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Session 1: Methodology & QA

Establishing Traceability Routes in Nuclear Medicine: The ETrain Project

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Keywords (3 max): Traceability, Calibration, Harmonisation

Abstract
Background and aim
Nuclear medicine plays a pivotal role in modern diagnostics and therapy, yet disparities in measurement traceability across Europe hinder its full potential. Traceability is critical to ensure harmonisation of measurements across Europe and to improve accuracy when using diagnostic or therapeutic techniques. Studies have shown that only 23 % of European participants tested could measure a reference source to within 5 % of the true activity [1,2]. The ETrain project, funded by Euramet, begins to address this challenge by establishing traceability routes for radioactivity measurements in nuclear medicine. Spanning 8 countries and involving 14 funded institutions, the project will develop calibration services for important clinical radionuclides with uncertainties of 2 % or better (at k=1), assess and improve uncertainty evaluation methods, and validate calibration routes through intercomparison exercises.
Methods
ETrain will support the introduction of three traceability models; distribution of reference solutions, calibration of user-supplied samples, and deployment of travelling secondary standards. The methods will be tailored to national legislative and infrastructural contexts. The project also targets harmonisation of measurement capabilities through engagement and training, with a goal for 80 % of participants from emerging metrology regions to achieve activity measurements within 10 % of reference values and provide uncertainty budgets for their measurements.
Results & Conclusion
Updates on progress will be presented including setup of services, and evaluation of uncertainty when using calibrators and imaging equipment. The outcomes will benefit clinical users, regulators, and industry, contributing to improved patient care, personalised therapies, and the EU's strategic goals in cancer and medical ionising radiation applications.
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Lu-177 PSMA Registry: a platform to support clinical decision for patients undergoing molecular radiotherapy

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Keywords (3 max): Theragnostic, Prostate cancer, Clinical data management

Background and aim: Lu-177 PSMA therapy is an emerging treatment for metastatic castration-resistant prostate cancer (mCRPC). To support clinical decision-making and improve patient outcomes, we aimed to develop a structured and scalable registry to capture data on imaging, dosimetry, and therapy outcomes for patients undergoing Lu-177 PSMA therapy.
Methods: The registry was initially prototyped in Excel to define key data fields and workflows, with input from clinicians and other stakeholders. It was implemented using REDCap, a secure web-based data capture platform hosted at Royal Surrey NHS Foundation Trust (RSFT). Data instruments were created to collect up to 330 validated data points per patient, covering demographics, clinical history, treatment details, and dosimetry. Retrospective data from 16 patients were used to test the prototype, revealing the need for additional fields for detailed dosimetry analysis. Features for PSA tracking, DICOM imaging storage, ECOG performance scoring, and built-in REDCap reporting were integrated. Access control based on user roles ensured robust data security.
Results: Testing with 16 patient records confirmed the registry's ability to capture core data and generate visualisations, including PSA trends and ECOG scores. Feedback guided improvements to the field structure and usability. Imaging and data export functions were validated for clinical and research use.
Conclusion: We developed a secure, user-friendly clinical registry for Lu-177 PSMA therapy, adaptable for future enhancements such as toxicity monitoring and multi-site deployment. It supports high-quality data collection for long-term studies of the prognostic potential of dosimetry in Molecular Radiotherapy.

Quantitative SPECT Harmonisation: Analysis of cross-vendor phantom data from the EARL ^{177}Lu SPECT/CT Accreditation pilot

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Keywords (3 max): SPECT imaging, Harmonization, EARL Accreditation

Abstract

Background and aim: Despite the growing importance of quantitative ^{177}Lu SPECT/CT imaging for dosimetry in radiopharmaceutical therapy, insufficient standardisation across systems and vendors remains a major obstacle to data comparability and broader clinical use. This study explores inter-system variability in the EARL Quantitative ^{177}Lu SPECT/CT accreditation pilot [1] using manufacturer and third-party reconstructions.

Methods: Curated phantom data from 14 systems (8 Siemens, 6 GE) across 11 centres were analysed in Python (v3.12.4). Image calibration factors (ICFs [2]; Jaszczak phantom) and recovery coefficients (RCs; NEMA IQ phantom with six spheres; 10-mm replaced by 60-mm sphere; no background) were calculated. RCs were derived with spherical VOIs matching nominal insert volumes, placed via a centre-of-mass method on CT-interpolated SPECT. All sites provided manufacturer reconstructions (OSEM, 20 iterations, 4 subsets, no post-filtering, CT-based attenuation correction, triple-energy-window scatter correction, resolution modelling). Additionally, data were reconstructed using vendor-neutral software (Hermia, Hermes Medical Solutions and PyTomography [3]) using equivalent settings.

Results: The analysis required a labour-intensive curation process due to the non-harmonised use of DICOM for quantitative SPECT and reconstruction protocol variations across participating sites. For each system and reconstruction software, ICFs and RCs were strongly correlated. ICFs agreed well between reconstruction methods. Manufacturer reconstructions yielded higher RCs for Siemens, while third-party reconstructions yielded higher RCs for GE systems.

Conclusion: This study demonstrates strong agreement between manufacturer and vendor-neutral reconstructions. Despite the technical challenges, the curated, cross-vendor phantom dataset offers a solid platform for imaging standardisation, supporting the upcoming EARL ^{177}Lu SPECT/CT Accreditation programme.

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FMEA (Failure Mode and Effects Analysis) for 177Lu marked PSMA and DOTATATE/TOC therapies for risk treatment assessment

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Aim: Radiometabolic 177Lu based treatment is a complex process that involves different specialists. Due to his high complexity and to the potential serious risk of health damages for patients and healthcare professionals, a global analysis of the whole process would allow to identify the weak point and then improve clinical standards. Risk analysis also fulfil the requirement of 2013/59/EURATOM directive. We performed a FMEA (Failure Mode and Effects Analysis) analysis for 177Lu therapies in order to identify the main critical points in the whole procedure.
Materials and methods: We divided the whole process of 177Lu base therapies into main steps and identified all possible failure-modes. Each failure-mode was scored for severity (S), occurrence (O) and detectability (D), range:1-10. Based on the Risk Priority Number (RPN=SxOxD) all failures were ranked. Both in home marked or already and ready for injection radiopharmaceuticals were considered. Both 177Lu-PSMA and 177Lu-DOTATATE/TOC therapies were considered.
Results: Failure mode with highest RPN score were: incorrect infusion supervision based on counts measurements; incorrect connection of catheters (vial-injection pump-patient); incorrect end of infusion; false negative of pregnancy test. Additionally, for home marked radiopharmaceuticals: incorrect selection of vial geometry calibration factor.
Conclusions: The FMEA analysis allowed the identification of the main failure mode in 177Lu treatment procedures. Based on the obtained results, strategies could be implemented in the clinical practice in order to further improve patient safety. The present results may help new implementation of 177Lu base therapy in the prospective of increasing use of this kind of therapies.

Uncertainty analysis of vertebral activity quantification in SPECT/CT imaging after [^{177}Lu]Lu-DOTATATE therapy using a physical phantom and simulations

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Keywords (3 max): uncertainty analysis, bone marrow dosimetry, 177Lu SPECT/CT imaging

Abstract

Background and aim: Accurate bone marrow dosimetry is essential in radiopharmaceutical therapy with [^{177}Lu]Lu-DOTATATE, where red marrow is a dose-limiting organ. This study evaluates errors in lumbar vertebra activity quantification using phantom measurements and Monte Carlo (MC) simulations.
Methods: A 3D-printed lumbar spine (L1–L5) and kidney phantom based on ICRP 145[1] was used. Attenuation of cortical bone was achieved using high-density printing material; spongiosa was modeled with a K_2HPO_4 solution containing 33 kBq/ml [^{177}Lu]$LuCl_3$ dissolved in DTPA. Standard-resin kidney phantoms were filled with 310 kBq/ml [^{177}Lu]$LuCl_3$ dissolved in HCl(aq). SPECT/CT imaging was performed in a water-filled IEC NEMA phantom using varying acquisition parameters. The influence of different acquisition parameters was assessed using SIMIND[2] MC simulations with Poisson noise (1000 realizations per setting), based on a digital model of the physical phantom. Two OSEM reconstruction algorithms with different scatter corrections were compared: A) PyTomography[3] with triple-energy-window scatter correction; B) a MC-based SARec reconstruction[4]. Activity quantification was evaluated by comparing SPECT-derived and true activities based on CT-based VOIs.
Results: Quantification in LV1-LV5 was mostly influenced by neighbouring high kidney activity, scatter, and noise behavior of OSEM reconstructions. Vertebrae overlaid by kidneys showed decreased activity. MC-based reconstruction showed higher accuracy (LV1-LV5 89%±1%; mean ±SD) than triple-energy-window reconstruction (79%±1%).

Conclusion: Our analysis reveals that the accuracy of activity quantification depends strongly on axial positioning of lumbar vertebrae and kidneys. When axial kidney and vertebra positions overlap, the vertebra's activity is underestimated. Quantification improves with MC-based scatter correction.

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Optimisation of ^{177}Lu post therapy CZT SPECT/CT dosimetry scan duration using qualitative and quantitative metric analysis

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Keywords (3 max): PRRT Dosimetry, optimisation, scan time

Abstract

Background and aim: Accurate dosimetry requires multiple scans throughout the course of peptide receptor radionuclide therapy (PRRT). Published post-therapy ^{177}Lu SPECT/CT scans range between 20–50 minutes duration and can be resource-intensive and challenging for patients. In this retrospective study the minimum scan time that maintains adequate qualitative and quantitative image quality was investigated for a selection of Neuroendocrine tumour (NET) patients.

Methods: Image data sets of five cycle 1 ^{177}Lu-Lutathera PRRT patients, 3 females and 2 males weighing 55–122 kg were used. SPECT/CT images (60 projections per head x 20s per projection (pp)) acquired on Days 1, 3-5 and 7 on a GE Discovery NM/CT 870 CZT SPECT/CT were iteratively reconstructed to simulate reduced acquisition time, with reconstructions ranging from 20s to 5s pp. Activity quantification and three time-point dosimetry was performed for lesions and organs with physiological uptake, for various combinations of reduced time protocols. Clinical image quality was visually assessed by both an experienced Nuclear Medicine physician and Radiologist and rated using the Likert scale.

Results: A scan time of 10s pp for Day 1 and Day 3-5 scans, and 15s pp on Day 7 were found to be qualitatively and quantitatively acceptable. The resultant absolute difference in kidney absorbed dose was 0.01 – 0.06 Gy (0.2 – 1.8%) across all patients. Results for lesions and other organs with physiological uptake will also be presented.

Conclusion: A significant reduction in scan duration has been achieved. Differential scan times for Day 7 facilitates improved quantification for reduced-time post therapy ^{177}Lu imaging.

Automated image segmentation for quantification of tumour burden in ^{177}Lu-PRRT patients

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Keywords (3 max): Segmentation, ^{177}Lu-DOTA-PRRT, Tumour

Abstract

Background and aim: There is an increasing interest for tumour dosimetry in ^{177}Lu peptide receptor radionuclide therapy (PRRT) and tumour delineation in ^{177}Lu SPECT images. The aim was to develop and validate an automated image segmentation method for dosimetry of the entire tumour burden.

Methods: The segmentation method utilized Difference of Gaussians (DOG) filtering applied at multiple scales, resulting in a series of high-pass filtered images. These were further processed using region-growing, with automatically identified seeds based on thresholding of DOG images. The set of binary masks from each DOG image were combined to construct the final tumour-burden mask. An option to exclude previously segmented organ VOIs from the DOG-filtered images was also incorporated. In this work, organ VOIs were obtained from CT-based segmentation with the TotalSegmentator software (1).

Optimization of DOG image thresholds was performed using simulated SPECT-images of three anthropomorphic XCAT-phantoms. Tumours were positioned within the phantoms in NET-typical locations, with shapes and volumes derived from patient ^{68}Ga-PET images. Phantoms were simulated both with and without respiratory motion. Tumour and organ activity concentrations were assigned according to a pharmacokinetic model, with inter-tumour variability based on random sampling.

The method's performance is currently being evaluated in patient SPECT-images acquired 24 h and 96 h p.i. This includes an operator study involving medical oncologists responsible of patient management.

Results: The tumour burden has currently been delineated in a total of 175 patients. Manual adjustment has been required in few cases and has typically been made due to modest radiopharmaceutical uptake. For the operator study 24 patients have been included, representing a variety of segmentation challenges.

Conclusion: The automated segmentation method has been found valuable to obtain a streamlined identification and delineation of tumours in SPECT images of ^{177}Lu-PRRT patients.

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Improving Lesion Quantification in ^{177}Lu-PSMA Therapy Through Adaptive Segmentation of SPECT Images

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Keywords (3 max): SPECT, Segmentation, Theranostics

Abstract

Background and aim: Quantitative assessment of tumor burden in ^{177}Lu-PSMA therapy is essential for dosimetry, response evaluation, and personalization of treatment. However, the lack of standardized and practical segmentation methods for post-therapy SPECT images limits clinical application.

Methods: We developed a semi-automated iterative thresholding algorithm for lesion segmentation on SPECT/CT SUV maps. The method dynamically adjusts thresholds based on lesion volume and contrast, refined through a phantom-derived calibration curve. Implementation was done in Python within 3D Slicer.

Results: The algorithm was tested on three phantom datasets and three patient scans with varying acquisition times and background levels, showing improved robustness over fixed-threshold techniques. Quantitative evaluation using Dice, TPR, Hausdorff Distance, and Mahalanobis Distance demonstrated good agreement with manual segmentations (e.g., Dice > 0.79, HD95 < 2 mm).

Conclusion: The proposed method enables reproducible and contrast-adaptive segmentation of lesions in post-therapy SPECT, making it suitable for clinical workflows where AI is not yet feasible. Future work will focus on extending this to patient datasets and integrating dosimetric calculations.

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Threshold-based Segmentation Method for Liver Tumors after [^{177}Lu]Lu-DOTA-TATE Therapy

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Abstract

Background and aim: Accurate tumor dosimetry is essential for optimizing outcome in molecular radiotherapy and it requires precise tumor segmentation. This study aimed to develop a threshold-based segmentation method for liver tumors after [^{177}Lu]Lu-DOTA-TATE therapy.

Methods: Monte Carlo simulations were used to generate 120 SPECT projections from 20 spherical liver lesions with varying volumes (1-16 ml) and tumor-to-normal tissue concentration (TNC) ratios (2-16). Simulated raw data were added to raw data from a patient without liver lesions and reconstructed. Lesions' known volumes were segmented using iterative thresholding and resulting thresholds were plotted against TNC ratios in the reconstructed images. A fitted equation was proposed for estimating thresholds for tumors based on TNC ratio, enabling segmentation of tumors with unknown volume. The method was evaluated on 160 additional simulated lesions in two patients without liver lesions across four imaging time points. Thresholds from the fitted equation were applied, and segmented volumes were compared to ground truth.

Results: The fitted equation showed strong correlation (R=0.88). For a TNC ratio of 8, mean segmented volumes (±SD) using the proposed method were 15.7±1.0 ml, 6.9±0.5 ml, and 4.1±0.5 ml for simulated volumes of 16 ml, 8 ml, and 4 ml, respectively. Similar results were observed for TNC=16. Accuracy declined substantially for smaller lesions or lower TNC ratios.

Conclusion: The proposed method showed promising results for tumors ≥4 ml, and TNC ratios ≥8. Segmentation accuracy for smaller and less avid tumors was limited by partial volume effects and noise.

Supporting figure / Table (optional)

^{177}Lu-SPECT with natural voxels for management of partial-volume effects

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Keywords (3 max): ^{177}Lu-PRRT, quantitative SPECT, tomographic reconstruction

Abstract

Background and aim: Natural voxels (na.v.) is an image-representation format in which values are assigned directly to volumes-of-interest (VOIs). The aim of this study was to demonstrate that SPECT reconstruction using na.v. is superior to the conventional method for activity-concentration estimation employing cuboid voxels (cu.v.) combined with post-reconstruction partial-volume correction (PVC) using recovery coefficients in ^{177}Lu-PRRT.

Methods: Two datasets were utilized. The first (dataset A) comprised a single patient undergoing ^{177}Lu-PRRT with SPECT acquired at 1 d, 4 d, and 7 d p.i. (dataset A) The second (dataset B) included eight patients with a single SPECT acquisition at 1 d p.i. Images were reconstructed using both cu.v. and na.v. formats. Natural voxels for normal organs were defined via segmentation of CT images using TotalSegmentator [1], while tumour na.v. were defined from segmentation of images reconstructed with cu.v. Activity-concentration estimates were compared for kidneys, spleen, and tumours. Patient studies were replicated using the SIMIND Monte Carlo program [2] by using SPECT (na.v.) and CT images serving as input for source and geometry definitions. Activity-concentration estimates were compared with concentrations defined in the simulation input.

Results: Tumour estimates are higher for na.v. than for cu.v. with PVC in patient data and demonstrate better accurate when evaluated using simulated data.

Conclusion: SPECT with na.v. yields superior activity-concentration estimates compared with post-reconstruction PVC using recovery coefficients.

