indicate a need for patient specific treatment optimisation.

ID89 (oral presentation)

Title
131I-mIBG 3D Voxel dosimetry in a patient with a high whole-body dose

Authors
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Abstract

Introduction: In the following we report a unique dosimetry 131I-mIBG case with whole body and tumour dosimetry of a single patient recruited onto the Veritas trial. VERITAS is a European multicentre phase II randomised trial for metastatic neuroblastoma patients. The 131I-mIBG arm includes a 444 MBq/kg administration with in vivo whole-body dosimetry and 0.7 mg/m2 of Topotecan daily until a second course of 131I-mIBG at day 15. The activity of 131I for the second course is based on the dosimetry of the first to deliver a combined whole-body absorbed dose of 4 Gy.

Method: The 9 year old female patient presented with a left supra renal neuroblastoma primary tumour and widespread metastatasis to the bone marrow and bones. For the first cycle, 12 GBq of 131I were administered uneventfully followed by serial whole-body counting using a ceiling mounted, collimated, Geiger counter. Count rate from the detector is converted to activity using the initial baseline measurement. Time integrated activity was calculated by integrating the chosen curve with the fitted parameters. S-values were calculated using a patient weight adjusted model based on the ORNL phantoms. SPECT data were acquired at 4,6,8,11 and 13 days post administration over the abdomen and thorax. A single low dose CT performed was used for attenuation correction at all imaging points. Images were reconstructed using an OSEM algorithm with attenuation, scatter correction and detector response modelling. Dosimetry was performed using locally developed dosimetry software, written as a 3D Slicer application and employing the EGSnrc Monte Carlo code. Images were converted to activity concentration maps and registered using a non-rigid registration algorithm. Exponential time activity curves were fitted and used to calculate voxel-based time integrated activities with associated uncertainty maps. Anatomical segments were generated using a semi-automated technique defining diseased bone, liver kidneys, spleen and primary tumour. Doses were calculated using both a convolution kernel and fully 3D Monte Carlo simulations.

Results: A whole-body dose of 5.6 Gy was calculated from the single cycle and therefore no further 131I-mIBG was administered. A maximum of 110 Gy (median 20 Gy) was estimated to be delivered to the diseased marrow and 46 Gy (median 23 Gy) to the primary lesion. Median organ doses were 4.3, 3.9 and 2.9 Gy for the liver, kidneys and spleen respectfully. The patient demonstrated mild thrombopenia and neutropenia but was otherwise symptom free. Stem cells were subsequently reinfused uneventfully on day 22 at an estimated retained activity of 130 MBq. Six months following treatment the patent showed stable disease with mildly reduced mIBG uptake on 123I imaging.

e-POSTERS

ID7 (e-poster)

Title
Extravasation of Lutetium-177-DOTATATE dosimetric evaluation and management

Authors
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Abstract

Introduction: The number of treatments in Molecular Radiotherapy (MR) is increasing with the extension of the indications for lutetium-DOTATATE , the arrival of lutetium PSMA , and the reimbursement for Radium223. This innovative treatment will also lead to an increase in the number of extravasations. A case of extravasation with lutetium-DOTATATE, dosimetric evaluation and management are described in the following study.

Material and methods: A patient was injected with 7.12 GBq lutetium-177-DOTATATE in a 23.1 ml solution. Extravasation was detected in the left arm on post-therapy whole-body scintigraphy 6.5 hours after injection. A quantitative SPECT/CT scan (xSPECT Quant, Siemens®) was therefore performed afterwards. Finally, 48h after injection, only a static image on the arm was performed (due to a technical failure). The transition factor between static, whole body and tomographic sensitivities were determined in collaboration with IRSN and Cochin Hospital. Different thresholds were used for the segmentation in order to evaluate the activity and the volume of interest. The influence of the dead time was estimated. In collaboration with the IRSN, the dosimetric evaluation of the patient was performed. The segmentation and activity measurements were carried out with esoft (Siemens), PlanetDose and 3DSlicer. Other calculation method Geant4, mird were compared.

Results: For a source of 35 mL and 100 MBq, in SPECT/CT, a thresholding at 20% of the maximum recover an activity with 15% uncertainty. A threshold of 55% allows the volume to be recovered to within 20%. In the range of activity measured, there is no significant influence of dead time. The effective half-life of the drug is estimated at 8.45 h, consistent with a recently published case (1). The activity in the extravased zone is estimated to be 310 MBq or 4% of the total injected activity. Considering a homogeneous dose distribution, the average absorbed dose distribution is 17 Gy in 19ml. SPECT/CT shows a heterogeneous distribution as an arc shape in the adipose tissue of the arm. The extravasated volume was therefore divided into two for dosimetric evaluation. One of 8 cm3 containing 79% of the activity and the other of 11 cm^3 containing 21% of the activity. A dose of 32 Gy is then achieved in the small volume. Other calculations method gave similar result.

Conclusions: The estimated dose received in the arm in a small volume is higher than the dose limit of 25 Gy (2), the threshold for the appearance of radiation-induced necrosis. A monthly follow-up of the patient is implemented over a period of 6 months and has not revealed any clinical skin signs to date. These results raise many questions about the management of extravasations during MR procedures, the influence of fixation heterogeneity, variable volume of distribution and tissue type on the expected adverse effects. Procedures have been implemented in case of extravasation.

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ID12 (e-poster)

Title
SPECT/CT system calibration for ^{131}I dosimetry — Robust routines and pitfalls

Authors
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Abstract
Introduction: Calibration is crucial in SPECT/CT dosimetry. Specific challenges are posed for ^{131}I, where high count rates require corrections for dead time and pulse pileup. The aims of this work are to enlighten some pitfalls and present routines that may offer robust ^{131}I SPECT/CT calibration.

Materials and methods: Series of ^{131}I phantom measurements have been performed on two GE Discovery 670 Pro SPECT/CT systems. Each series covered a two-month period, when only physical decay governed the ^{131}I source strength. Data collection and reconstruction were executed using clinical protocols for ^{131}I dosimetry, including attenuation and scatter corrections.

Projection data from a homogeneous Jaszczak phantom were analysed to establish dependences between total average spectrum count rate and ^{131}I peak losses from dead time and pulse-pileup. Established loss corrections were then applied on all reconstructed image stacks, whereby the systems' SPECT/CT sensitivity [cps/MBq] was analysed.

Results: Robust calibration was obtained for the homogeneous Jaszczak phantom at a ^{131}I content in the range 250 1500 MBq, see figure 1. At lower activities, deviations were introduced in the reconstruction procedure, whereas higher activities exceeded a selected loss-correction limit of 2.

The loss-correction scheme proved applicable also for a Jaszczak phantom with a 6-cm spherical insert with ^{131}I, see figure 2. This geometry may be useful for regular calibration control.

Conclusions and discussion:
Long-term phantom measurements may constitute robust routines for establishing a correction scheme for dead time and pulse pileup, while providing data for ^{131}I SPECT/CT calibration. Furthermore, several pitfalls have been identified.