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Supporting figure

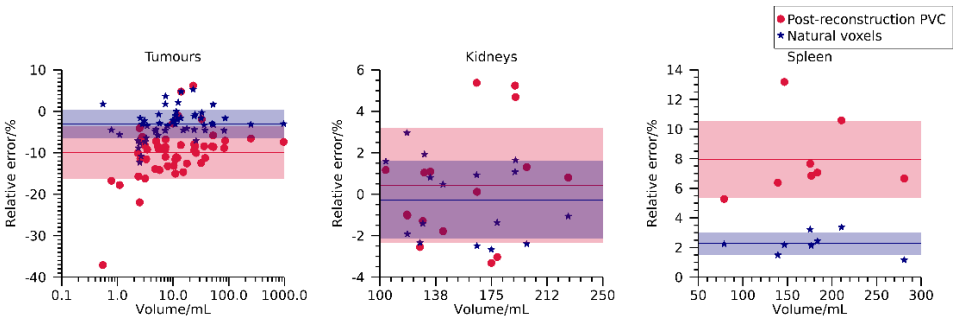

Figure 1: Relative errors for activity concentration estimates for images simulated from dataset B. Solid lines indicate means and shaded bands indicate one standard deviation.

Session 2 : Patient dosimetry and clinical trials

Landscape of clinical trials in molecular radiotherapy

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Keywords (3 max): MRT, Clinical trials, landscape

Abstract

Background and aim: Molecular radiotherapy has expanded significantly, evidenced by the surge in publications on agents including ^{177}Lu-PSMA and ^{177}Lu-DOTATATE. Despite promising industrial investments, the actual integration of molecular radiotherapy (MRT) into clinical research remains to be clarified.

Methods: We extracted data from ClinicalTrials.gov using "cancer" and "therapy" as keywords, creating a database of 58,648 clinical studies from 2000 to 2024. Using Python 3.12.2 scripts, we semi-automatically categorized studies into molecular radiotherapy (MRT, n=584), external beam radiotherapy (EBRT, n=2550), and drug therapy (DRUGS, n=48,668), to allow for in-depth analysis of these subsets.

Results: Over 20 years, the total number of MRT clinical trials increased fifteenfold, from 6 in 2000 to 89 in 2024. Although absolute numbers grew, the EBRT/MRT trial ratio fluctuated between 3 and 7, while the drug therapy/MRT ratio, initially 125 in 2000–2009, decreased to 60 by 2020–2024. Early-phase trials (phase ≤2) dominate MRT studies, constituting 87% overall, with phase 1 trials increasing from 12% to 53%. Prostate cancer leads indications studied (rising from 9 to 115 studies), followed by liver cancers and neuroendocrine tumors, with increasing cancer type diversity over time. Beta-minus emitters are the most predominant radionuclides used (75%), though the use of alpha emitting agents has risen since 2020. ^{177}Lu was the most frequently employed radionuclide in 2024, representing over 50% of MRT trials.

Conclusion: This review clarifies MRT's evolving role in cancer clinical research relative to other treatment modalities. Further detailed studies are needed to enhance understanding of this landscape.

INSPIRE – A prospective observational study of radiation dosimetry for radioiodine treatment of thyroid cancer

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Keywords (3 max): Thyroid, Clinical Trial, Radioiodine

Abstract

Background and aim: SELIMETRY and MEDIRAD were the first investigator-led multi-centre clinical trials incorporating dosimetry for radioiodine treatment of thyroid cancer. Investigating National Solutions for Personalised Iodine-131 Radiation Exposure (INSPIRE, ClinicalTrials.gov: NCT04391244) is a follow-up prospective observational study which aims to further explore dosimetry for organs-at-risk and target tissues in differentiated thyroid cancer patients and to establish dose-response relationships.

Methods: INSPIRE aims to recruit 150 patients. 10 UK sites were set up for quantitative imaging using support from the Radiotherapy Trials Quality Assurance (RTTQA) group. Flexible imaging protocols were developed due to differences in SPECT/CT availability and treatment schedules. Dosimetry is performed centrally using Hermes Hermia Voxel Dosimetry. Patients are treated with 1.1, 3.7 or 5.5 GBq of radioiodine after TSH stimulation. Follow-up is performed using standard-of-care thyroglobulin measurements. Salivary gland toxicity is assessed using Common-Terminology-Criteria-for-Adverse-Events (CTCAE) v5.

Results: 127 patients have been recruited to date. Initial results of the first 97 patients have shown a large range of absorbed doses for thyroid remnants (<1 to 1106 Gy) and salivary glands (Median 0.7 Gy, Range 0.2 to 12.1 Gy). Salivary gland toxicity data was available for 23 patients and CTCAE grade increased in 10. Excellent biochemical response rate at 9-12 months was found to be 71% in 33 patients with completed follow-up.

Conclusion: The interim results show that multi-centre investigator-led clinical trials are feasible and help to roll out quantification and dosimetry methodologies across UK centres. Empirical activity administrations result in a wide range of radiation doses and transient salivary gland toxicity is observed in 40% of patients.

^{124}I PET dosimetry to optimize ^{131}I therapy of metastatic differentiated thyroid cancer: an ongoing phase II trial

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Keywords: radioiodine therapy optimization

Abstract:

Background and aim: This study aims at demonstrating that the first two ^{131}I treatments of metastatic differentiated thyroid cancer (MDTC), optimized with ^{124}I planning, provide a response rate on soft tissue metastases at 6 months higher than the fixed activity method.
Methods: Patients are prepared with hormone withdrawal both for treatment planning and therapy. Oral administration of liquid ^{124}I (100 MBq) is followed by blood sampling and whole body counting at 2, 6, 24, 120 h. PET scans are taken at 24 and 120 h. Lesion post-therapy dosimetry is performed on dead time corrected SPECT/CT taken at 24 and 96 h. A composite response is evaluated with ^{18}F-FDG-PET, contrast-enhanced CT, ^{124}I PET and thyroglobulin level.
Results: Among 30 enrolled patients, 13 (43%) were dropped out for absence of ^{124}I uptake. Seventeen patients received 26 optimised treatments with median 10 GBq, range 4-20 GBq. Planning modified our usual activity for MDTC (8 GBq) in 22/26 treatments (85%). Three females over 70 exhibited G2/G3 haematological toxicity. Moderate sialadenitis was reported by 5 patients. Twelve patients reached the end of the study. We had 4 CR, 4 PR and 4 PD at ^{124}I PET.
Conclusion: ^{124}I PET detected more lesions than post-therapy ^{131}I SPECT/CT. This was essential for a perfect staging, essential to plan the maximal tolerable activity in presence of bone lesions. Blood dosimetry was more impacting than lesion dosimetry. This remarks its clinical usefulness even in absence of ^{124}I.
The study is funded by the AIRC Foundation.

Radioembolization of hepatocellular carcinoma with 90Y glass microspheres: an earlier administration day unexpectedly improves tumour control probability

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Keywords (3 max): 90Y glass microspheres, TCP, administration day

Abstract

Background and aim: 90Y glass microspheres can be administered after varying decay intervals. We investigated whether shorter intervals improve Tumour Control Probability (TCP) at fixed Tumour Absorbed Dose (TAD).

Methods: We compared lesion response in two cohorts differing only by decay interval (Day 4 vs Day 8), comparing TCP curves also stratified by lesion mass (cut-off 50 g). In totally perfused lesions, we evaluated TAD, spatial density ρ, specific activity as, and mass via univariate and multivariate analyses across CR+PR vs SD+PD, and CR vs PR+SD+PD.

Results: We studied 94 patients (150 lesions). TCP (TAD<600 Gy) was higher for 59 lesions treated on Day 4 than 91 on Day 8. In totally perfused lesions, TCP plateaued at 344 Gy (Day 8) and 160 Gy (Day 4). Considering the totally perfused lesions ROC analysis the CR+PR versus SD+PD classes gave poor AUC values: 0.62, p=0.01 for as, 0.63, p=0.01 for TAD, and 0.60 p=0.01 for M, non-significant for ρ. CR vs PR+SD+PD yielded significance only for M (AUC 0.71, p=0.01). At multivariate analysis, CR+PR gave significance only for as. Considering CR alone, only the significance of mass was confirmed. Our results are in agreement with recent experimental work on complete pathological necrosis but contrast with previously published simulations.

Conclusion: Day8 administration is discouraged. For tumours <50 g treated on Day 4, TAD >160 Gy does not improve OR. Larger lesions benefit from a maximal tolerable activity approach

References: Funded by Boston Scientific

MRI-based dosimetry for image guided ^{166}Ho-TARE, insights in methodology and preliminary results from the EMERITUS-2 trial

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Keywords (3 max): Radioembolization, image guidance, MRI dosimetry

Abstract

Background and aim: The use of dosimetry for transarterial radioembolization (TARE) has uniquely shown to improve patient outcomes. This emphasizes the need for high-precision dosimetry to deliver high tumour doses while sparing healthy liver tissue. However, optimal implementation remains challenging due to low resolution conventional imaging and lack of intraprocedural dose feedback. Holmium-166 microspheres (^{166}Ho-MS) enables rapid, high-resolution (2×2×4 mm³) MRI-based dosimetry. The EMERITUS-2 trial investigated the potential of MRI-guided TARE to safely escalate tumour dose and reduce dose heterogeneity through intra-procedural dosimetric assessment.

Methods: EMERITUS-2 was a phase 1 study in hepatocellular carcinoma patients undergoing TARE. ^{166}Ho-MS were administered in fractions while patients were positioned in an MRI scanner. Dose distribution was evaluated visually and through dose volume histograms after each ^{166}Ho-MS fraction using MRI-based dosimetry. Treatment continued until the normal liver dose limit (40 Gy to max 2/3 of volume) was reached, or tumour coverage was deemed sufficient. Primary endpoints were liver toxicity and dosimetric comparison to conventional whole-liver TARE (60 Gy).

Results: Four patients received mean whole-liver doses of 72–122 Gy (7.8–19.2 GBq). Tumour doses ranged from 133–334 Gy, exceeding conventional estimates (77–297 Gy). ^{166}Ho-MS were administered in 6–11 fractions. Intra-procedural MRI-based dosimetry exposed dose heterogeneity, allowing adjustments to improve tumour coverage. Side effects were mild (grade 1–2 nausea, fatigue, pain), and treatment ended upon reaching liver dose limits or full administration of ordered ^{166}Ho activity.

Conclusion: MRI-guided TARE enables intra-procedural, personalised dosimetry and controlled activity administration, offering a promising step forward in treatment individualisation using dosimetry.

Development of Terbium-161 SPECT/CT Protocols in Support of Two Early-Phase Clinical Trials: Towards Accurate Post-Therapeutic Dosimetry

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Keywords (3 max): Tb-161, NETs, mCRPC

Abstract

Background and Aim: Terbium-161 (^{161}Tb) is a promising therapeutic radionuclide, but its complex photon emission spectrum can complicate SPECT/CT quantification. This abstract summarizes our development of ^{161}Tb dosimetry protocols in two early-phase clinical trials at University Hospital Basel (USB), Switzerland (*1,2*).

Methods: A first SPECT/CT protocol was established at Sahlgrenska University Hospital, Sweden, in 2018 on a GE Discovery 670 Pro NM/CT system (*3*). During 2020–2024, the protocol was refined via phantom studies with standard geometries and 3D-printed inserts, assessing image quality and quantitative accuracy. Based on these results, a dedicated protocol was implemented on a Siemens Symbia Intevo system at USB in 2022, followed by extensive calibration and validation.

Results: Good visual image quality was achieved; however, the radionuclide's broad photon spectrum produced high count rates, and collimator choice strongly affected quantitative accuracy. Low-energy collimation caused septal penetration, further increasing count rates and, in some cases, leading to significant dead-time losses (>10% at 750 MBq for the GE system). A medium-energy collimator with a 75 keV ±10% window mitigated these effects and improved quantitative accuracy (LungSpine phantom w/ spherical inserts, n=24, V=2–8 mL: median error <1.9%, IQR: 0.92–4.8%).

Conclusion: High-accuracy ^{161}Tb SPECT/CT is feasible, but penetration, scatter, and dead-time must be managed, preferably through medium-energy collimation and/or Monte Carlo–based reconstruction, with dead-time correction if necessary. To date, >18 patients have been imaged at USB using the optimized protocol, enabling individualized dosimetry. Ongoing work aims to further improve accuracy and support broader clinical adoption.

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Dosimetry comparison of [^{177}Lu]Lu-rhPSMA-10.1 and [^{177}Lu]Lu-PSMA-617 in prostate cancer patients

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Keywords (3 max): [^{177}Lu]Lu-PSMA, Dosimetry, Radionuclide therapy

Abstract

Background and aim: Prostate-specific membrane antigen (PSMA)-targeting radioligands are increasingly used in prostate cancer therapy. However, differences in binding affinity and kinetics may influence efficacy and safety profiles. Given its relevance for clinical decision-making, this study compares the dosimetry of [^{177}Lu]Lu-rhPSMA-10.1 and [^{177}Lu]Lu-PSMA-617 using a standardized dosimetry protocol and single-center data.

Methods: Sixteen prostate cancer patients were retrospectively included. Eight metastatic castration-resistant patients received 7.4 GBq [^{177}Lu]Lu-rhPSMA-10.1, and eight oligometastatic hormone-sensitive patients received 3 GBq [^{177}Lu]Lu-PSMA-617. SPECT/CT imaging was performed at 4–5 timepoints post-treatment. Kidneys and salivary glands were segmented using a deep-learning tool (nnInteractive), lesions using a 42% thresholding method. Voxel-based dosimetry (Torch, Voximetry) was performed for kidneys and lesions >2 cm. For salivary glands and smaller lesions, absorbed dose (AD) was determined using the MIRD equation with oversized VOIs to correct for partial volume effects. S-values were based on ICRP 89 reference organ masses (salivary glands) or equivalent water spheres (lesions), using PET/CT-based volumes. Group comparisons were performed using the Mann-Whitney U test.

Results: The findings are illustrated in Figure 1. Kidney and lesion ADs were not significantly different between [^{177}Lu]Lu-rhPSMA-10.1 and [^{177}Lu]Lu-PSMA-617 (kidneys: 0.84 vs. 0.93 Gy/GBq, p=0.587; lesions: 2.36 vs. 3.49 Gy/GBq, p=0.425). The median salivary glands AD was significantly lower for [^{177}Lu]Lu-rhPSMA-10.1 (0.06 vs. 0.33 Gy/GBq, p=0.002).

Conclusions: [^{177}Lu]Lu-rhPSMA-10.1 demonstrated a significantly lower salivary gland AD compared to [^{177}Lu]Lu-PSMA-617, while achieving comparable kidney and lesion dosimetry. These findings suggest that rhPSMA-10.1 may offer a more favorable safety profile, particularly regarding salivary gland toxicity, without compromising tumor targeting.

Supporting figure / Table

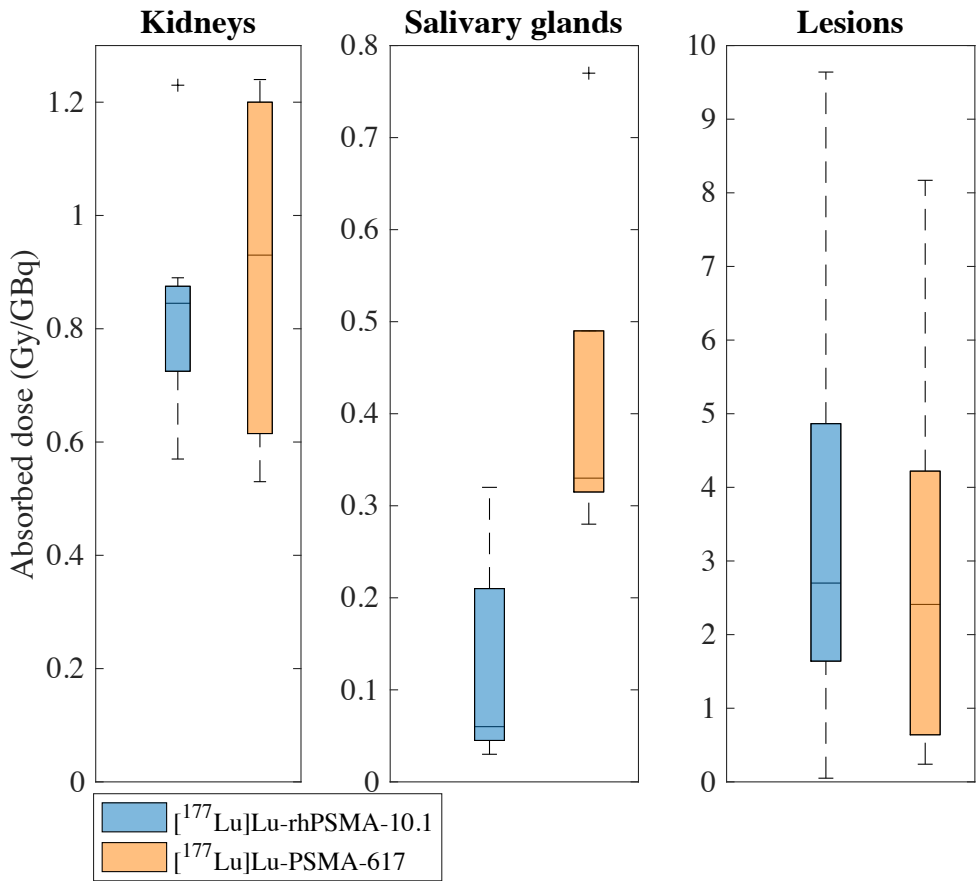

Figure 1: Boxplot showing the absorbed dose (Gy/GBq) for [^{177}Lu]Lu-rhPSMA-10.1 and [^{177}Lu]Lu-PSMA-617 in kidneys, salivary glands, and lesions.

Standard vs. kidney dosimetry-based activity prescription in PRRT: Current status of the DOBATOC trial

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Keywords (3 max): PRRT, DOTATOC, trial

Abstract:

Background and aim: The DOBATOC trial (ClinicalTrials.gov *NCT04917484*; CTIS *2024-517240-62-00*) is an ongoing prospective, randomized phase II trial for patients with progressive or symptomatic neuroendocrine neoplasms (NEN) referred for peptide-receptor radionuclide therapy (PRRT) at Aarhus University Hospital.
Patients are randomized 1:1 to either a standard treatment (4 treatment cycles of 7.4 GBq Lu-177 DOTATOC) or an experimental treatment (4 cycles with kidney dosimetry-based activity prescription). Here we present the protocol design and preliminary results for the first 50 patients included out of the 100 patients planned.
Methods: Kidney dosimetry in the experimental arm is based on 3 post treatment SPECT/CT scans for each cycle. We aim to reach a kidney biological effective dose up to 27 Gy by injection of up to 20 GBq Lu-177 DOTATOC in the first treatment cycle and up to 25 GBq in the following cycles.
Blood samples for biochemistry analyses are drawn every 2nd week after every treatment cycle. Renal function is monitored using Tc-99m DTPA clearance measurements (GFR) at baseline and after the treatment series, and by eGFR between treatments. Response or progression is evaluated by contrast-enhanced CT and Ga-DOTATOC PET/CT scans.
Results: The trial design will be presented along with preliminary results on prescribed activity, kidney dose and toxicity for the first 50 patients included in the study.
Conclusion: The current status is presented for the prospective randomized DOBATOC trial for the study of a kidney dosimetry-based treatment vs. a standard treatment with Lu-177 DOTATOC for PRRT of patients with NEN.

Tumour-to-kidney absorbed dose ratios for potential alpha-emitter DOTATATE therapies

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Keywords (3 max): Alpha, PRRT

Abstract

Background and aim: Kidney and tumour absorbed doses (ADs) may be simulated for potential alpha-emitter somatostatin receptor therapies by using biokinetics of patients receiving [^{177}Lu]Lu-DOTATATE and modelling daughter redistribution. Here, we estimate tumour-to-kidney AD ratios for ^{225}Ac, ^{227}Th, ^{212}Pb, ^{230}U, ^{226}Ac, ^{211}At, and ^{149}Tb DOTATATE therapies.

Methods: SPECT/CT images and probe measurements of 9 patients receiving ^{177}Lu-DOTATATE were analysed to estimate tumour, kidney, and whole-body time integrated activities (TIAs) and uptake and clearance rates. The time-activity curves were adjusted for the physical half-lives of potential radionuclides for targeted alpha therapy. Daughter redistribution was modelled according to ICRP biokinetic models in Simbiology (MATLAB v2023b, MathWorks), assuming all daughters were released for alpha decay, and 36% for beta decay. Release of daughter radionuclides from tumours were modelled at two different rates, corresponding to the fast and slow clearance rates of other soft tissues in the biokinetic models.

Results: The different tumour daughter release rates minimally impacted the ^{230}U and ^{226}Ac tumour AD estimates, but slow tumour daughter release strongly increased ^{225}Ac, ^{227}Th, and ^{212}Pb tumour ADs. Variation in the tumour-to-kidney AD ratios (Figure 1) increased with parent physical half-life, as the individual patient kinetics played a larger role. The inter patient variation may be attributed to the simplified tumours mass estimate, but this did not affect the difference between radionuclides.

Conclusion: The longer physical half-life radionuclides may be more beneficial for alpha-emitter DOTATATE therapies, but this is only with regards to kidney AD and our chosen kinetic models.

Supporting figure / Table (optional)

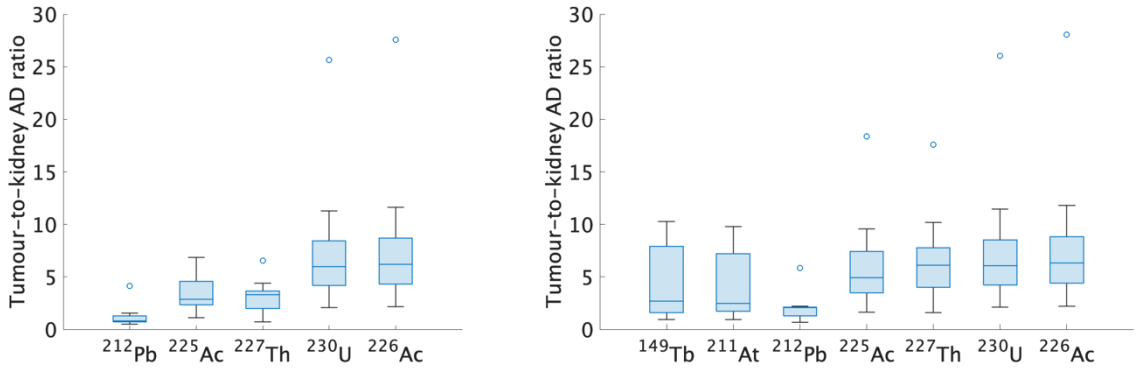

Figure 1: Tumour-to-kidney AD ratios for with the fast and slow daughter clearance from tumours on the left and right, respectively. Daughter redistribution was not modelled for ^{149}Tb and ^{211}At

PRRT Efficacy of ^{111}In-DTPA-Octreotide Auger and Internal Conversion Electron Emission after Intra-arterial Implementation in Liver Metastasized Colorectal NETs

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Introduction: Colorectal NETs less commonly metastatic but whenever present, survival is mediocre. Evidence guiding optimal treatment is practically lacking. We aimed to evaluate the efficacy of ^{111}In-DTPA-Octreotide Auger and Internal Conversion Electron Emission by assessing PRRT outcomes in patients with somatostatin receptor (SSTR) positive liver metastasized colorectal NETs.
Patients and Methods: Eleven patients (m=3, f=8, age range 49-79 years) included in the study had ^{111}In-DTPA-Octreotide avid disease (visual score IV). Morphologic (RECIST 1.1), SSTR imaging responses and toxicity were assessed, three-monthly post-PRRT. Kaplan-Meier estimate was used to determine progression-free survival (PFS) and overall survival (OS) from the beginning of the therapy. ^{111}In-DTPA-Phe^{1}-Octreotide was implemented after selective catheterization of the hepatic artery, in an average activity of 6.3±1.3 GBq per patient/per session, consecutively, with a time interval between sessions of 6-8 weeks. Infusion repetition did not exceed the 12 fold.
Results: None of the patients resulted in complete response. Partial response was assessed in eight (72.72%), disease stabilization in one (9.10 %) and progressive disease in two (18.18%). The median PFS and OS were 36 and 48 months, respectively. The organ average radiation dose was: (a) Liver Tumor 15.2 mGy/MBq, (b) Liver 0.14 mGy/MBq, (c) Kidneys 0.41 mGy/MBq, (d) Spleen 1.4 mGy/MBq and (f) Bone marrow 0.0032 mGy/MBq. A WHO toxicity grade 1 to 2 erythro-, leuko- and thrombocytopenia occurred in 9 (81.81%) cases observed about after the 9th session.
Conclusion: The high efficacy of ^{111}In-DTPA-Octreotide Auger emission due to high LET, results in minimal toxicity and encouraging survival in metastatic colorectal NETs, despite their mediocre prognosis.

Session 3: Software for patient dosimetry

A Joint EANM/EFOMP Dosimetry Tender Document for Software Evaluation and Procurement

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Keywords (3 max): dosimetry, software, tender

Abstract

Background and aim: As molecular radiotherapy continues to expand, there is increasing interest in the use of commercial software to meet regulatory expectations for personalised dosimetry. The expanding portfolio of available tools offers a wide range of capabilities, making it challenging for departments to identify software that aligns with their clinical, research, and operational needs. A structured and consistent approach to software evaluation is needed to support informed procurement.

Methods: A modular tender document has been developed jointly by members of the EANM Dosimetry Committee and EFOMP's Special Interest Group for Radionuclide Internal Dosimetry. This includes detailed, structured tender questions across key domains: hardware requirements, software environment, data input, application scope, image reconstruction, activity quantification, image registration, segmentation, data integration, and dosimetric calculations. Additional sections cover data output and practical usability. The questions are designed to be vendor-neutral and reflect the breadth of dosimetry software currently available.

Results: The completed tender document allows potential users to clearly define their requirements and enables vendors to transparently describe the functionality of their solutions. It will help departments understand the clinical, operational, and financial implications of different software features, supporting effective and context-appropriate decision-making.

Conclusion: By introducing a standardised framework for comparison, this initiative addresses a significant gap in current practice and supports broader efforts to adopt dosimetry in clinical workflows. Following consultation with vendors and stakeholders, a final guide and template will be published via the EANM in late 2025, with periodic updates to reflect technological advances and emerging standards.

Comparison of dosimetric assessments in 90Y-MICROSPHERE THERAPY IN HCC: preliminary results

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Keywords: 90Y-microsphere, dosimetry, HCC

Background and aim: To compare dosimetric assessments obtained by an in-house developed spreadsheet (IHDS) with a certified treatment planning system and a worksheet provided by a scientific committee, for radiometabolic treatments with 90Y-microspheres (RMT90Y).
Methods: HCC patients referred for RMT90Y were simulated by selective injection of 99mTc-MAA activity into the hepatic artery, followed by whole-body, SPECT and CT imaging. The datasets were used to assess tumor and healthy liver doses by using: the certified treatment planning system Voxel Dosimetry (Hermes, Sweden) (TPS), the calculation worksheet MIRDy90 (MIRD) and IHDS, the latter two systems based on two-compartmental model and MIRD formalism. 1GBq 90Y-microspheres was assumed to be administered to all the patients. TPS tumor and healthy liver doses were assumed as references for comparison with those evaluated by MIRD and IHDS, by means of Bland-Altman analysis as difference versus mean.
Results: 15 patients were evaluated, mean tumor volume was 285 [37; 1057]ml. Bias and limits of agreement of MIRD comparison with respect to TPS tumor and healthy liver doses were -30 [-125; 66]Gy and -1 [-7; 5]Gy, respectively. Bias and limits of agreement of IHDS comparison with respect to TPS tumor and healthy liver doses were -27 [-122; 67]Gy and -2 [-7; 4]Gy, respectively.
Conclusion: IHCS and MIRD demonstrated acceptable agreement with TPS in estimating tumor and healthy liver doses in HCC patients undergoing RMT90Y. Despite an underestimation trend, discrepancies remained within clinically reasonable limits. IHDS and MIRD demonstrated comparable performance, supporting their use as practical alternatives when TPS is unavailable.

Salivary Gland Dosimetry for Patients Receiving Lu-177 PSMA and I-131 NaI: An Impact Analysis of Differing Dosimetry Approaches and Software Solutions

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Keywords: Salivary, software-evaluation, comparison

Background and Aim: The aim of this study is to compare salivary gland dosimetry for patients undergoing treatment with radioiodine for thyroid cancer and Lu-177 PSMA for metastatic prostate cancer. A critical side effect of both therapies is unintended irradiation of the salivary glands, which can lead to varying degrees of xerostomia. The goal of this study is to evaluate different dosimetry software and methods, specifically those based on the Medical Internal Radiation Dose organ-level approach and voxel-based methods, focusing on their uncertainties and clinical applicability.
Methods: Preliminary data analysis has been performed using several dosimetry tools, both in-house and commercial. Organ level dosimetry was performed using an Excel-based spreadsheet, Hermes Organ dosimetry and DoDose (an in-house Python module within 3D Slicer). Voxel dosimetry was performed using Hermes Voxel dosimetry and a voxel module of DoDose. Both Hermes and DoDose voxel software also included options to use organ level fitting in a voxel level workflow.
Results: Preliminary results indicate variability in salivary gland dose estimates. Average ± SD absorbed doses to the salivary glands for Lu^{177}-PSMA when calculated at the organ level were 4.18±1.88Gy using the in-house spreadsheet, 2.76±1.55Gy using Hermes and 3.39±1.15Gy using DoDose. When using a voxel workflow, absorbed doses were 3.41±0.95Gy (Hermes) and 3.15±1.10Gy (DoDose). Hybrid workflows provided doses of 2.91±0.87Gy (Hermes) and 4.56±1.22Gy (DoDose).
Conclusions: Ongoing analysis aims to identify the most accurate and practical approach for clinical implementation, with recommendations to improve standardisation and reduce uncertainty in salivary gland dosimetry. Phantom validation studies are planned to further assess method accuracy.

Clinical application of PLANET® Dose V3.2 on Single-Time-Point dosimetry in patients treated with [^{177}Lu]Lu-DOTA-TATE

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Keywords (3 max): single-time-point dosimetry, molecular radiotherapy

Abstract

Background: An absorbed dose-effect correlation was observed for [^{177}Lu]Lu-DOTATATE treatments in patients with neuroendocrine tumours, using a four-time-point (4TP) dosimetry protocol. However, reducing the number of time points would ease the workload and patient burden. Simplified approaches such as single-time-point (STP) dosimetry should therefore be investigated. This study examines the feasibility of implementing STP dosimetry using patient-specific pharmacokinetics from the first cycle.

Methods: For 25 patients, 4TP dosimetry was performed for the first and second treatment cycles, using PLANET® Dose V3.2 (Dosisoft, Cachan, France) with images acquired at 4, 24, 72, and 192 hours post-injection. For the second cycle, two STP-based approaches were then evaluated and compared with the 4TP reference results.

The first approach used the 4TP-absorbed dose from the first cycle, scaled by the volume-to-total counts ratio at 24 hours from both cycles. The second approach used the STP tool of ANET® Dose to assign pharmacokinetics from the first cycle to a single point at 24 or 72 hours.

Results: At 24 hours, the second approach showed smaller deviations from 4TP dosimetry than the proportional scaling approach. However, the best agreement was obtained with the second approach at 72 hours, with relative differences below 9% for liver and kidneys, and up to 20% for spleen and tumours.

Conclusion: STP dosimetry offers logistical advantages. This study shows it can yield results in good agreement with MTP dosimetry. Further research is needed to confirm whether absorbed dose–effect relationships are preserved.

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Budiansah et al. EJNMMI Phys 2025 12.26

A Proposition of a Modular Digital Twin Pipeline for Dosimetry Protocol Optimization in Molecular Radiotherapy

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Keywords (3 max):

Abstract

Background and aim: Accurate and standardized dosimetry represents a major challenge in molecular radiotherapy (MRT). This work introduces a modular digital twin pipeline for the dosimetry process, enabling *in silico* optimization of protocols and standardization of dosimetry practices.

Methods: The current pipeline includes 3 core modules: (1) Anatomical, which generates a patient-specific anatomical model using CT acquisitions, registered to the anthropomorphic digital model XCAT; (2) Functional, which integrates advanced PBPK (Physiologically-Based Pharmacokinetic) models to simulate activity distribution based on patient-specific parameters and SPECT/PET acquisitions; (3) Virtual clinical trials, which simulates clinical-like images and absorbed dose maps. These modules form an interoperable workflow, where each component can be updated or refined independently.

Results: Preliminary implementation demonstrates feasibility across all modules. The fitting operation of the functional module parameters still needs to be tuned. Full validation is ongoing, focusing on replicating clinical workflows. As shown in Figure 1, this will enable the assessment of dosimetry protocols through sensitivity analyses, allowing the evaluation of the impact of parameter variations on absorbed dose calculations. The digital twin can also serve as a common ground truth for multi-center studies, facilitating protocol harmonization across centers.

Conclusion: The digital twin pipeline offers a scalable and modular benchmark test for MRT dosimetry optimization, combining anatomical and pharmacokinetics modeling to generate virtual clinical trials. By providing a shared ground truth and the ability to modify key parameters, it supports personalized treatment planning, multi-center validation, and standardization of clinical practices.