ID19 (e-poster)

Title
Septal penetrations correction for ^{225}Ac quantitative images

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Abstract
Background/Purpose: To establish a dosimetry protocol for ^{225}Ac targeted alpha-particle therapy, one need to rely on quantitative images of the activity distribution in the patient. ^{225}Ac not being a gamma emmiter, two of its daughters are used: ^{221}Fr and ^{213}Bi [1]. However, the presence of high energy of ^{213}Bi's gammas (440 keV) entails for a septal penetration correction method in SPECT imaging, high energy collimators not being effective enough to reduce the apparition of artefacts at that energy.

Methods: We used a Richardson-Lucy iterative deconvolution filter (RL) to relocate septal gammas where they should have been detected in the image [2,3]. Gate (v9.2) was used to simulate septal kernels and planar images with simple shape sources in different geometric configurations and media. After assessing its efficiency with these simulated planar images, we used the RL filter SPECT projections with a 20 MBq ^{225}Ac source acquired with DISCOVERY NM/CT670 equipped with HEGP collimators.

Results: Using RL filter, we managed to highly reduce septal penetration artefacts. Indeed, septal gamma proportion in acquired images decreased from 75.7% to 8.4% after applying RL filter (50 iterations), while maintaining the same total count per projection. It's worth noting some low statistic artefacts and the loss of Poisson noise in the projections.

Discussion/Conclusions: It seems that the loss of the Poisson noise in the projections doesn't impair the visual quality of the reconstruction. The impact of attenuation correction still needs to be evaluated in order to properly quantify the reconstructed images.

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ID25 (e-poster)

Title

Use of whole-body retention data for personalized lesion dosimetry: evaluation for iodine-131 treatments from the MERAIODE clinical trial

Authors

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Abstract

Purpose: To estimate lesion absorbed dose using external whole-body retention measurements when a series of post-treatment fixation images is not available.

Methods: Patients from MERAIODE1 study were treated for metastatic thyroid cancer with 5.5 GBq of I-131 after receiving a redifferentiation therapy. Radioiodine biokinetics in lesions was assessed using 4 post-treatment planar images scaled in activity using a SPECT/CT acquired on day 4. The cumulated activity was computed by fitting a monoexponential time-activity curve (TAC). On another hand, the effective whole-body half-life assessed from external measurements, associated to SPECT-quantified activity, also enabled determination of a monoexponential TAC for each lesion. Absorbed dose was estimated by Monte Carlo simulation in a realistic model of the patient.

Results: Absorbed doses obtained for 7 patients and 25 lesions ranged from 16 Gy to 2900 Gy (median: 270 Gy) using planar images. Relative differences in results using external measurements remained acceptable for 16 lesions (-13% to +42%) and even smaller for 11 of them (-13% to +17%). However, discrepancies were substantial (+99% to +991%) for the 9 remaining lesions developed by the 4 patients whose whole-body half-lives were <20h.

Conclusion: This comparison indicates that external measurements associated with SPECT could be, for some patients, a surrogate of serial images for a personalized absorbed dose calculation to lesions. However, these measurements cannot characterize every lesion-specific biokinetics and can lead to inconsistent results when whole-body half-lives are short, which might be a relevant indicator to determine whether a sufficiently reliable dosimetry can be performed this way.

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ID26 (e-poster)

Title

Number of projections, total projection time, and reconstruction settings for quantitative 177 Lu SPECT: Systematic and random errors

Authors

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Abstract

Background/Purpose: The aim was to study systematic and random errors of SPECT-based activity- concentration estimation of 177 Lu for different acquisition times, number of projections, and reconstruction settings using Pareto optimization.

Methods: Six spheres (0.5mL-26.9mL) in a NEMA phantom were filled with 177 Lu (5.8MBq/mL). 120 projections á 180s were acquired, using a medium-energy collimator and 15% energy window (208keV). List- mode was used for creating datasets with total acquisition times of 600s-2400s and 20-120 projections with 32 noise-realisations, using bootstrapping. Reconstruction was performed using OS-EM with compensation for attenuation, scatter [1], and distance-dependent resolution. Even-integer number of subsets were considered, and number of iterations set such that number-of-projections×number-of-iterations≤2400. In total, 1900 combinations of number of projections and reconstruction settings were evaluated for three total acquisition times. Volumes-of-interest following the spheres were defined. The activity-concentration mean and standard deviation were calculated over bootstrap-realizations, and Pareto fronts established with respect to coefficient of variation (CV) and mean error. The procedure was reproduced for a Monte Carlo simulated anthropomorphic phantom with three tumours (2.8mL-40mL), mimicking the activity distribution for patients undergoing 177 Lu-DOTA-TATE therapy [2].

Results: Pareto-optimal points with a low CV had a low number of subsets, while Pareto optimal points with a low bias had a high number of subsets. The number of projection angles had little explanatory power. Discussion/conclusion: The parameters of main interest for quantitative SPECT are the total acquisition time (rather than how that time is distributed over projections) and reconstruction settings (number of subsets and iterations).

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ID27 (e-poster)

Title
The wearable individual dose monitoring apparatus: a new approach to the internal radiation dosimetry

Authors
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Abstract
In Molecular Radiotherapy, a personalized internal radiation dosimetry (IRD) increases local tumour control and lowers overall toxicity. IRD is performed using standardised numerical computations or, at best, is based on a time sequence of 4-6 SPECT imaging scans.

A new approach for a more precise radioagent biokinetics determination has been proposed with the Wearable Individual Dose Monitoring Apparatus (WIDMApp) [Morganti et al, Med Phys 2021]. The WIDMApp project aims to develop an apparatus for the continuous mapping of activity transit and accumulation in organs and precise assessment of the organ-level absorbed doses.

The WIDMApp system is designed as i) a wearable, non-invasive multi-sensor device for in-vivo radiation detection; ii) a Monte Carlo simulation using a SPECT-CT scan of the patient as input to model the real structures, simulate the particle path in the body and calculate the radiation detection of each sensor; iii) a processing algorithm using detected signals and simulation data to reconstruct the actual biokinetics in target and organs.

A proof-of-principle of the WIDMApp approach was realized with a detector sensor prototype and IEC/NEMA body phantom with three spheres filled with different radionuclides (54 MBq of 18F, 53 MBq of 99mTc and 28 MBq of 64Cu) to mimic volumes with different wash-out.

WIDMApp was effective in identifying the three emitting volumes and the decay constants with uncertainties in the range 3%-8%.

Reconstruction of the individual biokinetics using small, portable, and simple detectors is in principle possible. The high rate of data sampling would increase the level of accuracy in internal dose estimation. Optimized sensors and multi-channel acquisition electronics are under development to enable tests on patients.

ID30 (e-poster)

Title

Quantification accuracy evaluation of Yttrium-90 PET for post-therapeutic voxelised dosimetry on three generations PET/CT scanners

Authors

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Abstract

Although accurate quantification of 90Y distribution is challenging regardless of the imaging modality, multiple studies have shown that PET/CT imaging of low incidence positrons emitted by 90Y (0.003% branching) outperforms Bremsstrahlung SPECT/CT. We evaluate the quantification accuracy of post-therapeutic dosimetry calculation using voxelised local energy deposition models (LDM) of 90Y for three generation PET/CT systems: analogue, digital and long axial field of view (LAFOV).

Materials and Methods: One uniform (6.2 L) and one NEMA-IQ phantoms was filled with 0.24 and 0.22/2.92 MBq/ml of 90YCl3, respectively. They were scanned for 30 minutes, reconstructed with 15 and 30 minutes frames (EARL2 protocol), and postfiltered with an all-pass, 7- or 9-mm Gaussian filter. Quantitative accuracy was assessed by means of Coefficient of Variation (COV) in the uniform and mean Recovery Coefficient (RC-mean) in the NEMA-IQ phantom. Theoretical LDM dosimetry within NEMA-IQ spheres was compared to CE-marked software calculations, with and without partial volume effect (PVE) correction.

Results: In the uniform phantom, COV, activity concentration and total activity accuracies were [127%/9,7%/12%; 36%/1.7%/11%; 28%/6,8%/-6%] (analogue), [58%/-3%/11.1%; 20%/-2.5%/11.2%; 13%/-0.1%/3.5%] (digital) and [76%/-0.3%/-0.3%; 24%/-2.0%/3.0%; 17%/-0.2%/3.2%] (digital-LAFOV), for all-pass, 7 and 9 mm filtered reconstruction, respectively. Absorbed dose error varied from 13%-75% for all scanners, without differences in the mean, yet significant uncertainty variations between the scanners. For the 22mm sphere, dosimetry error decreased from 27% to 13% after PVE correction.

Conclusion: Despite variations in noise levels for 90Y scans between tested PET/CT scanners, the average activity concentration remained comparable. Accurate quantification of 90Y PET/CT dosimetry with clinically relevant tumour size range requires PVE-correction.

ID32 (e-poster)

Title

Comparison of 99mTc-MAA SPECT-CT and 90Y resin -microsphere PET-CT dosimetry for selective internal radiation therapy (SIRT) for hepatic tumours

Authors

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Abstract

Purpose: This study compared predictive and post-treatment dosimetry calculated at voxel level, based on 99mTc-MAA SPECT-CT and 90Y- resin microsphere PET-CT.

Materials And Methods: In this analysis, we compared 99mTc-MAA SPECT-CT with 90Y PET-CT dosimetry for 21 treatment sessions (17 HCC and 4 mCRC). Predictive and post-treatment dose calculations were performed using MIM 7.2 (MIM Software Inc.). The mean doses in tumour (DmT) and normal liver (DmNL) were determined and compared on the 99mTc-MAA SPECT-CT and the 90Y PET-CT. Bland-Altman analysis was used to evaluate the agreement between the mean absorbed doses in T and NL, in predictive and post-treatment dosimetry.

Results: The DmT were 242 ± 100 Gy and 249 ± 94 Gy for 99mTc-MAA SPECT-CT and 90Y PET-CT respectively and DmNL were 24±16 and 25±12 Gy. The correlation between predicted and post-treatment DmT and DmNL was strong (r = 0.936 and r = 0.921, respectively). Bland-Altman analysis gave a mean difference of −7.3 Gy with −76.7 Gy and 61.9 Gy (95%CI) for DmT; and -1.3 Gy with −13.9 Gy and 11.3 Gy for DmNL.

Conclusions: Comparison between 99mTc-MAA SPECT and 90Y-microsphere PET, in terms of dose distribution, showed a good correlation and Bland-Altman analysis indicates lower variations for NL than for T (1.96 SD equal to 11.3 Gy and 61.9 Gy respectively) allowing to predict the irradiation of the involved liver regions and to estimate the maximal 90Y activity to be administered in order to give not exceed 40 Gy to the NL and, if possible, deliver more than 120 Gy to the tumour.

ID33 (e-poster)

Title

Trustworthy Artificial Intelligence in hybrid imaging Theranostics: the emerging role of medical physicists in AI ethics' auditing

Authors

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Abstract

Introduction: The approach of Theranostics continuously proves its significant impact on the gradually increasing number of RadioPharmaceutical Therapies (RPTs) worldwide. Artificial Intelligence (AI) appears to be a game changer in facilitating all tasks of the Theranostics workflow and, therefore, the personalization of RPTs. However, the acquisition of adequate knowledge, skills and competences in the fields of biomedical sciences and technology by the medical physicists actively engaged in the Theranostics' process does not suffice. It is essential to be complemented by adequate education and training in the related cornerstone ethical principles and key requirements for trustworthy AI Theranostics' systems. The current study focuses on highlighting the emerging role of medical physicists in this novel AI ecosystem, to effectively address not only the scientific but also the ethical considerations associated with its use.

Materials and Methods: Contemporary scientific publications on the role of AI Theranostics' systems and the underlying ethical principles were selected. Special emphasis was put on European Commission ethics' guidelines, Council of Europe relevant reports and joint European and North American bodies published documents, highlighting the enhanced role of medical physicists actively involved in the process.

Results: Our study revealed that initial certification of AI Theranostics' systems, although essential, can never replace responsibility. It is, therefore, imperative that certification is complemented by accountability frameworks throughout the AI Theranostics' system entire life cycle. Such frameworks, which are based on both internal and external auditing procedures, should not only focus on the assurance of scientific efficacy and technical robustness. They should also assure that the use of AI Theranostics' systems adheres to the four core ethical principles, rooted in fundamental rights: respect for human autonomy, prevention of harm, fairness and explicability. Respect of the core ethical principles should be continuously monitored, by filling in trustworthy AI Theranostics' assessment reports. Health professionals that will bear the specific auditing burden and resulting enhanced role should be literate in the fields of both AI and ethics.

Conclusion: Traditionally, medical physicists are considered to be actively involved in quality assurance programs of imaging/therapy systems, as well as the corresponding procedures. However, the role of medical physicists in the AI Theranostics' era is expected to be further enhanced. Medical physicists will be expected to produce AI Theranostics' systems required specifications' documents, fully respecting the core ethical principles, which they should consequently understand in depth. In addition, filling in trustworthy AI Theranostics' assessment reports requires interdisciplinary knowledge, in order to comprehend and put forward ethical challenges effectively. Therefore, in case that medical physicists aim to take over full AI Theranostics' auditing role, they should be able to stand up to the challenge of proving prior adequate training in the fields of both AI and ethics.

ID41 (e-poster)

Title
Accuracy of thyroid uptake calibration method: a multi-centric study with realistic phantoms.

Authors
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Abstract
Aim/Introduction: The assessment of the thyroid uptake is required for the diagnostic and treatment of benign thyroid disease. Performed directly in air or in standard neck phantoms, calibrations of these measurements do not consider thyroid anatomy. The aim of this French multi-centric study is to assess the accuracy of thyroid uptake measurement using a set of realistic thyroid phantoms with varying size, and for two radionuclides (Tc-99m and I-123). Measurements were carried out according to the site-specific procedure (Local) and to a standardized protocol (Std). The objective of the task group is to characterize the parameters influencing the results and to give recommendations to move towards standardization of quantification methods.

Material and methods: Measurements were carried out from October 2020 to Mars 2022 on twenty-six NaI gamma-cameras and three CZT cameras with parallel and pinhole collimators. Five thyroid phantoms with volume between 3 and 30 mL, a syringe and local phantoms were used. The 700 generated acquisitions were centrally analyzed. A 3DSlicer module has been developed to perform automatic segmentation and calculation of the sensitivity.