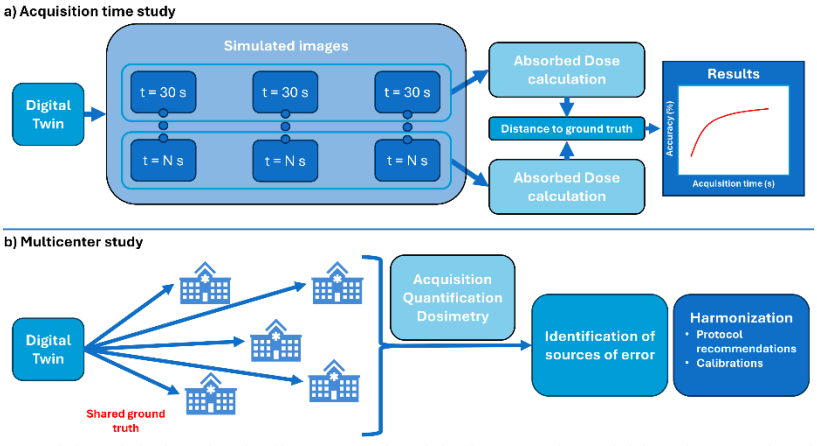

Figure 1 : Potential uses of the Digital Twin pipeline. a) Study of the impact of acquisition time on absorbed dose calculation. b) Using the Digital Twin as a common ground truth to assess the impact of variations in clinical practices on absorbed dose calculations

Development of a Bayesian network for a comprehensive uncertainty assessment in personalized dosimetry after targeted radionuclide therapy

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Keywords (3 max): Bayesian network ; uncertainty ; Lu-PSMA

Abstract

Background: To develop an innovative method enabling a comprehensive uncertainty budget associated to personalized absorbed doses for ^{177}Lu-PSMA therapy and providing probability distributions of all dosimetric quantities, particularly for lesions which may be characterized by a high uncertainty on their estimated volume.

Methods: In Targeted Radionuclide Therapy (TRT), three measurable and input variables contribute to the uncertainties on the final dose estimate: the calibration factor of the gamma camera, the count rate inside the lesional or healthy tissue measured on patient's images, and the anatomical volume of this tissue. Uncertainties associated with the input variables were evaluated notably by sensitivity analysis. A Bayesian Network (BN) was developed to propagate these uncertainties to the computed absorbed dose, using deterministic or probabilistic relationships between variables involved in the dosimetric workflow. The uncertainty on each dosimetric estimate was defined as the standard deviation of the corresponding probability distribution generated by the BN.

Results: Results were obtained for 707 individual metastases after the first ^{177}Lu-PSMA cycle of 18 patients from 2 hospitals. For these lesions with a median volume of 1.9 mL, uncertainties on absorbed dose ranged from 20% to 110%. The BN enabled to quantify that the uncertainty on the lesion volume contributes mainly to the uncertainty on the absorbed dose.

An innovative BN has been developed to evaluate the uncertainties on personalized absorbed doses in TRT. The obtained result for 707 lesions showed that dose uncertainties can reach more than 100% and should be essential to refine dose-effect relationships in TRT.

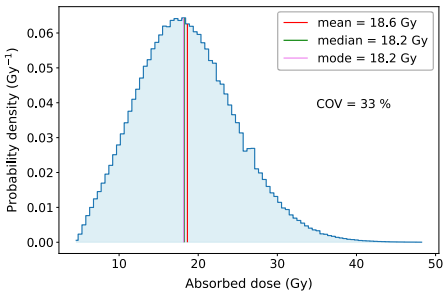

Figure title: Probability distribution of the absorbed dose obtained from the Bayesian network for a lesion treated by ^{177}Lu-PSMA. The Coefficient Of Variation (COV) is the relative standard deviation of the distribution.

MIRDrpt simplified dosimetry and bioeffect modelling for ^{177}Lu (-DOTATATE and -PSMA) – a standardized dosimetry calculation toolkit

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Keywords (3 max): Lu-177; dosimetry; standardization

Abstract

Background: Patient-specific dosimetry is essential for optimizing radiopharmaceutical therapy (RPT), yet widely adopted standardized protocols remain scarce. MIRDrpt, a modular toolkit developed within the MIRDsoft suite, delivers a reproducible end-to-end workflow for calculating absorbed doses (AD), biologically effective dose (BED), and equieffective doses (EQDx) in ^{177}Lu-DOTATATE/PSMA treatment settings.
Methods: MIRDrpt, an organ-level dosimetry worksheet tailored to specific RPTs, supports single-/multi-timepoint dosimetry for liver, kidneys, spleen (LKS), salivary glands (PSMA only), bone marrow (BM; blood-/image-based), and ≤ 5 tumors. Upto five SPECT/CT timepoints and ten ex-vivo blood measurements per administration are accommodated. Automated best time-activity fits (trapezoidal, mono-, bi-exponential) driven by Akaike information criterion generate time-integrated activity coefficients (TIAC) that feed mass-scaled S-values. Recovery-coefficient–partial-volume correction and sphere-model tumor self-doses are optionally included. BED/EQDx are derived from dose-rate curves with default or user-configurable α/β and repair constants. Validation of ^{177}Lu-DOTATATE (first in MIRDrpt series) used 53 treatment cycles from Hadassah Medical Center, containing multiple (1–8d) SPECT/CT imaging (LKS segmented) and two blood samples for BM dosimetry.
Results: MIRDrpt computes tumour TIACs, AD, BED, and EQDx, from typical post-treatment data. In 53 ^{177}Lu-DOTATATE cycles, MIRDrpt reproduced TIACs and AD within 6% for LKS. BM TIAC/AD differed by ~17%, reflecting ~18 % difference in assumed marrow masses.
Conclusion: MIRDrpt offers a validated, freely available platform for standardized dosimetry of ^{177}Lu-based RPT, suitable for independent calculations or benchmarking. Preliminary implementation for ^{177}Lu-PSMA is underway. Future expansions, pending MIRD Committee endorsement, will extend this framework to additional radiopharmaceuticals, fostering community-wide consistency and traceability in personalized dosimetry.

Supporting figure / Table (optional)

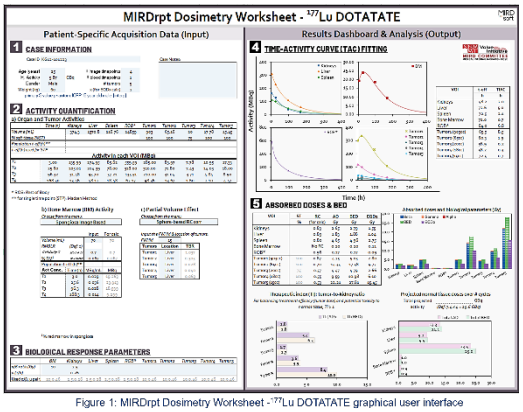

Figure 1: MIRDrpt Dosimetry Worksheet - ^{177}Lu DOTATATE graphical user interface

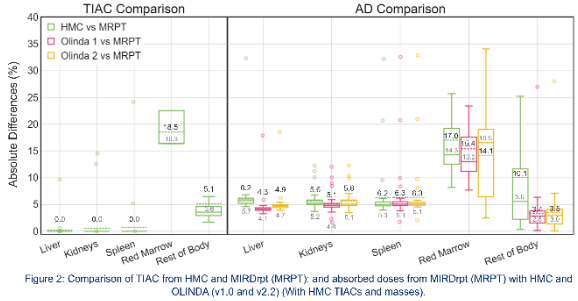

Figure 2: Comparison of TIAC from HMC and MIRDrpt (MRPT): and absorbed doses from MIRDrpt (MRPT) with HMC and OLINDA (v1.0 and v2.2) (With HMC TIACs and masses).

Difference % = (XX-MRPT)/MRPT XX = OLINDA v1.0, OLINDA v2.2, HMC. The solid and dashed horizontal lines in the box plot represents the median (text in grey) and mean (text in black) values, respectively.

OpenDose Core: a library for implementing model-based internal dosimetry calculations

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Keywords (3 max): internal dosimetry software

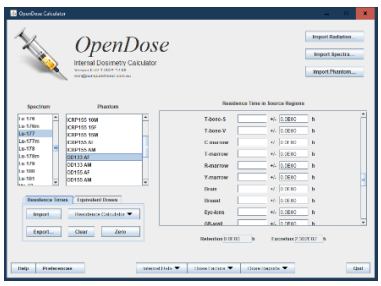
Abstract:

Background and aim: The OpenDose collaboration is developing several applications requiring internal radiation dose calculations, including a flexible desktop dose calculator application, a web site providing reference dosimetry based on specific absorbed fractions (SAFs) calculated by collaboration members and a general purpose image-processing platform used for generating validation data for image-based internal dosimetry workflows. To simplify development and testing, this core functionality is implemented in a single library to be included in each separate project.

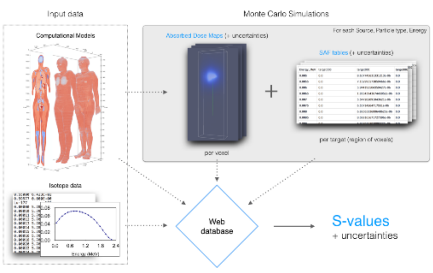
Methods: The ocd.jar library is written in Java and uses JSON for data storage and exchange. It performs internal dose calculations using the MIRD scheme, by combining absorbed fractions and emission spectra to create dosimetry models, then using these to calculate equivalent dose to model targets due to radioactivity in model sources. Calculations are performed on values with user-specified uncertainties. The library includes utility functions to build models from user-supplied data. It also provides a command line interface (CLI) supporting end-user validation.

Results: Test scripts supplied with the library use the CLI to evaluate user-defined test cases for calculation of dose factors (S-values), and absorbed, equivalent and effective dose distributions. Extensive spreadsheet calculations are used to generate data for test cases, which are packaged by utility scripts as JSON files defining test inputs and expected outputs.

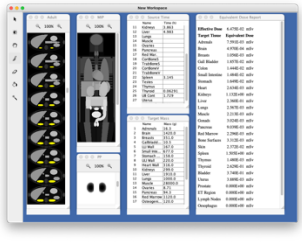
Conclusion: A library implementing internal radiation dose calculation has been developed and incorporated into several OpenDose software projects. The distribution includes tools for users to construct and evaluate their own test cases.



OpenDose Calculator



OpenDose Web Database


OpenDose Workbench

The OpenDose 3D Roadmap

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Keywords (3 max): OpenDose 3D, personalised dosimetry

Abstract:

Background and aim: *OpenDose 3D* is a free, open-source software for image-based dosimetry in nuclear medicine. Its active community drives continuous development and roadmap definition.

Methods: Five new key features were developed and validated.

1) **CT calibration tool:** Generates scanner-specific HU-to-density curves from CIRS.062 phantom automatic segmentation. Validation was performed on CT images at 120 kV and 140 kV (2.5 mm).
2) **Tumour segmentation module:** Generates VOIs in functional images based on volumes defined in anatomical images. The module was tested on a patient with a range of tumours from 2.05 to 20.95 cm³.
3) **Voxel-level time integration** performed within SingleTime-Point approaches allows the creation of voxel-based absorbed dose (AD) maps and Dose-Volume Histograms.
4) **Radiobiological indices** are now available, such as the Biological Effective Dose (BED). These 2 modules were tested on an anthropomorphic phantom (5220-RS800T) during the development of external/internal radiotherapy combination.
5) **Reporting function:** Generates PDF reports with workflow information and results per-VOI

Results: For 120 kV and 140 kV, HU-density curves were generated and tested against experimentally-obtained values and the calibration of HU CT units for radiotherapy (Schneider *et al.,* 1996). Tumour segmentation yielded <1% relative difference with known volumes (2.07 to 20.94 cm³). Voxel-based absorbed dose maps, BED, and DVHs were generated and yielded consistent results. Reports are now integral parts of OpenDose3D processing. The amount of information generated can be adjusted in the settings.

Conclusion: These developments will be integrated into OpenDose3D next stable release. Suggestions from users are welcome to plan further implementations.

References:

Schneider *et al.* Phys Med Biol. 1996 41(1):111-24.

Session 4: Absorbed dose effect relationships

Correlation between absorbed dose and response in thyroid cancer patients treated with radioiodine – A systematic review

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Keywords (3 max): Thyroid, Radioiodine, Systematic Review

Abstract

Background and aim: Treatment response of radioiodine therapy for thyroid cancer patients should correlate with the absorbed doses delivered to targets, the thyroid remnants or metastatic disease. Nevertheless, the majority of treatments are still performed using empiric activity levels. The aim of the present work was to perform a systematic review and meta-analysis of absorbed dose and outcome for thyroid cancer patients treated with radioiodine.

Methods: The study was registered with PROSPERO (CRD42024554956). PubMed, Web of Science and OVID MEDLINE were searched for studies reporting both the absorbed doses delivered and treatment outcome.

Results: The database search identified 3621 studies. 17 were deemed eligible for analysis. The remnant ablation publications included a total of 1138 patients, while the combined metastatic patient cohort was smaller with only 214 patients. A delivery of at least 300Gy and 80Gy to thyroid remnants and lesions, respectively, resulted in success rates of 78% to 96% and 46% to 98%.

Conclusion: Individual studies have demonstrated relationships between absorbed doses delivered and outcome from radioiodine for differentiated thyroid cancer. Nevertheless, no conclusive absorbed dose effect relationship could be established in the present systematic review. We hypothesise that a lack of standardisation and validation of dosimetry methodologies and differences in follow-up criteria in the studies result in this obscured relationship. It is proposed that large-scale observational prospective studies are required to determine the absorbed doses required for successful personalised treatments of thyroid cancer patients with radioiodine.

Mechanistic Prediction of Nephrotoxicity in Radiopharmaceutical Therapy Using a Preclinical Nephron Substructure NTCP Model

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Keywords (3 max): Nephrotoxicity, absorbed dose-effect relationships

Abstract

Background and aim: Nephrotoxicity is a dose-limiting factor in radiopharmaceutical therapy (RPT), especially as RPT is integrated earlier into treatment regimens. Current kidney absorbed dose thresholds, extrapolated from external beam radiotherapy (EBRT), do not account for RPT-specific absorbed dose heterogeneity, dose rate effects, or substructure-level radiosensitivity. We developed a mechanistic normal tissue complication probability (NTCP) model incorporating substructure-specific dosimetry and radiobiology at the nephron level.

Methods: The model calculates nephron substructure survival based on absorbed dose to glomeruli and proximal tubules (PT) with the Linear-Quadratic formalism. Absorbed doses to nephron substructures were calculated with a previously developed nephron substructure-level dosimetry framework. Whole-nephron survival was calculated with the weighted survival of the substructures based on their functional relevance. Individual nephron survival probabilities was aggregated into kidney-level NTCP using a relative seriality NTCP formulation. Parameters were fitted using preclinical nephrotoxicity data for [^{177}Lu]Lu-DOTA-TATE.

Results: The model showed good agreement between NTCP predictions and observed histopathology (R^2 = 0.97). Sensitivity analysis revealed glomerular radiosensitivity and the seriality parameter as dominant contributors to predicted NTCP. Model robustness was validated using a stochastic nephron-level simulation and an independent dataset of radiolabeled folate-receptor targeting cm09 nephrotoxicity data. The model accurately predicted substructure-specific injury and whole-kidney toxicity.

Conclusion: The developed framework enables radiobiological NTCP prediction under RPT-specific conditions and may support the refinement of absorbed dose limits by accounting for heterogeneous nephron response to irradiation. While developed using murine data, the model is conceptually adaptable to clinical translation through incorporation of patient-specific substructure dosimetry and correlation to nephrotoxicity.

Semi-Quantitative I-123 SPECT Suggest Subtherapeutic Absorbed Dose in Recurrent Thyroid Cancer Patients and Highlight Need for Individualized I-131 Therapy

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Keywords (3 max): radioiodine, dosimetry, SPECT

Abstract

Background and aim: While most patients with differentiated thyroid cancer (DTC) have favorable outcomes, those with distant metastases may become refractory to iodine uptake, thus resulting in sub-tumoricidal absorbed doses from conventional I-131 treatment. This study aimed to extend prior work on personalized dosimetry-based combined I-131-EBRT therapy (n=5) by retrospectively estimating I-131 uptake and absorbed dose in a larger cohort using a semi-quantitative I-123 SPECT method in patients with recurrent DTC.

Methods: Imaging and clinical data were retrieved from institutional PACS and electronic health records. Lesion volumes of interest (VOIs) were contoured on ^{123}I SPECT/CT. SPECT counts were measured in lesion VOIs, whole-body regions (normalized to patient weight), and background. Lesion-to-whole-body count ratios were then scaled to a conventional therapeutic activity (5.55 GBq; 150 mCi). Time-integrated activity coefficients (TIACs) were derived by applying pharmacokinetic curves from the prior I-131 multi-timepoint SPECT/CT cohort to the I-123 24-hour uptake data. TIACs were input into MIRDCALC v1.22 to estimate lesion self-absorbed dose.

Results: Eighteen patients included 22 analyzable lesions. Only a minority (n=2) approached the tumoricidal threshold of 80 Gy (Maxon et al.). Median lesion volume was 13.3 ml (range 7.7–49.0 ml), median TIAC was 0.28 hr (range 0.03–11.54 hr), and median absorbed dose was 8.6 Gy (range 1.6–313.6 Gy).

Conclusion: Absorbed dose and TIAC varied widely across lesions, revealing limitations of fixed-activity, single modality I-131 treatments. Most lesions received subtherapeutic doses. These findings support the need for patient- and lesion-specific dosimetry to optimize therapeutic efficacy. Ongoing analysis will explore correlations with biomarkers and clinical outcomes.

Supporting figure / Table

Table 1: Summary of patient-specific parameters and calculated activity and absorbed dose

	Lesion size (ml)	Fraction of Activity in Tumor (-)	Tumor Activity Assumed at 24 h (mCi)	Tumor TIAC (Hr)	Absorbed dose (Gy)
Min	7.7	5.52E-04	0.03	0.03	1.59
Max	49.0	1.98E-01	10.72	11.54	313.58
Mean	17.8	1.82E-02	0.99	1.06	35.87
Median	13.3	4.86E-03	0.26	0.28	8.55

Are Trabecular Bone Volume and Trabecular Metabolic Activity on [18F]FDG PET/CT predictive of Hematological Toxicity in PSMA Therapy?

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Keywords (3 max): Bone marrow, toxicity, 177Lu-PSMA

Background and Aim: This exploratory study aimed to determine whether [18F]FDG PET/CT examinations could predict haematological toxicities in patients with metastatic castration-resistant prostate cancer (mCRPC) prior to treatment with [177Lu]Lu-PSMA.

Methods: We selected 45 mCRPC patients between July 2022 and March 2025 who underwent [18F]FDG PET/CT scans as part of pre-treatment assessment before receiving [177Lu]Lu-PSMA therapy. The TotalSegmentator plugin in 3DSlicer was used to segment the entire skeleton on CT images; the trabecular bone was extracted using Hounsfield unit thresholding and morphological operations. For each patient, we calculated the percentage of trabecular bone (percent_trab) and the mean standardized uptake value (SUVmean) in trabecular structures on the [18F]FDG images. The median SUVmean (SUV_BM) across all trabecular structures was determined. Haematological toxicities were graded following CTCAE v5 and correlated with percent_trab and SUV_BM.

Results: Seven patients developed grade 3 (G3) anaemia or thrombocytopenia, with four experiencing both. No leukopenia was observed in our population of patients. Spearman correlation coefficients between percent_trab and G3 toxicities were -0.512 ($p<0.001$) for anaemia and -0.433 ($p=0.003$) for thrombocytopenia. Correlations between SUV_BM and G3 toxicities were +0.373 ($p=0.012$) and +0.436 ($p=0.003$) for anaemia and thrombocytopenia, respectively.

Conclusion: These preliminary results suggest that trabecular bone assessment based on CT images may help predict G3 haematological toxicity in mCRPC patients treated with [177Lu]Lu-PSMA therapy. As few G3 events occurred in this cohort, further data collection is ongoing to validate these encouraging findings.

Personalized dosimetric workflow for ^{177}Lu-PSMA treatments considering the cross-irradiation from bone metastases to red bone marrow

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Keywords (3 max): Lu-PSMA ; red bone marrow ; Monte Carlo

Abstract

Background and Aim: This work aimed at developing an innovative workflow for ^{177}Lu-PSMA personalized dosimetry to lesions and organs at risk (OAR) simultaneously, considering the cross-irradiation from bone metastases to red bone marrow, especially for patients with a high skeletal tumor burden.

Methods: Patients were treated for a metastatic castration-resistant prostate cancer with approximately 7.4 GBq of ^{177}Lu-PSMA. Biokinetics in lesions and OAR was assessed using 3 SPECT/CT images acquired at about 4h, 24h and 6 days post-injection. Since bone metastases are often numerous and difficult to identify on CT, they were delineated using an in-house adaptative thresholding algorithm on SPECT/CT images. Absorbed doses were estimated by Monte Carlo simulation in a realistic model of the patient, and contribution of cross-fire radiation from bone lesions to red bone marrow was also evaluated.

Results: Absorbed doses were obtained for 707 individual lesions after the first ^{177}Lu-PSMA cycle of 18 patients from 2 hospitals, ranging from 0.04 to 48 Gy/GBq (median: 2 Gy/GBq). In addition, absorbed doses to red bone marrow were between 0.01 Gy and 0.3 Gy/GBq (median: 0.03 Gy/GBq), and bone metastases cross-irradiation contributed significantly (p-value = 4e-6) from 0.5% to 57% of these dose values.

a) These results indicate the possibility to perform a comprehensive and personalized computation of absorbed dose to lesions and OAR. Furthermore, this workflow allows consideration of bone lesion contribution to the red bone marrow dose, which might be non-negligible especially in presence of a high skeletal tumor burden as often observed for ^{177}Lu-PSMA patients.

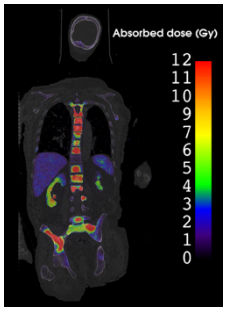

Figure title: Coronal slice of the absorbed dose map for a patient after the first ^{177}Lu-PSMA cycle.

Bone marrow patient-specific dosimetry for [^{177}Lu]Lu-DOTA-TATE therapy

Susana Veloza-Awad[1, 2, 3, 4] , José A Fragoso-Negrín[1, 2, 3], Aristida Adjalla-Vignikin[1, 2], Kevin Hébert[1], Emmanuel Deshayes[1, 2], Jean-Pierre Pouget[2], Pierre-Olivier Kotzki[1, 2], Stephan Nekolla[4], Manuel Bardiès[1, 2], Lore Santoro[1, 2]

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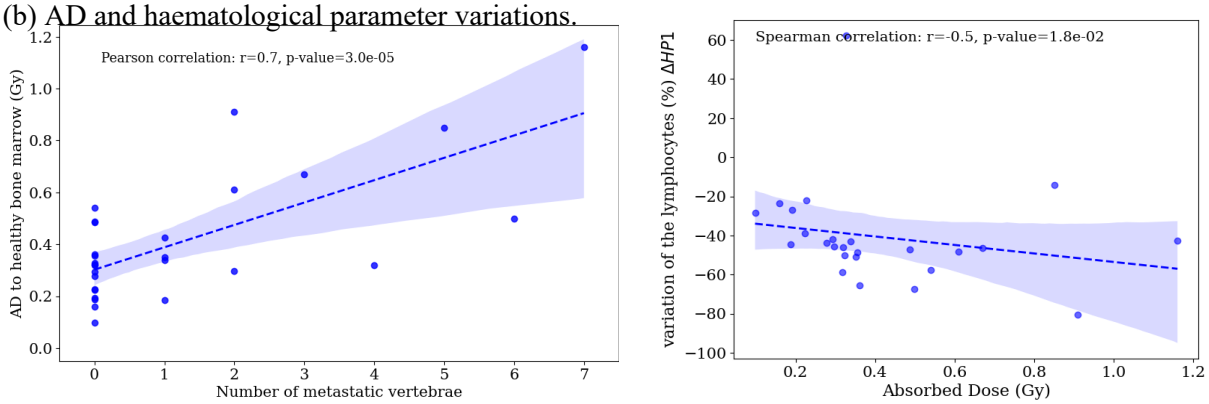
Keywords (3 max): bone marrow, patient-specific dosimetry

Abstract:
Background and aim: In molecular radiotherapy, bone marrow (BM) is an absorbed dose-limiting organ [1]. This study evaluates the impact of segmentation strategies on BM absorbed dose (AD) and the influence of AD on clinical outcomes.
Methods: We analysed 28 patients treated with [^{177}Lu]Lu-DOTA-TATE from 2016 to 2023 [2]. 4 SPECT/CT images from the first treatment cycle were used.
Each vertebra was classified as healthy or metastatic. AD was analysed per vertebra, and correlations were assessed between: (a) number of vertebral metastases and AD to healthy BM; (b) AD and haematological parameter variations.
Patients were grouped based on the location of metastases, and ADs were compared across a range of vertebral volumes of interest (VOIs).
Fully patient-specific dosimetry was performed using OpenDose3D. The study was approved by the local ethics board (ICM-ART 2025/12).
Results: ADs higher than 1.6 Gy (up to 8 Gy) were found in vertebrae affected by metastasis; healthy BM remained below 0.6 Gy. VOI definition (L2-L4, lumbar and/or thoracic vertebrae in the field of view) did not impact the average BM AD. A strong positive correlation (r = 0.7) was found between the number of metastases and *healthy* BM AD; a moderate negative correlation (r = –0.5) was found between BM AD and lymphocyte variation.
Conclusion: Patient-specific healthy BM dosimetry is needed, especially in metastatic patients. BM dosimetry can be performed even for tumour involvement in L2-L4.
References:
[1]Wahl *et al.* JNM 2021 62(S3) 23S-35S

[2]Hebert *et al.* JNM 2024 65 (6) 923-930

Supporting figure: correlations between (a) the number of vertebral metastases and AD to healthy BM (b) AD and haematological parameter variations.



Investigation of the predictive value of pre-therapy of ^{68}Ga-DOTATOC PET/CT in ^{177}Lu-DOTATATE peptide receptor radionuclide therapy dosimetry

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Keywords: PRRT Dosimetry, Machine Learning, Dose Prediction Model
Background: The standard treatment for Gastro-Entero-Pancreatic Neuroendocrine Tumours (GEP-NETs) involves four fixed administrations of *7.4* GBq ^{177}Lu-DOTATATE every *8* weeks, lacking individual optimisation. This retrospective study assessed whether pre-therapy ^{68}Ga-DOTATOC PET, commonly used for eligibility, could predict post-treatment dosimetry.
Methods: Correlations between *8* PET-derived metrics and *5* ^{177}Lu absorbed dose (AD) values were examined in over *400* lesions. Patients underwent PET and blood tests within six months prior to therapy. After the first ^{177}Lu-DOTATATE administration, SPECT/CT scans were performed at *20* and *162* hours post-injection. Lesions and organs-at-risk (OARs) were segmented on PET using MIM Software (semi-automatic for lesions, automatic for OARs), and adjusted on SPECT via CT-based registration. Bland-Altman and Spearman tests assessed agreement and correlation. A machine learning (ML) model incorporating VOI statistics and biomarkers was also explored.
Results: Among PET-AD correlation pairs, a strong association was found between total-lesion-somatostatin-receptor-expression TLSRE [*SUVbw*ml*] of PET and the first SPECT time-point ($r=0.90$). Another curious correlation was found between TLSRE and the post-therapy time-integrated activity coefficient (τ) ($r = 0.51$), improving with *Ki-67* stratification ($r\_G1 = 0.52$, $r\_G2 = 0.62$). The ML approach for dose prediction is under refinement.
Conclusions: τ prediction was insufficient due to physiological and technical differences between PET and SPECT (acquisition time: 1h vs 20h, somatostatin-analog ligand: TOC vs TATE, kidney protection: absent/present). The evolving ML model holds promise for improved personalised dosimetry.

Impact of Simplified Post-Therapy Dosimetry Protocols in [177Lu]Lu-DOTATATE PRRT on absorbed doses results and clinical outcomes

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Keywords (3 max): PRRT; dosimetry; Neuroendocrine tumours

Abstract:

Background and Aim: Peptide receptor radionuclide therapy (PRRT) with [^{177}Lu]Lu-DOTATATE is a standard treatment for progressive, well-differentiated gastro-entero-pancreatic neuroendocrine tumours (NETs). In a previous study[1], we demonstrated a correlation between tumour absorbed doses and progression-free survival (PFS) and overall survival (OS) on 34 patients, using a 4 time-points (4TP) SPECT/CT imaging protocol. The current study aims at assessing how decreasing the number of TP impacts absorbed doses and correlations with clinical outcomes, including PFS and OS.

Methods: The reference protocol consisted of four imaging time points, respectively d_0 (4h), d_1, d_3, and d_8 post-injection. The simplified protocols included:

- three-time-point approaches: d_0-d_1-d_8 or d_1-d_3-d_8,
- two-time-point approaches: d_1-d_8 or d_0-d_8.

Absorbed doses to target lesions and organs at risk (liver, spleen, kidneys, bone marrow) were calculated using mono-exponential fitting and the local energy deposition assumption with Planet dose software (Dosisoft) in patients with NETs overexpressing somatostatin receptors. Concordance analyses included Bland–Altman plots, Pearson correlation coefficients. Associations between absorbed doses and PFS or OS were explored using survival analysis techniques.

Results: Simplified protocols showed concordance with the 4TP reference for lesion and organ dosimetry. Preliminary analyses showed trends between absorbed doses and PFS/OS that were consistent with those previously observed using the 4TP approach.

Conclusion: Simplified post-therapy dosimetry protocols may provide reliable absorbed dose estimates while reducing the number of post-therapeutic imaging timepoints. Correlations with clinical outcomes highlight their potential for supporting individualized PRRT optimization.

References:

[1] Hebert et al. JNM 2024 65 (6) 923-930

Feasibility and challenges of a cumulative dosimetry using different dosimetry software after External Beam Radiotherapy (EBRT) and Molecular Radiotherapy (MRT) treatments

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Keywords (3 max): Cumulative dosimetry, Radiobiology, Software

Abstract

Background: External Beam Radiotherapy (EBRT) and Molecular Radiotherapy (MRT) are cancer treatments with distinct irradiation patterns. This study investigates a methodology enabling voxel-based biologically effective dose (BED) superposition on 2 different software.

Methods: An anthropomorphic thorax/heart phantom (5220-RS800T) containing various ^{177}Lu inserts was imaged at 4 time-points (SPECT/CT). EBRT planning was performed using Eclipse V15.6. MRT and cumulative dosimetry was performed using PLANET® Dose V3.3 and OpenDose3D V1.0 (independently).

The EBRT CT was registered (rigid) against the MRT CT reference (D0), thereby allowing EBRT segmentations and absorbed dose (AD) maps to be aligned with the MRT dataset. 3D cumulative BED maps and BED-volume histograms were generated using the linear-quadratic model.

Results: AD maps to liver, lungs, tumours (2) were calculated for EBRT and MRT. On OpenDose3D, the larger tumour received 10 Gy and 21.7 Gy from MRT and EBRT, respectively, while the liver and lungs exposition was smaller (≤ 2.8 Gy for the liver, <0.1 Gy for lungs). On PLANET® Dose, the results were consistent, with mean ADs in tumours and OARs differing by less than 0.2 Gy compared to OpenDose3D. After BED conversion on OpenDose3D, the larger tumour reached 10.1 Gy and 60 Gy from MRT and EBRT, respectively. OARs remained below 4 Gy.

Conclusion: This work represents a proof of concept of combined EBRT and MRT integration in treatment planning systems. Applications to 7 patients with various cancers treated by combined radiotherapy are currently processed and will be presented.

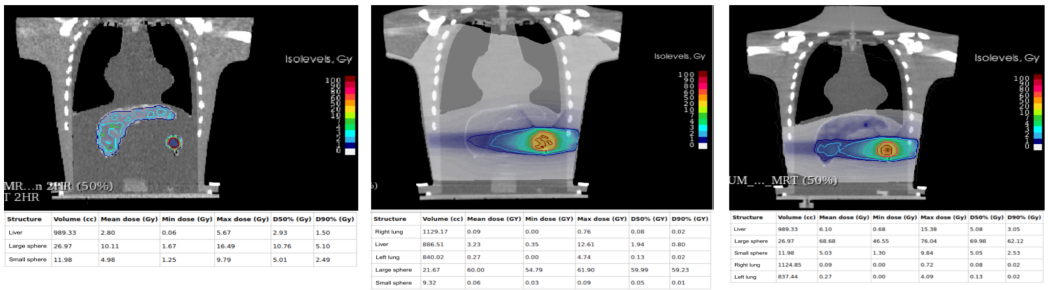

Figure 1: 3D voxel-level BED maps generated in OpenDose3D (left: MRT BED, center: EBRT BED, right: BED sum)

The re-irradiation paradigm, considerations and challenges in the inclusion of MRT in the equation, as demonstrated through a case study

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Keywords (3 max): PRRT Dosimetry, Re-irradiation, SABR

Background and aim: Approximately 15% of neuroendocrine tumour (NET) patients referred for peptide receptor radionuclide therapy (PRRT) in our institution have undergone previous therapeutic exposures, most commonly external beam radiotherapy (EBRT) and PRRT. Kidneys can receive a significant dose during stereotactic EBRT (SABR) of the liver. As the kidneys have no recovery factor, consideration of absorbed doses (ADs) received from previous therapeutic exposures is necessary prior to proceeding with PRRT. Incorporating previous ADs from EBRT in the cumulative dose calculation can be challenging due to the difference in calculation methods, metrics, limits and uncertainties. This case study presents dosimetry for a PRRT patient with three previous SABRs.

Method: Kidney activity at 3 time-points post-PRRT was measured using quantitative SPECT/CT and time-activity curves generated. Total cumulative AD, including the previous therapeutic exposures, was determined in terms of BED and EQD_2 (equivalent dose in 2Gy fractions) after each cycle of PRRT.

Results: Maximum organ ADs are combined in EBRT re-irradiation protocols, however for this patient the kidney AD PRRT threshold was exceeded if this is used. In consultation with treating physicians, a SABR AD which better reflected the heterogeneity of the kidney AD was identified through examination of the dose volume histogram. Assessment of differential renal function also contributed to the decision on treatment progression.

Conclusion: Ideally EBRT re-irradiation guidelines should incorporate molecular radiotherapy. Consideration needs to be given as to the optimum and safest AD metrics to be combined. This case study highlights the challenges that need to be considered to facilitate it's inclusion.