Results: Fifty configurations (a gamma-camera, a radionuclide and a collimator) from twenty clinical centers were analyzed. Four configurations were excluded due to incomplete data. Images of the five thyroid phantoms and syringe in std conditions were processed by height thresholds (between 5% and 40%) and an optimal threshold of 10% was defined to eliminate scattered radiation and volume effect. The geometry of the phantom and its filled volume has an impact on the sensitivity results. For pinhole collimator the sensitivity decreased when the thyroid volume increased, whatever the radionuclide and protocol. Filling the phantom may result in radioactive inhomogeneity or incomplete volume, which is considered in the analysis. The sensitivity in air, obtained with the simple syringe (Sair) and for the threshold of 10% can be compared for the different geometries. For pinhole Tc-99m (n=11 configurations), the mean sensitivities Sair are 103 ±41 counts/MBq/s (Std) and 105 ±86 counts/MBq/s (Local). The difference being mainly due to different measurement distances of the protocols. For parallel collimators, differences are smaller, independent of protocol, radionuclide and parallel collimator model. For I-123 measurements with parallel collimators (n=14 configurations), the mean sensitivities Sair are 70 ±11 counts/MBq/s (Std) and 68 ±11 counts/MBq/s (Local). Finally, the analysis compares the thyroid uptakes obtained in standardized conditions with those obtained by the centers according to their local method.

Conclusion: With parallel collimators, sensitivity is relatively independent of the thyroid volume. For pinhole collimators the calibration is strongly influenced by the volume and quantitative measurement is of limited accuracy. The study should show if a simple syringe can be considered as a surrogate for thyroid phantoms and to suggest recommendations to improve the accuracy of the calculation of the thyroid uptake.

ID43 (e-poster)

Title

The relevance of Internal Bremsstrahlung in evaluating Dose Point Kernels and Voxel S-Values for ^{90}Y and ^{32}P

Authors

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Abstract

Background/Purpose: In nuclear medicine, Dose Point Kernels (DPKs) and Voxel S-Values (VSVs), representing the energy deposited all around an isotropic source, are extensively used for internal dosimetry and are usually obtained by Monte Carlo (MC) simulations. For beta-decaying nuclides, they are estimated neglecting Internal Bremsstrahlung (IB), during which photons having a continuous spectral distribution are emitted simultaneously to the beta-decay by the parent nucleus. The role of IB emission in DPKs [1,2] and VSVs [3] estimation in the case of ^{32}P and ^{90}Y is investigated; DPKs and VSVs updated values are reported.

Methods: DPKs for ^{32}P and ^{90}Y were estimated via GEANT4-based Monte Carlo simulations using the respective standard beta decay spectra. Subsequently, an additional source term accounting for IB photons and their spectral distribution was defined and simulated, highlighting the discrepancies between the two approaches. A similar procedure was followed to evaluate ^{90}Y VSVs of different voxel sizes, leading also to an analytical model incuding IB contribution and extending the calculation to any voxel size of practical interest.

Results: For distances within the maximum range of beta particles, IB does not significantly contribute to DPK and VSVs; conversely, for larger distances, values are higher by 30–40% for ^{32}P and by 20-34% for ^{90}Y, with respect to the estimations neglecting IB.

Discussion/Conclusions: The presented DPKs and VSVs include for the first time the contribution due to IB, providing a more accurate set of dosimetric factors for three-dimensional internal dosimetry of ^{32}P- and ^{90}Y-labelled radiopharmaceuticals and medical devices. Furthermore, the analytical model constitutes an easy and fast approach for 90Y-VSVs estimation for non-standard voxel dimensions.

ID44 (e-poster)

Title
Single centre study of the quantification accuracy of 99mTc-MAA for the pre-treatment of 90Y liver embolization

Authors
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Abstract
Background and objective: EANM guidelines to optimize MAA-^{99}mTc SPECT/CT protocol for pre-treatment Y90 dosimetry were followed to obtain the higher recovery coefficient (RC), while keeping noise (in terms of coefficient of variation) to an acceptable level.

Subsequently, we analyzed how total activity, activity concentration ratio and spatial position, acquisition duration and reconstruction parameters affect SPECT/CT quantification variability of whole VOI metrics, either using self image calibration and global SPECT calibration.

Materials and methods: First, a homogeneous phantom was acquired for SPECT/CT sensitivity calibration. Then, we acquired the IEC body phantom filled with hot spheres (Ac from 1.8 to 0.2 MBq/ml) in 2 positions, with different background-to-sphere concentration ratio (Acratio from cold to 3:1) on a GE NM/CT 850 SPECT/CT. Frame duration (T) varied from 5" to 45"/proj (60 projection totally). The 128x128 reconstructed OSEM images were scatter, attenuation and resolution recovery corrected. 14 different reconstructions were tested: updates (p=s*i) from 20 to 240 with and without Butterworth filter. All analyses were carried out with MIM Software.

Results: Scatter, attenuation and resolution recovery corrections do guarantee that the activity distribution is spatially invariant. Self image and global SPECT calibration perform similarly.

100 updates with no filter maximize RC, while keeping noise at an acceptable level. Ac and Acratio do influence quantification accuracy (10% and 20% variations, respectively, in the clinical range).
Interestingly, no differences were measured with T in the tested range.

Conclusions: Pre-treatment MAA-^{99}mTc SPECT/CT was optimized for whole VOI metrics, factors affecting activity quantification issues were highlighted. Further analyses are needed to quantify accuracy and pitfalls in voxel-level metrics.

ID46 (e-poster)

Title
A Geant4 Monte Carlo simulation that imports DICOM ROIs to define detectors and primary sources

Authors

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Abstract

Monte Carlo (MC) simulations are the gold standard for dosimetric estimation in several therapies. Geant4 is one of the most commonly used toolkits for developing MC simulations in medical application, especially for research purposes. We developed a Geant4 based MC code that, besides importing DICOM files to describe the patient as a voxelized geometry, converts the Regions Of Interest (ROIs) from the same DICOM files into Geant4 native "solids" and place them in a parallel world, i.e. independent to the voxels. We use a dual approach depending on the kind of shape each ROI is describing. If the ROI describes a smooth volume, we use the Poisson Surface Reconstruction1 (PSR) algorithm from the CGAL library to find a triangular facets water tight tessellated solid, which is then converted into a G4TessellatedSolid. PSR does not provide excellent results in reconstructing sharp edges. For this reason, if the ROI describes a known figure, such as a cylinder or a parallelepiped, we use another approach: we estimates the figure parameters, including its' orientation in the 3D space, using the RANSAC[2] algorithm. This way, the detectors are described independently from the voxel geometry and there are no aliasing problems in representing them and it is possible to use a smart tracking in the voxel. The code has been developed for the WIDMApp project, aimed at monitoring Molecular Radiotherapy, but we think it could be of interest for other applications. Therefore, it will be released as open source.

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ID49 (e-poster)

Title

Robustness of a method for tumour delineation in ^{177}Lu SPECT images acquired on a StarGuide

Authors

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Abstract

Robust and accurate delineation methods are needed for tumour dosimetry after radiopharmaceutical therapy. In this work, we evaluate the performance of a previously proposed technique for delineating tumours on 177Lu SPECT images acquired on a ring-shaped CZT-based camera (StarGuide) [1].

Six spherical inserts of a NEMA phantom (1.2-113.1 mL) were filled with 1.8 MBq/mL of ^{177}Lu. Six acquisitions of 60 minutes each were performed over one month (0.25-1.8 MBq/mL) on a StarGuide. Using the Lister tool, the acquired projections were reframed into five independent sets of projections of 12 minutes each (total: 30 sets) and reconstructed with the manufacturer protocol (Q.Clear with attenuation and scatter correction). After manually drawing a first over-sized volume of interest (VOI) around each sphere, the PERCIST SUV Peak tool in MIM (MIM Software Inc.) was used to calculate the largest mean value in a 1 mL-spherical VOI inside each contour. VOIs corresponding to each sphere were delineated using a 30%-isocontour of the previously determined mean value. For each sphere and reconstruction, the relative percentage difference between the measured and nominal volume was calculated.

Median differences over 30 scans were below 5% and 12% for the four largest spheres (5.6-113.1 mL) and the 2.6 mL sphere, respectively, with a maximum difference of 34%. For the smallest sphere (1.2 mL), the median difference exceeded 200%.

The method proved to be reliable for tumour delineation in ^{177}Lu SPECT images acquired on a StarGuide in a clinically relevant range of activity concentrations, as long as volumes >5.6 mL are considered.

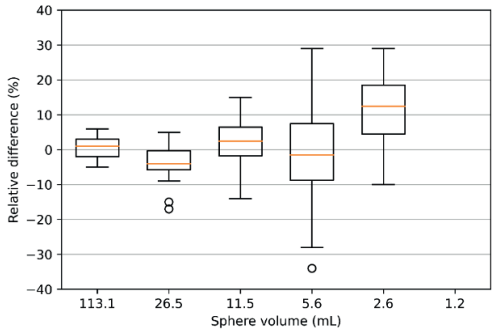

Figure 1: Boxplots representing the distribution of the relative percentage difference for each spherical insert of the NEMA phantom. The orange lines represent the median of the data. The boxes extend from the lower to upper quartile values, while the whiskers show the range of the data. Flier points are those past the end of the whiskers. Data for the 1.2 mL spherical insert are out of range.

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ID58 (e-poster)

Title

A head-to-head comparison of three CE-certified dosimetry software solutions for ^{177}Lu-labelled radioligand therapies

Authors

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Abstract

Aim: The goal was to test three CE-certified commercially available software solutions (Hermia, QDOSE, SurePlan-MRT) for ^{177}Lu dosimetry.

Method: A NEMA phantom with 6 spheres (177Lu activity concentration: 2.14 MBq/ml) was used for the analysis. Six image-sets (5/6 image-sets including 4 SPECT/CTs, 1/6 image-set including 6 SPECT/CTs) with variable scan-dependent acquisition durations, camera sensitivity factors and phantom positions were created. All scans were reconstructed either with FLASH-3D (6i6s) or with xSPECTquant (12i3s) with attenuation and scatter correction without post-filtering. The accuracy of count-based activity determination, alignment, fitting, activity, time-integrated activity coefficients (TIACs) and absorbed dose (ADs) calculations was investigated. The resulting activities, fitting parameters, TIACs and ADs were compared to the results obtained from NUKDOS.

Result: All codes handled activity- and count-based data correctly and performed dosimetry calculations for all image-sets, except for the image-set with different reconstructions. Small positioning differences were aligned automatically whereas large differences required either manual image alignment (2/3) or drawn segment based (3/3) adjustments. The relative difference (R) in activity quantification, TIACs and ADs was <±5% for the four-scan data sets. For the data with six scans, R in activity was < ±5%, Rs in TIAC and AD w ere higher (~10% for Hermes, ~130% for QDose, ~19% for SurePlan-MRT).

Conclusion: Independent of the used dosimetry-software, performing similar workflows result in differences in the same order of magnitude. Selected imaging protocol, segmentation method and fitting have a major impact on dosimetry. Improvements in fitting process are desirable for all software.

ID62 (e-poster)

Title

Safety and efficacy of non-carrier added (n.c.a.) 177Lutetium-PSMA-I&T radioligand therapy in hormone resistant metastatic prostate cancer patients

Authors

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Abstract

Aim: In metastatic castration-resistant prostate-cancer patients (mCRPC), failing conventional therapies, radiopeptide treatment with 177Lutetium seems to be the management of choice. We aimed to assess the safety and efficacy of n.c.a. 177Lutetium-PSMA-I&T in mCRPC patients for the establishment of this treatment novelty in Greece.

Patients and Methods: In nine men (median age 73 years) with progressive mCRPC, n.c.a. 177Lutetium-PSMA-I&T was i.v. infused. Whole-body scintigraphy was obtained immediately, 24 and 48 hrs p.i. In a median of 6 sessions (mean activity 6.8 ± 1.2 GBq/session), a mean cumulative activity of 40.8 ± 14.3 GBq was reached. For dosimetry OLINDA/EXM 1.1. code was used.

Results: In 4/9 (44.4%) and 5/9 (55.6%) patients a 28% and 40% PSA drop respectively was observed, 16 weeks after the initial session. Median imaging-based progression-free survival (PFS) was 8 and median overall survival (OS) 13 months. WHO Grade-3 myelotoxicity was noticed in 2/9 (22.3%) patients after their last (sixth) treatment session. The median absorbed dose for the lacrimal and parotid glands was 2.6 ± 1.4 and 2.1 ± 1.2 Gy/GBq respectively, for kidneys 0.81 ± 0.28 Gy/GBq, for liver 0.14 ± 0.36 Gy/GBq, for spleen 0.18 ± 0.24 Gy/GBq, for osseous metastatic lesions in a range of 2.20 –12.38 Gy/GBq and for bone marrow 0.038 ± 0.009 Gy/GBq.

Conclusion: In mCRPC patients, n.c.a. 177Lutetium-PSMA-I&T is well tolerated and effective, offering new horizons for a longer PFS, OS and quality of life. Lacrimal, salivary glands and bone marrow consist the critical organs. Thus, dosimetry should be a necessary appendage.

ID63 (e-poster)

Title
Cyclotron produced radionuclides

Authors
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Abstract
Aim: Nuclear Medicine (NM) is based on a great variety of radiopharmaceuticals. The aim of this presentation is to provide an updated overview of cyclotrons and radionuclides.

Method: Information about the cyclotron technologies and radiopharmaceutical trends according to practice experience and IAEA.

Results: In total 200 cyclotrons are operated around Europe, whereas 4 are in Greece by industrial companies. Most of them run up to 18 MeV accelerating protons, to high speeds directing them on liquid/solid targets producing radionuclides that can be separated from the target and processed in synthesis modules. The main advantages of cyclotrons-produced radionuclides rely on:
(a) Easy programmable operating facility for irradiation
(b) Recovering and recycling target material
(c) Automated modules for synthesis, purification all in one integrated pre-loaded disposable cassette.
(d) Small amount of long-lived radioactive waste

Concerning to production of radionuclides ^{18}F-FDG is the main demand but nowadays examples of more ^{18}F-tracers such as ^{18}F-Flutemetamol, ^{18}F-PSMA, ^{18}F-Flortaucipir, are in development, and 18 MeV cyclotrons are suitable for the production of many radionuclides such as ^{11}C, ^{64}Cu, ^{68}Ga, ^{89}Zr, etc.