Session 5: AI and modelling

DL-SC: A Deep Learning-Based Scatter Correction Method for Quantitative 177Lu SPECT/CT Imaging

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Keywords (3 max): Deep Learning, Quantitative SPECT, Scatter correction

Abstract

Background and aim: Monte Carlo (MC)-based scatter correction is the most accurate method in SPECT scatter correction (SC); however, it is computationally intensive. The aim of this work is to develop a deep learning-based scatter correction (DL-SC) that facilitates rapid and accurate SC for ^{177}Lu SPECT/CT imaging.
Methods: 1000 random activity distributions [1] were used to simulate projection sets of photopeak (187.2-228.8keV) and two scatter windows (166.4-187.2keV; 228.8-249.6keV) using the SIMIND MC program [2]. Two different projection sets were created for the photopeak: (i) all (scattered+unscattered) photons; (ii) scatter only. By using scatter-window projections, a triple-energy-window scatter estimation (TEW-SC) (iii) was created. Based on this dataset, a 3D-u-net was trained [input: projections(iii), output: projections(ii)]. For simulated projection data of 50 unseen activity distributions, OSEM reconstructions were performed using PyTomography [3] with 4 subsets, 20 iterations, resolution modeling, and attenuation correction using different approaches for SC: (a) “perfect” scatter estimate (reference, generated using (ii)); (b) TEW-SC; (c) DL-SC (proposed method). SPECT reconstructions (b) and (c) were compared to (a) by calculating SSIM, NRMSE and voxel activity accuracy (VAA) [1]. Additionally, the total FOV activity deviation (TAD) to ground-truth activity was calculated for all SC-methods.
Results: DL-SC outperforms the TEW-SC in all comparison metrics. Analysis of the AD shows that the accuracy of activity quantification is within ±5% for both (a) and DL-SC, whereas for TEW-SC it lies within ±15%.
Conclusion: DL-SC is a promising method to perform fast and accurate SC for quantitative ^{177}Lu SPECT imaging.

References

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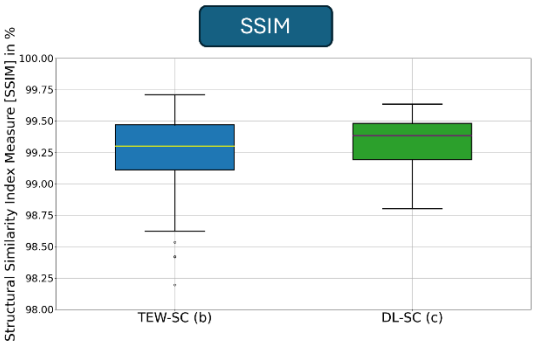
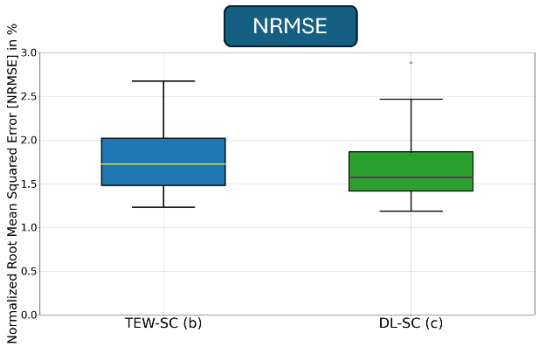
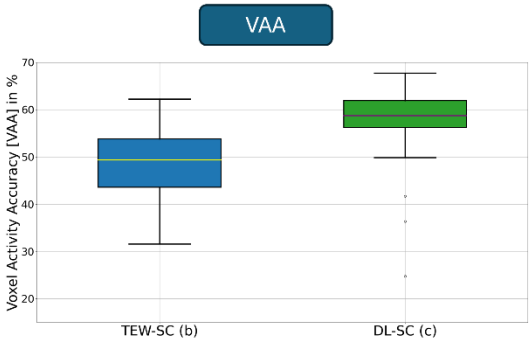
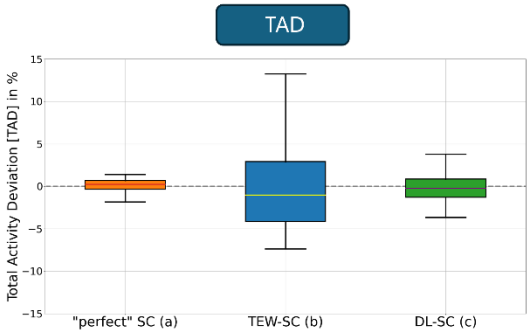
[2]: Ljungberg, ComputMethProgBio(29(4),1989)
[3]: Polson, SoftwareX(20:102020,2025)

Supporting figure / Table (optional)


SSIM
Structural Similarity Index Measure [SSIM] in %
100.00
99.75
99.50
99.25
99.00
98.75
98.50
98.25
98.00
TEW-SC (b)
DL-SC (c)


NRMSE
Normalized Root Mean Squared Error [NRMSE] in %
3.0
2.5
2.0
1.5
1.0
0.5
0.0
TEW-SC (b)
DL-SC (c)


VAA
Voxel Activity Accuracy [VAA] in %
70
60
50
40
30
20
TEW-SC (b)
DL-SC (c)


TAD
Total Activity Deviation [TAD] in %
15
10
5
0
−5
−10
−15
"perfect" SC (a)
TEW-SC (b)
DL-SC (c)

Development of a deep learning-based automatic segmentation tool for total tumour volume delineation in imaging of metastatic prostate cancer

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Keywords (3 max): Total tumor volume, ^{68}Ga-PSMA PET/CT, deep-learning segmentation

Abstract

Background and aim: ^{68}Ga-PSMA PET/CT scans are used to select patients with metastatic castration-resistant prostate cancer for ^{177}Lu-PSMA treatment, as well as for follow-up using RECIP 1.0 criteria. This evaluation is based on the assessment of the total tumour volume (TTV). This study aimed to evaluate a deep learning-based automatic segmentation method on ^{68}Ga-PSMA PET/CT scans.
Methods: A nnU-Net convolutional neural network (CNN) deep-learning method was trained for automatic TTV segmentation. The reference volumes were segmented by a nuclear specialist on 24 PET/CT scans using a visual adaptive threshold method. Three labels were included: kidneys, salivary glands and lesions.
A 5-fold cross-validation was applied, with up to 21 scans used for training (80% training, 20% validation) and 3 for testing. Predicted segmentations were evaluated using the Dice Similarity Coefficient (DSC) against expert references, and compared to a standard threshold-based method (rpt-tmtv).
Results: The DSC against expert reference were found to be equal to 92.0%, 94.6% and 89.6% for the three tests, and respectively, with TTV relative error equals to -13.9%, +6.0% and +14.9%. For comparison, the DSC for rpt-tmtv were 75.8%, 82.8% and 93.7%, respectively. The main difference lays in the segmentation of liver lesions.
Conclusion: The nnU-Net model provides fast and accurate segmentation improving repeatability and reducing intra-observer variability. Three nuclear physicians will review the predicted segmentation in a blind study to evaluate the model's efficiency and its impact on clinical decision-making. Further training will be conducting on post ^{177}Lu-PSMA SPECT-CT scans for dosimetry purposes.

Precision and accuracy in one-point kidney dosimetry for NET patients receiving later-session ^{177}Lu-DOTATATE therapy

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Keywords (3 max): ^{177}Lu dosimetry, precision and accuracy, one-point dosimetry

Abstract:

Background and aim: Calculated absorbed doses (AD) may support ^{177}Lu-DOTATATE therapy optimization. This study aims to analyse the precision and accuracy of various AD calculation methods using one single timepoint in later therapy sessions.
Methods: Time-activity curves for right and left kidneys were analysed from 407 patients treated with ^{177}Lu-DOTATATE at Uppsala University Hospital. The patients had undergone three-timepoint dosimetry after the 1st and 4th therapy sessions, with imaging about 24, 96 and 168 h after infusion start. Focusing on the 4th session, using three-point dosimetry as a reference, comparisons were made to one-point dosimetry at each timepoint using; (i) the effective half-life (t_{eff}) from the first therapy session; (ii) a standard, fixed-value t_{eff} of 51 h, and; (iii) the Hänscheid method [1]. The percentage deviation from the reference AD was calculated for all sets, and the median, 5%, 25%, 75% and 95% percentiles were extracted.
Results: Using t_{eff} from session 1 in one-point dosimetry 24 or 96 h after injection returned ADs within ± 21% (5% to 95% percentiles) from reference, and so did Hänscheid at 96 h (see Figure 1). However, Hänscheid at 24 or 168 h systematically underestimated the AD, while the standard, fixed-value t_{eff} returned larger uncertainties.

Conclusion: One-timepoint dosimetry returns data within ±20% from three-timepoint dosimetry, provided that the single timepoint is carefully selected and a reliable analysis method is applied.

References:

[1] H. Hänscheid et.al., J Nucl Med (2018) 59:75-81, DOI: 10.2967/jnumed.117.193706

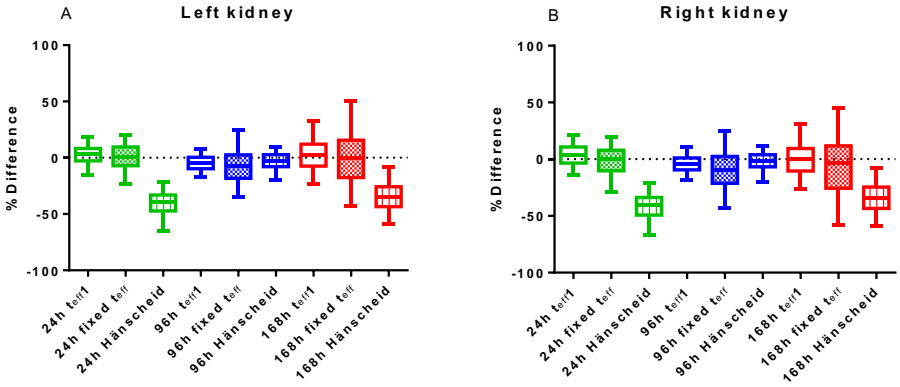

Figure 1. Differences of absorbed dose calculations using various one-timepoint-dosimetry methods, applied at various imaging timepoints, versus three-timepoint dosimetry for (A) Left kidney and (B) Right kidney

PET-based single-time-point dosimetry using a physiologically-based pharmacokinetic model, machine learning and a non-linear mixed effects model for [^{177}Lu]Lu-PSMA-I&T Therapy

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Keywords (3 max): Global Sensitivity Analysis, ^{177}Lu-labelled PSMA Therapy, Dosimetry

Abstract

Aim: This study evaluates the accuracy of predicting time-integrated activity (TIA) for [^{177}Lu]Lu-PSMA-I&T therapy using pre-therapeutic [^{68}Ga]Ga-PSMA-11 PET/CT data within a hybrid framework combining physiologically based pharmacokinetic (PBPK) modeling [1], non-linear mixed-effects modeling (NLMEM) [2,3], and machine learning (ML) techniques.
Methods: Thirteen patients with metastatic prostate cancer underwent PET/CT imaging approximately 0.9±0.1 hours after injection of 115±16 MBq (1.6±0.3 nmol) [^{68}Ga]Ga-PSMA-11 prior to injection of 7.3±0.3 GBq (91±5 nmol) [^{177}Lu]Lu-PSMA-I&T therapy. Post-therapy, whole-body planar scintigraphy was acquired at 3–5 time points to derive reference TIAs (rTIAs) for kidneys and tumors using a PBPK model. Three single-time-point (STP) dosimetry strategies were assessed: (1) STP with PBPK and NLMEM ($STP_{PBPK\text{-}NLMEM}$), (2) support vector regression-based ML (STP_{ML}), and (3) a hybrid method combining both ($STP_{PBPK\text{-}NLMEM+ML}$). For ML-based methods, patient-specific covariates (e.g. age, weight, hematocrit, and administered activity) and ML hyperparameters were investigated. Accuracy was evaluated by comparing STP-derived absorbed doses (sADs) to rADs using root-mean-square errors (RMSEs) and mean absolute percentage errors (MAPEs).
Results: RMSEs (MAPEs) for kidneys and tumors were 11% (8%) and 193% (92%) for $STP_{PBPK\text{-}NLMEM}$; 15% (9%) and 158% (87%) for STP_{ML}; and 8% (5%) and 19% (16%) for the $STP_{PBPK\text{-}NLMEM+ML}$, respectively.
Conclusion: A single PET/CT scan acquired ~1 hour after injection can yield accurate renal TIA estimates when analyzed with a hybrid PBPK-NLMEM-ML framework, with improved performance also observed for tumor estimates.

References:

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Population-Based Pharmacokinetic Modelling of Zr-89 Labelled Antibodies Using Non-Linear Mixed-Effects Approaches for Optimized Imaging and Quantification

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Keywords (3 max): molecular antibody, pharmacokinetic modelling, immuno-PET

Abstract

Background and Aim: Zr-89-labelled monoclonal antibodies enable whole-body immuno-PET for biodistribution and therapy response assessment. However, low injected activity (15–37 MBq) and long circulation times often require multi-time-point imaging over 4–10 days, creating logistical and patient burden when new conpounds are evaluated. Population-based pharmacokinetic modelling with non-linear mixed-effects (NLME) offers a promising way to extract meaningful data from sparse scans.

Methods: A prospective study of 10 patients (40 scans) receiving Zr-89-atezolizumab (35.0 ± 1.9 MBq, protein dose 10 mg) was performed (1). Imaging was performed up to 4 time points (1–186 hours post-injection) on a digital PET/CT system using ^{89}Zr-EARL reconstruction (2). Liver, kidney, and total-body activities were segmented using a MONAI-AI-model. NLME models (2- to 4-parameter, mono- and bi-exponential) were trained (n = 32) and tested (n = 8) using body weight as a covariate; physical decay –fixed. Performance was evaluated using R^2, RMSE, AIC, BIC, and OFV, and benchmarked against MIRDfit.

Results: All models achieved $R^2 > 0.85$ (train) and > 0.93 (test). A 3-parameter bi-exponential model, separating biological and physical decay via weighting factor α (determines influence of two processes), performed best for liver (R^2 0.95/0.97, RMSE 0.0004/0.0003, AIC -459/-106), kidneys (R^2 0.85/0.93, RMSE 0.0011/0.0006, AIC -396/-62), total body (R^2 0.96/0.99, RMSE 0.024/0.007, AIC -244/-70) kinetics, outperforming MIRDfit and generalizing across patients.

Conclusion: NLME modelling enables accurate, patient-friendly quantification of Zr-89 antibody kinetics from limited data, supporting protocol simplification − especially in clinical trials. This highlights the potential for applicability of population-based NLME models.

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Prediction of [^{177}Lu]Lu-DOTA-TATE time-integrated activity using PBPK modelling and pre-therapeutic [^{68}Ga]Ga-DOTA-TATE PET/CT

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Keywords (3 max): PRRT, PBPK model, single-time-point TIA prediction

Abstract

Background and aim: Time-integrated activity (TIA) is essential for absorbed dose (AD) calculations, and is important for individualising peptide receptor radionuclide therapy (PRRT). This study aims to predict the TIA of [^{177}Lu]Lu-DOTA-TATE from a single [^{68}Ga]Ga-DOTA-TATE PET/CT image and population information used in a whole-body physiologically based pharmacokinetic (PBPK) model.

Methods: Data from twelve patients with neuroendocrine tumours (NETs) who underwent a pre-therapeutic [^{68}Ga]Ga-DOTA-TATE PET/CT and PRRT with [^{177}Lu]Lu-DOTA-TATE were used [2]. A PBPK model for [^{68}Ga]Ga-DOTA-TATE and [^{177}Lu]Lu-DOTA-TATE was implemented, including all organs and NETs [1]. Ten model parameters were estimated through a fitting procedure using measured single [^{68}Ga]Ga-DOTA-TATE organ and tumour activities. Reference TIAs were determined by fitting the model with both single [^{68}Ga]Ga-DOTA-TATE and [^{177}Lu]Lu-DOTA-TATE time-activity measurements, while predicted [^{177}Lu]Lu-DOTA-TATE TIAs were estimated based solely on single [^{68}Ga]Ga-DOTA-TATE PET/CT time-activity measurements and population information. Relative prediction error (RPE) and mean absolute percentage error (MAPE) were calculated.

Results: The mean and standard deviation of RPE for TIAs were (-5±51)%, (-4±22)%, (-13±40)%, and (-10±21)% for tumours, kidneys, liver, and spleen, respectively. The MAPE values for tumours, kidneys, liver, and spleen were 43%, 18%, 31%, and 17%, respectively.

Conclusion: Single-time-point [^{68}Ga]Ga-DOTA-TATE PET/CT imaging offers a valuable prediction of TIAs, and consequently ADs, to organs, such as the kidney, during [^{177}Lu]-DOTA-TATE-targeted therapy. There is potential to enhance the prediction accuracy for tumours and the liver.

References

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Global sensitivity analysis with correlated input parameters in a whole-body PBPK model for [^{177}Lu]Lu-DOTA-TATE therapy

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Keywords (3 max): global sensitivity analysis, PBPK model, PRRT

Abstract

Background and aim: Accurate dosimetry with low absorbed dose (AD) uncertainty is essential for optimising radiopharmaceutical therapy. The use of physiologically based pharmacokinetic (PBPK) models is a valuable tool for endeavour. This study aimed to identify key correlated PBPK parameters most influencing AD in peptide-receptor radionuclide therapy (PRRT) using global sensitivity analysis (GSA).
Methods: Twelve patients with neuroendocrine tumours (NETs) who underwent a pre-therapeutic [^{68}Ga]Ga-DOTA-TATE PET/CT and PRRT with [^{177}Lu]Lu-DOTA-TATE were analysed [1]. Peri-therapeutic SPECT/CT images were acquired at 1 h, 1 d, 4 d, and 7 d after administration.
Ten correlated PBPK model parameters [2] were analysed using GSA based on Kucherenko's method [3] implemented in UQLab [4]. Pharmacokinetics were simulated and AD to organs and tumours estimated. Main and total sensitivity indices (S_i and S_{tot}) were calculated.
Results: According to the GSA, key parameters influencing the ADs to the kidneys, liver and spleen were the respective receptor densities (median [minimum, maximum] over 12 patients): kidneys (S_i=0.17[0.09,0.24], S_{tot}=0.88[0.77,0.97]), liver (S_i=0.19[0.04,0.29], S_{tot}=0.91[0.77,0.96]) and spleen (S_i=0.24[0.10,0.36], S_{tot}=0.95[0.87,1.00]). For tumours, the key parameters were also tumour receptor density (S_i=0.59[0.20,0.77], S_{tot}=0.93[0.63,1.00]). Receptor density of muscle and fat mainly affected total body AD (S_i=0.19[0.01,0.64], S_{tot}=0.38[0.02,0.96]).
Conclusion: GSA highlights receptor density as the primary influencing parameter of ADs. Variability in S_i and S_{tot} across patients underscores the need for personalised PRRT strategies.

References

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Intra-Patient Global Sensitivity Analysis of a PBPK Model for ^{177}Lu-labelled PSMA Therapy: Impact of Parameter Correlation

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Keywords (3 max): Global Sensitivity Analysis, ^{177}Lu-labelled PSMA Therapy, Dosimetry

Abstract

Aim: Physiologically based pharmacokinetic (PBPK) models are fundamental to digital twins and support personalised radiopharmaceutical therapy. This study employs intra-patient global sensitivity analysis (GSA) to assess the effect of model parameter correlations on kidney and tumour absorbed doses (ADs) in [177Lu]Lu-PSMA-I&T therapy.

Methods: Data from ten patients with metastatic castration-resistant prostate cancer who received pre-therapeutic [^{68}Ga]Ga-PSMA-I&T PET/CT and [^{177}Lu]Lu-PSMA-I&T therapy, followed by SPECT/CT scans at 2 and 4 days post-injection, were analysed. A whole-body PBPK model with tumours was implemented. Fifteen parameters, standard errors, and inter-parameter correlations were estimated via fitting to measured time-activity data and subsequently evaluated using Kucherenko GSA in UQLab [1]. Correlations were first ignored to identify direct influences of model parameters on ADs; then, they were included to capture indirect effects from interdependencies. Pharmacokinetics were simulated to estimate kidney and tumour ADs, main- and total-effect indices (S_i, S_i^T).

Results: Including parameter correlations (range: -0.6 − 0.6) yielded kidney ADs of 3.0 − 7.2 Gy (SD: 0.4 − 0.9 Gy) and tumour ADs of 2.0 − 26.8 Gy (SD: 0.6 − 4.9 Gy). Neglecting correlations significantly increased uncertainty in ADs ($p < 0.001$) by a factor of 1.2[1.0-1.7] (median[range]), while ADs showed no significant change. Kidney ADs were influenced by receptor density ($S_i = 0.3[0.1 - 0.6]$, $S_i^T = 0.7[0.6 - 0.8]$) and filtration rate ($S_i = 0.2[0.1 - 0.3]$, $S_i^T = 0.3[0.1 - 0.4]$). Tumour ADs were affected by receptor density ($S_i = 0.7[0.1 - 1.0]$, $S_i^T = 0.8[0.3 - 1.0]$); in five patients, tumour flow density was also influential ($S_i = 0.8[0.1 - 0.4]$, $S_i^T = 0.3[0.3 - 0.6]$). Neglecting correlations increased main-effect indices, particularly for kidney receptor density ($S_i = 0.5[0.5 - 0.6]$).

Conclusion: Incorporating parameter correlations into GSA reduced uncertainty in AD estimates. Dominant parameters influencing kidney and tumour ADs remained consistent regardless of correlation inclusion.

References: [1] Marelli et al., ICVRAM 2014

Deep Learning-Based Partial Volume Correction for Quantitative ^{177}Lu SPECT/CT Imaging: Cross-Scanner Transfer Learning Approach

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Keywords (3 max): Transfer learning, Partial volume correction, Deep learning

Abstract:

Background and aim: Partial volume effects pose a major challenge in quantitative ^{177}Lu SPECT/CT imaging, limiting the accuracy of radiopharmaceutical therapy dosimetry. Deep learning-based partial volume correction (DL-PVC, [1]) has shown great potential to mitigate partial volume effects, but existing models are typically tailored to specific camera types. This study investigates the generalizability of DL-PVC across two manufacturers using transfer learning.

Methods: Realistic ^{177}Lu SPECT projections were Monte Carlo simulated as described in [1] with SIMIND [2] to replicate acquisitions on GE Discovery D670 (MEGP collimator) and Siemens Intevo Bold (MELP) systems. Projections were reconstructed using PyTomography [3] with OSEM (20 iterations, 4 subsets), CT-based attenuation correction, triple-energy-window scatter correction, and resolution modeling. R2UNet models were trained separately on 1900 synthetic images per scanner. Transfer learning was then applied using 25-500 images from the alternate scanner, along with experiments using mixed-scanner datasets. Performance was assessed on 100 test images using SSIM, NRMSE, and VAA (volume activity accuracy [1]).
Results: Native models performed well on their own scanner's test data but degraded on cross-scanner test data. Fine-tuning with only 25 images improved generalization substantially, approaching native training levels for 500 images. However, single-scanner transfer learning caused a slight performance drop for the original scanner. Mixed-scanner transfer learning improved cross-scanner performance while maintaining or enhancing performance on the original scanner.

Conclusion: DL-PVC models can be effectively adapted across scanners using transfer learning. Mixed-scanner training offers a promising approach for developing scanner-agnostic models for quantitative ^{177}Lu SPECT/CT.

References

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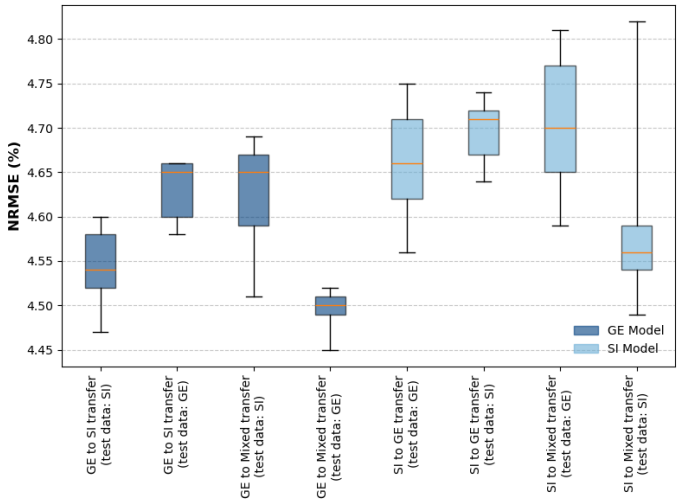
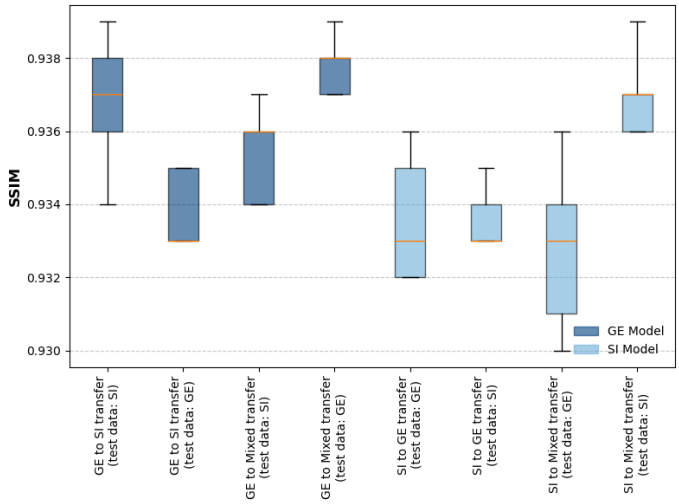
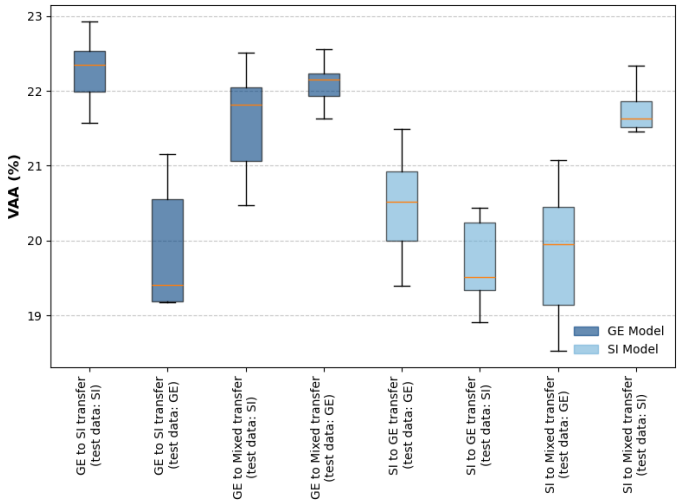
[3] Polson. SoftwareX 2025;29:102020.

Supporting figure / Table (optional)


NRMSE (%)
4.80
4.75
4.70
4.65
4.60
4.55
4.50
4.45
GE Model
SI Model
GE to SI transfer (test data: SI)
GE to SI transfer (test data: GE)
GE to Mixed transfer (test data: SI)
GE to Mixed transfer (test data: GE)
SI to GE transfer (test data: GE)
SI to GE transfer (test data: SI)
SI to Mixed transfer (test data: GE)
SI to Mixed transfer (test data: SI)


SSIM
0.938
0.936
0.934
0.932
0.930
GE Model
SI Model
GE to SI transfer (test data: SI)
GE to SI transfer (test data: GE)
GE to Mixed transfer (test data: SI)
GE to Mixed transfer (test data: GE)
SI to GE transfer (test data: GE)
SI to GE transfer (test data: SI)
SI to Mixed transfer (test data: GE)
SI to Mixed transfer (test data: SI)


VAA (%)
23
22
21
20
19
GE Model
SI Model
GE to SI transfer (test data: SI)
GE to SI transfer (test data: GE)
GE to Mixed transfer (test data: SI)
GE to Mixed transfer (test data: GE)
SI to GE transfer (test data: GE)
SI to GE transfer (test data: SI)
SI to Mixed transfer (test data: GE)
SI to Mixed transfer (test data: SI)

Towards More Personalized Bone Marrow Dosimetry Using Deep Learning-Based Segmentation Tools

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Keywords (3 max): Bone marrow, toxicity, 177Lu-PSMA

Background and Aim: Image-based bone marrow (BM) dosimetry shows improved correlations with hematological toxicities compared to blood-based approaches. A common technique estimates BM cumulated activity by segmenting L2-L4 trabecular bones on CT and combining this with quantitative SPECT imaging. It is commonly assumed that the trabecular portion of L2-L4 constitutes 6.7% of the total trabecular volume of all bones in a patient. This study aimed to verify this assumption within our patient cohort.

Methods: We included mCRPC patients undergoing [177Lu]Lu-PSMA therapy with dosimetry. Full skeleton segmentation on CT images was performed using TotalSegmentator (3DSlicer), extracting trabecular bone volume with Hounsfield unit thresholding and morphological operations. For each patient, the ratio of L2-L4 trabecular volume to total trabecular BM was calculated and compared to the 6.7% reference.

Results: In our cohort, the mean L2-L4 trabecular volume was 5.6% (±1.6%) of total trabecular BM, 16.3% less than the expected value. Quartile deviations from the reference were -21.4%, -12.4%, and -0.02%, meaning that the reference value was accurate for only one quarter of the patients. Individual discrepancies ranged from -92.5% to +14.9%. Considering each patient's specific percentage would yield more personalized BM dosimetry and potentially improve correlations with haematological toxicities.

Conclusion: Our results suggest that freely available artificial intelligence-based tools, such as TotalSegmentator, enable a more personalized and precise calculation of absorbed dose in the trabecular portions of bones, enhancing patient-specific BM dosimetry and yielding better correlations with haematological toxicities.

Session 6: Preclinical & miscellaneous

Pre-clinical physiologically based pharmacokinetic (PBPK) modelling of PSMA radioligands

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Keywords (3 max): PBPK modelling, PSMA radioligands, pre-clinical data

Abstract:

Background and aim: In radiopharmaceutical therapy, physiologically based pharmacokinetic (PBPK) modelling has mostly been used to study clinical data. However, clinical data is often limited by few measurements, which limits the complexity of applicable PBPK models. The aim of this study was to perform PBPK modelling on, more extensive, pre-clinical PSMA radioligand data, to reveal unstudied dynamics of PSMA radioligands.

Methods: The data was obtained at Paul Scherrer Institute, for the PSMA radioligands ^{177}Lu-PSMA-617, ^{177}Lu-PSMA-I&T, ^{177}Lu-SibuDAB, ^{177}Lu-PSMA-ALB-53 and ^{177}Lu-PSMA-ALB-56. The data has previously been published and contained activity concentrations of 13-14 tissues at 5-6 time-points post-injection, from mice injected with the radioligands, and albumin affinity measurements. A clinically studied radioligand PBPK model structure [1] was used to build a pre-clinical baseline model. Unspecific uptake and two different albumin binding models, with multiple binding sites, was developed as modifications. Combinations of the modifications were built in SimBiology/MATLAB, and regressions were performed between the models and the data. The modifications were evaluated through the performances of the regressions.

Results: Akaike weights showed significant improvements with the unspecific uptake for all radioligands, except ^{177}Lu-PSMA-ALB-56, and the modified albumin binding models significantly improved the regressions for ^{177}Lu-PSMA-I&T, ^{177}Lu-SibuDAB and ^{177}Lu-PSMA-ALB-53. Upon visual inspection of the time-activity curves, the baseline model was insufficient to describe the data, and the modifications helped improve the fit.

Conclusion: The improvements with unspecific uptake and multiple albumin binding sites may suggest unstudied dynamics, which significantly affects the biodistribution of the PSMA radioligands. However, these suggested dynamics require further research to be confirmed.

References

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Assessing the generalizability of a preclinical PBPK model for DOTA-TATE-based radiopharmaceuticals: applications to ^{161}Tb, ^{177}Lu, and ^{68}Ga

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Keywords (3 max): pharmacokinetic, DOTA-TATE, preclinical

Abstract

Background and aim: ^{177}Lu-DOTA-TATE is the current Peptide Receptor Radionuclide Therapy (PRRT) agent for neuroendocrine tumors, while other radionuclides like ^{161}Tb labeled to DOTA-TATE are under investigation. Hereafter, we assess whether a generic preclinical physiologically-based pharmacokinetic (PBPK) model can accurately predict organs and lesions uptake of various DOTA-TATE-based radiopharmaceuticals.

Methods: Starting from a published model (1), a PBPK model was developed and verified for [^{161}Tb]Tb-DOTA-TATE in healthy mice and mice bearing a CA20948 rat pancreatic tumor (2). Kinetic parameters and SSTR2 densities were fitted to corresponding [^{161}Tb]Tb-DOTA-TATE preclinical biokinetic data. Model generalizability was assessed using studies of DOTA-TATE labeled with ^{68}Ga and various β-emitters.

Results: The PBPK models successfully described the pharmacokinetics of [^{161}Tb]Tb-DOTA-TATE: the relative errors for time-integrated activities ranged from -22% to +27% in the kidneys and tumour. Relative SSTR2 levels between organs remained reasonably constant across mice strains with relative simulated expressions of 14±3% for the pancreas, 10±6% for the lungs, 2±0% for the liver, and 1±1% for the spleen (mean ± SD), using kidneys expression levels as reference. Our findings also indicate that the PBPK model is applicable to [^{68}Ga]Ga-DOTATATE, with variable accuracy across studies, and to [^{177}Lu]Lu-DOTATATE, with reasonable (within two-fold) prediction errors.

Conclusion: These results confirm that [^{161}Tb]Tb-DOTA-TATE shows comparable pharmacokinetics to clinical analogs, supporting its translation for PRRT and encouraging broader clinical use of a generalized PBPK model for dosimetry-based personalization of DOTA-TATE radiopharmaceutical therapies.