Considering however the growth in NM, and theragnostic pairs, there is a necessity beyond 177Lu-peptides for further agents and therapy tools such as alphas (^{225}Ac, ^{221}At, ^{67}Cu), leading to greater expansion of cyclotron technologies.

Conclusion
- Isotopes are the key components of an NM department both for imaging and therapy
- Theragnostic pairs allow better dosimetry and understanding of pharmacokinetics
- Development needs collaboration between physicians, physicists, biologists, and chemists from production up to bed.

ID63 (e-poster)

Title

Co–Infusion of DTPA solution during PRRT with ^{177}Lu-, ^{90}Y- and ^{111}In- labelled peptides reduces the trivalent ionic (free) contaminants, aiming to the myelotoxicity protection

Authors

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Abstract

Aim: PRRT is being routinely performed in our Institution with ^{111}In-DTPA-Phe1-Octreotide, ^{90}Y-DOTATOC, and n.c.a. ^{177}Lu-DOTATATE/DOTANOC. According to the manufacturers their solutions contain ~ 0.1 % trivalent free ions of ^{111}In (Tph1/2 = 2.83 d), ^{114}In (Tp1/2 = 49.5 d), ^{90}Y (Tph1/2 = 64.1 hrs), ^{177}Lu (Tph1/2 = 6.7 d) or ^{177m}Lu (Tph1/2 = 160.4 d). Since the infused activities/session range from 4070-7030 MBq, the amount of these free ions/contaminants might provoke undesirable myelotoxicity. Therefore we aimed to highlight the dosimetric differences.

Material and Method: The tandem, in trip-trop, i.v. co-infusion of 75mg of DTPA, in 250 ml normal saline, on the course of PRRT sessions, competes with transferrin, forms DTPA-contaminants-complexes, rerouting the ionic (free) Indium, Yttrium and Lutetium fraction to renal clearance.

Results: Indium-111, n.c.a. Lu-177 and Yttrium-90 activity and exposure rate half-life (hrs.), were (with and without adding DTPA), accordingly as follows: blood (rapid), blood (slow) and whole body phase for Indium-111: 2,8 ± 0,7/4,6 ± 1,2 ($p < 0,05$); 26,2 ± 5,6/28,0 ± 7,2 ($p > 0,05$); 9,4 ± 1,6/13 ± 2 ($p < 0,001$), for n.c.a. Lu-177: 1,5 ± 0,3/2,8 ± 0,4 ($p < 0,05$); 16,3 ± 5,4/18,0 ± 8,1 ($p > 0,05$); 13,4 ± 1,5/16,2 ± 3,5 ($p < 0,05$) and for Y-90: 2,8 ± 0,7/4,6 ± 1,2 ($p < 0,05$); 26,2 ± 5,6/28,0 ± 7,2 ($p > 0,05$); 9,4 ± 1,6/13 ± 2 ($p < 0,001$).

Conclusion: Co–Infusion of DTPA solution during PRRT with ^{177}Lu, ^{90}Y or ^{111}In should be a necessary appendage, reducing unwanted bone morrow irradiation.

ID65 (e-poster)

Title

Evaluation of treatment effect prediction based on voxel dosimetry in liver radioembolization with Y-90 resin microspheres

Authors

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Abstract

Background: Recent studies on liver radioembolization with Y-90 microspheres validate the correlation between organ and lesion absorbed doses during the therapy and the treatment effects (radiological response, adverse events and patient survival). However due to diversity in data collection, result comparison is challenging. Furthermore, a lack of studies on resin Y-90 microspheres is observed, since more studies focus on glass ones. The purpose of this study is to optimise and standardise Y-90 pre- and post- dosimetry protocol in our institution and evaluate prediction of treatment effects based on voxel dosimetry for resin Y-90 microspheres.

Methods: A retrospective study is performed in which pre- and post- treatment voxel based dosimetry data, clinical data and patient outcome is collected for 98 HCC patients treated with Y-90 resin microspheres from 2013 to 2021.
The protocol of dosimetry and image reconstruction is optimised based on EANM guidelines. A correlation between dosimetry results and treatment effects is searched for using statistical analysis.

Results: Following EANM guidelines, optimal Siemens 'Symbia' SPECT/CT image reconstruction for pre-treatment dosimetry with Tc-99m MAA is found - FLASH 3D, 8 subsets, 8 iterations, no filtering. Post-treatment dosimetry is performed on PET/CT images using the same VOIs as for pre-dosimetry. During statistical analysis a correlation between lesion dose and radiological response is found. No correlation between dose and adverse events or patient survival is observed. A good agreement between pre- and post- dosimetry is found.

Conclusions: Radiological response of liver radioembolization with resin Y-90 microspheres can be predicted based on voxel dosimetry.

ID67 (e-poster)

Title

Evaluation of Eye Lens Dose Using TRIPOLI-4® for Nuclear Medicine Professionals: ^{177}Lu Molecular Radiotherapy

Authors

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Abstract

Occupational exposure to low-dose ionizing radiation may increase the risk of cataracts. Correct estimation of radiation dose to the lens of the eye is then important for nuclear medicine professionals. A lutetium-labelled radiopharmaceutical is a type of medicine that contains a radioactive element called ^{177}Lu attached to a carrier molecule that can target specific tissues in the body. ^{177}Lu emits beta particles that can destroy cancer cells while sparing healthy ones. On March 23, 2022, the FDA approved ^{177}Lu-PSMA-617 for the treatment of patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer. The recommended ^{177}Lu-PSMA-617 dose is 7.4 GBq intravenously every 6 weeks for up to six doses

[1]. The ^{177}Lu-PSMA-617 was also approved for medical use in the European Union in December 2022. TRIPOLI-4®** is a Monte Carlo radiation transport code developed at CEA-Saclay

[2]. To study radiation protection dosimetry in human tissues and organs, voxel computational phantoms from the ICRP publication 110 were modeled using TRIPOLI-4®. To easily use the voxel phantoms in different exposure scenarios, a newly developed phantom option in TRIPOLI-4® was helpful to model one or more phantoms [3]. The increasing use of ^{177}Lu-PSMA-617 for prostate cancer treatment is now confirmed. The radiation dose to the lens of the eye and to the thyroid for nuclear medicine professionals may follow this rising trend because ^{177}Lu and ^{177m}Lu also emit rays, especially for staffs preparing ^{177}Lu-PSMA-617 from a shielded vial for injection. In this study the eye and eye lens model of ICRP 116 were first inserted into the TRIPOLI-4® voxel phantoms.

Then, using the 177Lu sources, before and after the injection of 177Lu-PSMA-617 to the patient (phantom), the eye lens dose values of male and female nuclear medicine staff phantoms were evaluated and compared with the Hp(3) values.

** TRIPOLI-4® is a registered trademark of CEA. The author thanks EDF for partial financial support. The author would like to thank Dr. P. Ferrari of ENEA for providing related exposure scenarios information.

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ID69 (e-poster)

Title

The Pre-Therapeutic introduction of n.c.a. ^{177}Lu-PSMA I&T ("LuteScan") as a SPECT compatible radioligand for PSMA Imaging in Metastatic Prostate Cancer Patients

Authors

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Abstract

Aim: Intense PSMA activity on ^{68}Ga-PSMA functional imaging counts as the crucial inclusion criterion for implementing ^{177}Lu PSMA radioligand therapy, ensuring adequate PSMA expression on the tumoral lesions. We aimed to introduce ^{177} Lu-PSMA as a diagnostic whole body scan, alternative to the prerequisite ^{68}Ga-PSMA staging PET/CT scan, principally where the latter is not available.

Materials and Methods: After institutional review board approval and informed consent in 17 patients with metastatic castration-resistant prostate cancer (mCRPC), candidates for radiopeptide therapy (median age 76 years), 444 MBq (12 mCi) of n.c.a. ^{177}Lu-PSMA I&T, called by us ("LuteScan"), was pre-therapeutically, i.v. infused. For dosimetry, whole-body acquisitions followed immediately, 24 and 48 hr p.i; in addition, a 24 and 48 hr tomo-scintigraphy over (a) the lower part of the head, including the lacrimal and all salivary glands, and (b) the upper abdomen/lumbar region, including kidneys, was performed.

Results: In 15 out of 17 (82, 2%) mCRPC patients, "LuteScan" demonstrates them to be PSMA-avid. The absorbed dose for the lacrimal and parotid glands was 2.6 ± 1.4 and 2.1 ± 1.2 Gy/GBq respectively, for kidneys 0.81 ± 0.28 Gy/GBq and for bone marrow 0.038 ± 0.009 Gy/GBq.

Conclusion: The pre-therapeutic "LuteScan" in mCRPC patients refers them for further ^{177}Lu-PSMA therapy and might represent a diagnostic alternative to ^{68}Ga-PSMA, where the latter is restricted or not available. Dosimetry of kidneys, lacrimal and salivary glands exhibiting high physiological uptake of radiolabeled PSMA-ligands, considered dose-limiting organs, should be a necessary appendage.

ID70 (e-poster)

Title
Dosimetry of Liver and Hepatic Metastases in Ho-166 Microspheres Radioembolization Treatments

Authors
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Abstract
Holmium-166 microspheres (Ho-166-ms) are used in radioembolization, having the advantage with respect to Yttrium-90-ms of quantitative imaging using the same microspheres in both Scout and Therapeutic Administrations (SA and TA). The study goals are to report the mean absorbed dose (mAD) to liver and metastases and to confirm the high-power prediction of the SA on the TA.

Fifteen patients underwent SA and TA, in two weeks' time. SPECT/CT acquisitions were corrected for scattering and attenuation and taken when the activity was lower than 1 GBq. The SA acquisition was used to calculate the maximum administrable activity, keeping the liver mAD under/equal to 60 Gy, and to simulate the absorbed dose distribution. The TA acquisition was analyzed to determine the mAD to liver and metastases transferring the contours via rigid registration from SA to TA. All dose calculations have been performed using the Local Deposition Method. Furthermore, a local gamma-function analysis was conducted, with 10% dose difference and 10 mm Distance to Agreement.

The activity values of the TA ranged in a (median[min;max]) 4.6[1.9;6.5] GBq , while the tumor and liver mAD was 155[58.6;326.2] and 35[17.6;59.5] Gy respectively. A linear correlation of the liver mAD in SA and TA was found, with an R2 equal to 0.92 for the liver and to 0.91 for the metastases. The local gamma-function analysis showed a pass rate of 95.2[100.0;87.2].

This study confirmed the high predictive power of the Ho166 SA in terms of liver and metastases mAD assessment, within an activity of 6.5 GBq.

ID73 (e-poster)

Title
Clinical platforms in NET patients treated with radioligand therapy: a dosimetric comparison

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Abstract
Background: this work aims to compare absorbed doses between different platforms developed for Radioligand Therapy (RLT). Data analysis concerned dosimetric monitoring of kidneys and significant lesions (ROIs) in NET patients treated with Lu-177-DOTATOC. We compared absorbed doses between a pure voxel dosimetry approach [1], HMS® OLINDA/EXM 2.0, PLANET® Onco Dose and MIM® MRT [2].

Materials and method: we analyzed data of 10 patients performing sequential SPECT-CT dosimetry at 3 time points. To obtain dose rates with our voxel dosimetry approach, the convolution [1] between the Dose Voxel Kernel (DVK) and patient SPECT data was performed for each time point.

Then, the dose-rate curves have been fitted with a bi-exponential function and by integrating this function, the absorbed doses were derived. Finally, we compared these results with those returned by the clinical platforms, processing the same ROIs for each patient.

Results: the comparison highlights a discrepancy between the voxel dosimetry approach and PLANET® Onco Dose and MIM® MRT, when the phantom-based voxel dosimetry approach is used. Moreover if MIM® MRT employs the patient-specific voxel dosimetry approach, results agree with the other two procedures.

Conclusion: a discrepancy in dosimetry results appears when different workflows are used. An overestimation of absorbed doses within kidneys seems to appear when a phantom-based voxel dosimetry approach is used. For significant lesions, however, it seems not to be a systematic trend. Results need to be validated by increasing the patient cohort dimension.

Keywords

1. RLT, internal dosimetry, Lu-177-DOTATOC, clinical platforms.

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ID77 (e-poster)

Title
Development of a computer application for the dosimetry assessment of internal radiotherapy treatments with ^{177}Lu

Authors

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Abstract

Cancer is one of the diseases that affect many people, making it one of the leading causes of death in the world [1,2]. Nowadays, radiopharmaceuticals which incorporate the radionuclide ^{177}Lu are applied to treat different types of cancer by internal radiotherapy. For a long time, in Mexico, the internal dose assessment at organ level has been carried using a set of computational tools, such as, OLINDA/EXM V1.1, ImageJ, Osirix MD, etc [3,4]. Although these tools have been very useful so far, the need to unify the dose assessment process and provide more detailed information of treated patients is imperative. For this reason, the present work describes the development of a computational application for the dosimetry assessment of internal radiotherapy, using the App Designer in Matlab and data provided by the OpenDose project [5,6].

The developed app allowed to process and quantify planar and Single Photon Emission Computed Tomography/ Computed Tomography (SPECT/CT) nuclear images in a semi-automatic manner. Planar scans were quantified by the conjugate-view method, after applying corrections for scattering, attenuation, and decay. SPECT images were quantified by the three-dimensional quantification process, using images corrected for scattering, attenuation, decay, and partial volume effect [7,8].

Following a hybrid approach [7], the app obtained radiopharmacokinetic models, nuclear transformations and absorbed doses in organs and sites of interest, applying the MIRD scheme and the s-values reported by OpenDose for ^{177}Lu. The preliminary tests have allowed to analyze the absorbed doses of ^{177}Lu-DOTA-TOC and ^{177}Lu-DOTA-HYNIC-iPSMA in organs of interest of male and female patients under treatment.

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ID79 (e-poster)

Title
Retrospective verification of image-based dosimetry for SIRT using Simplicit90Y

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Abstract
Introduction: Selective internal radiotherapy (SIRT) is used to treat tumors of the liver by delivery of Y90-labelled microspheres. At the University Hospital Leipzig, Simplicit90Y® (Boston Scientific) is used for pre-SIRT dosimetry since 2021.

Methods: 41 patients were treated with SIRT, 29 male (71%) and 12 female (31%), mean age (± SD) was 67.8 years ± 7.6 years. Treatment was based on SPECT imaging of the distribution of Tc-99m – magroaggregated albumin (MAA). After SIRT, patients received SPECT and/or PET imaging. Personalized dosimetry was carried out with the software Simplicit90Y®. Doses are calculated by multiplying the activity by the constant $50\frac{Gy\ kg}{GBq}$ and a relative count rate, and dividing by the mass of the volume of interest. Volumes are calculated from MR- or CT-image based liver segmentations, density is assumed to be $1.03\frac{g}{cm^3}$. Only patients with post-therapeutic PET imaging were included in the analysis (23 out of 41). Each catheter position was considered separately. We compared doses to the perfused tumors and in to the normal tissue after treatment to the doses previously planned, using the same segmentations for both.

Results: Planned and actually measured absorbed doses to the tumors were 187.4 Gy ± 62.4 Gy and 156.4 Gy ± 66.7 Gy, respectively. Planned and actually measured doses to the normal liver tissue were 20.8 Gy ± 11.8 Gy and 23.8 Gy ± 12.8 Gy, respectively.

Conclusion: We performed a simple retrospective comparison of planned to actually absorbed doses in tumors and tissue at risk using Tc99m-MAA-SPECT for treatment planning and Y90-PET-imaging for post-therapeutic dosimetry. We found an agreement in the order of magnitude as achievable by the accuracy determined by the methodology.

ID81 (e-poster)

Title
^{131}I-mIBG therapy in children

Authors
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Abstract
I-131 MIBG is currently the gold standard therapy regarding neuroblastoma, a neuroendocrine tumor, in children.

The protocol of handling I-131 MIBG (VERITAS protocol, SIOPEN study) involves numerous steps: the handling of the radiopharmaceutical, the delicate process of segmentation and administration of it at particular flow rates, the preparation of the child wrt medicines and instructions regarding its weekly stay within the therapy room, the safety radioprotection instructions that parents/caregivers and involved staff will have to observe, the dosimetry of the child, child's exit from the radiotherapy unit, the handling of patient's radioactive trash and the follow up of child's being in the clinic with respect to dosimetry and radioprotection rules. All above steps and procedures require a well studied plan and reliable execution. Lack of fulfillment of the engaged requirements could jeopardize the treatment of the patient as well as the treatment of following programmed patients.

The Whole-body dosimetry guidelines of the protocol will be discussed. Whole-body absorbed dose calculations are made according to standard MIRD methodology. The activity-time data are plotted and integrated to determine the cumulated activity Ã. Issues regarding: i) background reading prior to administration, ii) geometry reading, iii) timing and conditions of readings, iv) equipment used, v) reproducibility of measurements, etc will be touched upon.

The used therapy protocol involves two cycles of I-131 MIBG administration, with 4 Gy allowed total absorbed whole body dose. Issues regarding whole-body dosimetry and the accuracy of therein calculations will be discussed.

ID83 (e-poster)

Title

The Experience in a Single Institute ("Aretaieion" Univ Hosp) Over Two Decades of Individualized GEP-NET Radio-peptide Therapy: From Bench to Bedside

Authors

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Abstract

Introduction: Radio-molecular-therapy (RMT) has firmly established its position as first class treatment for the management of neuroendocrine tumors (Netter-1).

Patients and Methods: Our initial experience [1997-2011, ~70 GEP-NET-patients, >800 sessions] was based on [111In-DTPA-D-Phe-1]-octreotide, (5.4 ± 1.7 GBq) intra-arterially infused in 12 consecutive sessions within an 8-10 weeks' time interval. For myeloprotection, 70mg DTPA in 250 ml normal saline was co-infused, to reroute the tri-valent ionic contaminants from blood-pool to urine and 1000 ml aminoacids for nephroprotection. Optionally, a port system was temporary subcutaneously implanted, ending at the common hepatic artery, exonerating patients from catheterization discomfort. (The "Aretaieion Protocol"). For dosimetry the OLINDA/EXM 1.1 code was used.

A decade later [2012-2016], we started working with non- carrier added (n.c.a.) ^{177}Lu-DOTATATE/TOC (54/16 infusions), in-house-labelled (per-patient/per-name).

Results: The organ average radiation dose (mGy/MBq) , expressed as ^{111}In /^{177}Lu ratios were: liver-tumor 11.2/35.0; liver 0.14/0.03-0.1; kidneys 0.41/0.02-0.5; spleen 1.4/0.02-1.2; bone-marrow 0.0035/0.008-0.04; port-system-cases vs. simple-arterial-infusions (sai) (^{111}Insai / ^{111}Inport ratios), were: liver-tumor 11.2/15.4; liver 0.14/0.18; kidneys 0.41/0.39; spleen 1.4/1.6; bone-marrow 0.0035/0.0032. Tumor-shrinkage (TS) with [^{111}In-DTPA-D-Phe-1]-octreotide and ^{177}Lu-DOTATATE appeared at the 8th and the 3rd-^{4th} session, respectively. CgA and Ki-67 levels correlated to the TS%, as follows: 50.0% for 2-3cm mean tumor size (MTS) and 450 Gy mean absorbed dose (MAD); 70.0% for 3-4cm MTS and 150 Gy MAD and only a 20.0% for a 6cm MTS and a 450 Gy MAD.

Conclusion: In RMT, accurate quantitative imaging and dosimetry must be regarded as an essential integral part of the whole therapy procedure.

ID87 (e-poster)

Title

Management of outpatients and radioactive waste following Lu-177 DOTATATE PRRT: the approach of Attikon University Hospital

Authors

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Abstract

Introduction: The present study summarizes the experience from the management of patients and radioactive waste, following a considerable number of Lu-177 DOTATATE therapies on outpatients at Nuclear Medicine Unit of ATTIKON University Hospital.

Materials and methods: The study includes therapies performed between 2019 and 2022. According to the followed protocol, patients were released 5h post injection, based on a measurement of the dose rate at 1m (DR-1m). The liquid radioactive waste during therapies was discharged directly into the public sewage system. Annual effective doses to sewage sludge workers and members of the public were assessed as indicated in relevant guidelines of the national regulatory authority. Regarding dry radioactive waste, empty vials and biohazard containers were separately held in storage until their residual activity was in compliance with the exemption criteria.

Results: A total of 172 therapeutic doses have been administered. The mean annual administered activity was 318.85±0.11 GBq. The mean DR-1m at the time of release was 18.30±2.80 μSv/h. The radiation burden for sewage sludge workers and the members of the public was estimated at 22.40±10.10 μSv/y and 0.45±0.20 μSv/y respectively. 6 months post administration, the mean dose rate at 10 cm from the surface of biohazard containers was measured 0.07±0.05μSv/h. For the empty vials the respective dose rate was 0.14±0.04 μSv/h and the mean residual activity 59.20kBq.

Conclusion: ^{177}Lu-DOTATATE therapy may be safely performed on outpatients. The radiation burden to critical groups was in compliance with the regulatory requirements. However, prolonged storage may be required for used vials.

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