References

(1) Zaid et al. 2021. https://doi.org/10.3390/pharmaceutics13122132. (2) Bernard et al. 2000. https://doi.org/10.1097/00006231-200011000-00015

Supporting figure / Table (optional)

Computed dosimetry for the preclinical assessment of silver-111 in the context of the ISOLPHARM project

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Keywords (3 max): dosimetry, silver-111, molecular radiotherapy

Abstract:

Background and aim: The ISOLPHARM collaboration in Italy aims at producing innovative radiopharmaceuticals using the radionuclides obtainable at the SPES facility of INFN-LNL with the Isotope Separation On-Line (ISOL) technique. Currently, silver-111 is being studied as a therapeutic agent for molecular radiotherapy in preclinical experiments (in vitro and in vivo) and an accurate dosimetric characterization is required.
Methods: Using Monte Carlo codes such as Geant4, MCNP, PHITS and MIRDcell, applications are developed to compute the absorbed dose in the cell compartments during radiobiology experiments and murine organ S-values for in-vivo tests. Also, voxel S-values and dose point kernels are being used to compare silver-111 to other medical beta emitters.
Results: The results of these simulations are successfully used to plan preclinical experiments and to understand the observed outcomes. The dosimetric features of silver-111 are similar to the ones of commonly used medical radionuclides such as lutetium-177 or iodine-131, and almost equal to those of rhenium-186, already studied in phase I/II clinical trials.
Conclusion: The dosimetric evaluation of silver-111 as a therapeutic (and maybe theragnostic) radionuclide gives encouraging results, which justify the ongoing experimental campaign conducted by the ISOLPHARM collaboration.

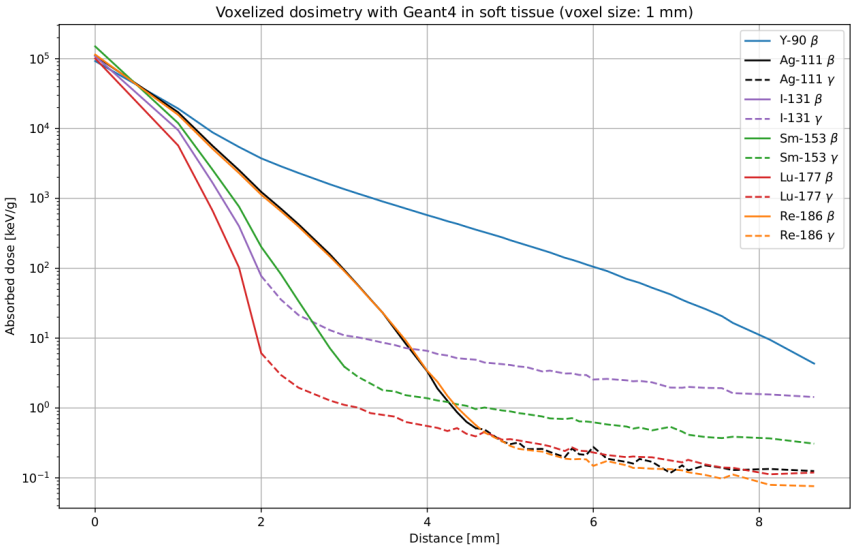
References

https://doi.org/10.1016/j.apradiso.2025.111979

https://dx.doi.org/10.25434/arzenton-alberto_phd2024-11-11

A. Arzenton, L. Morselli, M. Lunardon, G. Russo, A. Andrighetto (2021). “A free Geant4 database of S-values for voxelized dosimetry of nonuniform activity distributions from PET/CT and SPECT/CT imaging”. In: LNL Annual Report 2021, p. 59.

Supporting figure / Table


Voxelized dosimetry with Geant4 in soft tissue (voxel size: 1 mm)
Absorbed dose [keV/g]
Distance [mm]
Y-90 β
Ag-111 β
Ag-111 γ
I-131 β
I-131 γ
Sm-153 β
Sm-153 γ
Lu-177 β
Lu-177 γ
Re-186 β
Re-186 γ

Development of a PBPK-Based Mouse Digital Twin for Individualised Dosimetry of [^{177}Lu]rhPSMA-10.1 Therapy

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Keywords: PBPK modelling, Digital twin, Radiopharmaceutical dosimetry

x

Abstract:

Background and Aim: Prostate-specific membrane antigen (PSMA)-targeted radiopharmaceuticals have shown promising therapeutic potential for metastatic castration-resistant prostate cancer (mCRPC), although patient response remains highly variable. This study aimed to develop a physiologically based pharmacokinetic (PBPK) model for mice and generate digital twins to estimate absorbed dose (AD) distributions following rhPSMA-10.1 administration.
Methods: Five CB-17 SCID mice with LNCap tumour xenografts were injected with ^{nat}F[^{177}Lu]rhPSMA-10.1 and underwent biodistribution analysis. A PBPK model implemented in MATLAB SimBiology, with key physiological parameters, such as receptor densities and blood flows, was individually fitted to experimental data to create digital twins. Synthetic time-activity curves (TACs) were generated (ground truth), from which activities at 1h, 4h, and 24h were obtained, and noise levels (σ = 0–35%) were added using Gaussian distributions to replicate measurement variability. The model was refitted 1000 times per noise level, and the mean absolute percentage error (MAPE) of the time-integrated activity coefficients (TIACs) and ADs were calculated with reference to the ground truth. **Results:** The model demonstrated high robustness, with median TIAC deviations under 5% and the MAPE consistently below 50% of the added noise. Mean AD calculations for both tumour and kidney remained accurate across all noise levels, with maximum discrepancies of 0.96% and 2.32%, respectively. Standard deviations increased with noise but remained below the added noise.
Conclusion: PBPK-based mouse digital twins can reliably estimate AD for ^{nat}F[^{177}Lu]rhPSMA-10.1 therapy, even under high-noise conditions. This approach supports preclinical dosimetry and offers a computationally efficient tool for individualised treatment planning.

Simultaneous Alpha- and Beta-Particle Digital Autoradiography for Evaluating Co-Therapy and Diagnostic Uptake: Pre-Clinical Studies with Ac-225, Lu-177, and PET Tracers

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Keywords (3 max): digital autoradiography, Ac-225, RPT combination therapy

Abstract:

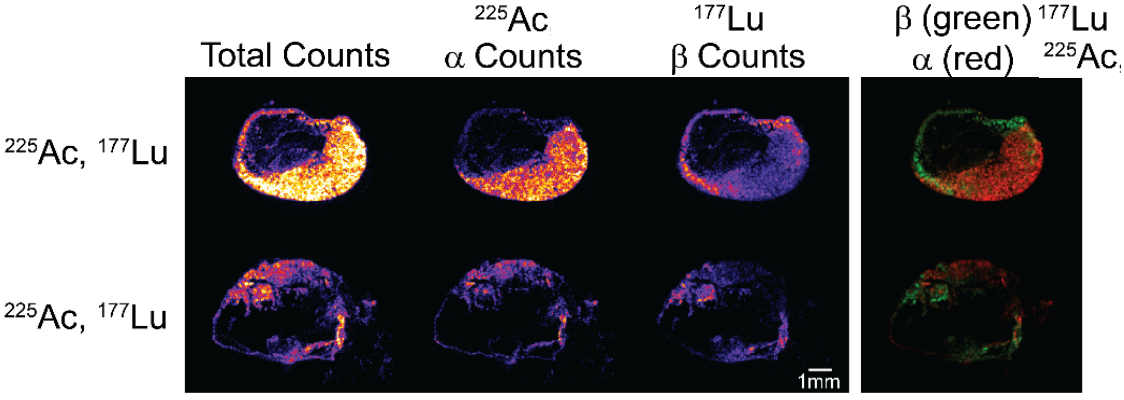
Background: The ionizing-radiation Quantum Imaging Detector (iQID) is a quantitative digital autoradiography system that enables simultaneous imaging of alpha and beta particles with high spatial resolution and particle-specific quantification. This capability supports pre-clinical evaluation of radiopharmaceuticals and small-scale dosimetry at near-cellular levels.

Methods: We used the iQID system to image tissue sections from pre-clinical models co-injected with Ac-225-labeled radioligands and beta-emitting analogs labeled with Lu-177 (therapeutic electron), Zr-89, or Ce-134 (diagnostic positrons). Monoisotope controls were included. At 24 hours post-injection, tissue was collected, flash-frozen in OCT, sectioned (7 μm), and mounted on Gadox (Gd2O2S) scintillation paper, which detects both alpha and beta emissions. Listmode data recorded individual particle events, with event area and total signal used to discriminate particle type. Digital autoradiographs were generated for alpha-only, beta-only, and total-count images.

Results: Distinct spatial uptake patterns were observed between alpha and beta emitters in tumors and normal organs, reflecting differences in localization and retention of therapeutic and diagnostic radioligands. These variations, visible at sub-organ resolution, highlight limitations of conventional PET and SPECT imaging for evaluating co-therapies and emphasize the need for higher-resolution approaches.

Conclusion: The iQID system enables concurrent, high-resolution imaging of alpha and beta emissions, supporting detailed analysis of radionuclide distribution and small-scale dosimetry. It offers a powerful tool for optimizing radiopharmaceutical design and evaluating co-therapy and diagnostic/therapeutic radionuclide pairs in pre-clinical studies.

Supporting figure



Evaluation of post-injection urinary excretions in a cohort of patients treated with ^{177}Lu-PSMA PRRT

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- Author 4 : Mathieu Frindel, ICO, France

- Author 5 : Aurore, Rauscher, ICO, France

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Keywords (3 max): ^{177}Lu-PSMA, urine, activity

Abstract

a) Background and aim

Patients undergoing ^{177}Lu-PSMA therapy routinely receive a nominal activity of 7.4 GBq (±10%). This posology implies that "one dose fits all," but what does it actually look like in practice? We prospectively collected urine between injection and the first SPECT/CT scan for accounting for administered, excreted, and imaged bladder activity with the goal to characterize urinary elimination dynamics, thereby clarifying the amount of residual "therapeutic" activity present at first imaging.

b) Methods

A total of 62 urine samples were collected from 14 patients, each receiving between one and five treatment cycles. Urine container mass and blood samples were measured, and ^{177}Lu activity quantified using a calibrated activity meter. The total activity excreted between injection and first imaging was calculated. All activities were decay-corrected to the imaging time and compared with the injected activity.

c) Results

Across all treatments, the mean injected activity was 6859 ± 252 MBq. Mean urinary elimination (including bladder content at imaging) was 2317 ± 733 MBq—representing 33.7 ± 10% of the administered dose within 4.8 ± 0.8 hours post-injection. A robust correlation was observed between urinary excretion and glomerular filtration rate (Pearson r = 0.88, p = 0.002).

d) Conclusion

^{177}Lu-PSMA therapy exhibits considerable interpatient variability in urinary excretion, yet enables meaningful quality assurance in image quantification. Ongoing work, which will be achieved before the symposium, will expand the cohort and incorporate total tumor burden at injection for further analysis.

Validation of a Wearable Individual Dose Monitoring System for Molecular Radiotherapy Using a Custom Dynamic NEMA Phantom

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Keywords (3 max): internal dose monitoring, dynamic phantom, biokinetics

Abstract:

a) WIDMApp (Wearable Individual Dose Monitoring Apparatus) is an innovative system under development for personalized internal dosimetry in Molecular Radiotherapy. It integrates patient-specific computational models with real-time data from wearable sensors to determine radiopharmaceutical biokinetics. This approach addresses the limitations of the poor temporal sampling of current methodologies based on nuclear imaging. A preliminary experimental verification of the WIDMApp approach was carried out using a customised dynamic phantom capable of replicating both the physical radionuclide decay and the biological washout.

b) The NEMA-IEC body phantom was equipped with two 3D-printed modified spheres filled with 6 MBq of ^{177}Lu solution and connected to Arduino-controlled peristaltic pumps. These pumps diluted the sphere's activity to simulate biological clearance, with flow rates exceeding the physical decay (one water drop every 25-50 s). The background from the activity within the body was simulated by filling the main phantom cavity with 13 MBq of ^{177}Lu solution. Ten WIDMApp sensors -comprising p-terphenyl scintillators and SiPM arrays with dedicated electronics- were positioned on the phantom surface to monitor photon emissions over time. A commercial Polimaster PM1610B dosimeter was used as reference.

c) The observed decay rates reflected a combination of physical decay and simulated washout, validating the system's ability to detect dynamic changes in activity. The WIDMApp prototype showed good agreement with the commercial dosimeter, demonstrating its effectiveness in tracking time-dependent radiopharmaceutical distributions.

d) These findings support WIDMApp as a promising tool for real-time, individualized dose monitoring, and a step toward future application in vivo.

Main reference: *Morganti et al. Med. Phys. 2021* https://doi.org/10.1002/mp.15311

Preparation of ^{225}Ac phantoms by gravimetric drop-on-demand inkjet deposition and imaging by digital autoradiography

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- Author 4 : R. Michael Verkouteren, National Institute of Standards and Technology, USA

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Keywords (3 max): digital autoradiography; resolution phantom; traceable activity

Abstract:

a) Background and aim

Direct imaging of alpha-particle emissions with near-cellular scale spatial resolution can be achieved with modern digital autoradiography instrumentation. With accurate quantitation of activity, preclinical research into radiopharmaceutical therapies can exploit high resolution imaging to advance beyond qualitative biodistribution studies and achieve high-precision dose mapping.

b) Methods

A Jetlab-4 benchtop dispenser is used for gravimetric drop-on-demand inkjet preparation of 2D autoradiography phantoms with activity directly traceable to primary standards. Printed features (^{225}Ac in 0.1 mol/L HCl on nickel substrates) were spaced 0.25 mm to 1.5 mm apart. Phantoms were imaged with three systems: an ionizing-radiation quantum imaging detector (iQID), a quantitative particle identification (QPID) spectral autoradiography system, and a Typhoon biomolecular imager.

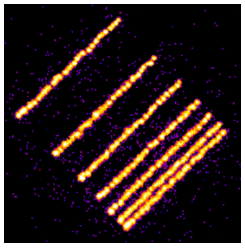
c) Results

The digital autoradiography systems (iQID and QPID) achieved comparable spatial resolutions (~ 20 µm). With appropriate corrections for cross-fire and timing, image count rates correspond to deposited activities. With filtering, alpha-only imaging show improved spatial resolution and near 100 % 2 π counting efficiency. Printed features were fixed in place, showing resistance to physical disturbance when mylar coverings were applied and removed.

d) Conclusion

Phantoms for digital autoradiography are prepared by drop-on-demand inkjet metrology and used to compare quantitation in different systems.

Certain commercial equipment, instruments, or materials are identified in this paper to foster understanding. Such identification does not imply recommendation by the National Institute of Standards and Technology, nor does it imply that the materials or equipment identified are necessarily the best available for the purpose.



Supporting figure

Autoradiography image of a lined phantom (^{225}Ac printed on nickel) acquired with a QPID system with particle identification filtering. The closest lines are spaced 0.25 mm apart.

Distribution predictions of alpha emitting radiopharmaceuticals and detached radionuclides

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Keywords (3 max): Dosimetry, PBPK-modelling, targeted alpha therapy

Abstract

a) Background and aim: Physiologically based pharmacokinetic (PBPK) models are essential tools for predicting distributions of radiopharmaceuticals and have been effectively applied to beta-emitting radionuclides (e.g. ^{177}Lu, ^{90}Y). Alpha-emitting radiopharmaceuticals pose additional challenges: 1) their short particle range requires higher spatial resolution in model compartments, and 2) alpha decay increases the likelihood of dechelation, necessitating the modelling of both bound and detached radionuclides.

b) Methods: An existing PBPK model for somatostatin receptor targeting vectors[1] was optimized for ^{212}Pb-DOTAMTATE[2]. The model is enhanced by including physiological substructures of the kidney such as the glomeruli and the tubules. Additionally, a dechelation-function is implemented to simulate the distribution of detached radionuclides. Currently, dechelation is limited to ballistic recoil using the beta-spectrum and assumed binding energy of DOTAM.

c) Results: The refined kidney model enables sub-tissue distribution predictions. The total renal activity remains comparable between both original and refined model. Simulations show 8% of the renal activity localizes in the glomeruli and 70% in the tubules. Incorporating dechelation into the PBPK model increased renal uptake by 8.2%.

d) Conclusion: We presented an optimized PBPK model for predicting the distribution of ^{212}Pb-DOTAMTATE. This model improves quantification of the distribution heterogeneity of the radiopharmaceutical at sub-tissue level and accounts for the contribution of released radionuclides. It was demonstrated that ballistic recoil potentially also affect the distribution of therapeutical radionuclides even via beta-emissions. Further validation is needed to confirm its predictive accuracy and potential for broader applicability.

e) References (optional)

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Comparison and Evaluation of n.c.a. ^{111}In-DTPA-Phe^{1}-Octreotide vs. n.c.a. 177Lu-[DOTA0, Tyr3] TATE] in (GEP-NENs) Treated Patients

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Aim: To compare the dosimetry profile and efficacy of ^{111}In-DTPA-Phe^{1}-Octreotide vs. n.c.a. Lu-177 DOTA-TATE in GEP-NETs, initially i.a. treated with ^{111}In-DTPA-Phe^{1}-Octreotide and after a median progression-free-survival of more than 39 mo, further retreated with i.a. infusions with n.c.a. Lu-177 DOTA-TATE, to confrontate the relapse observed.

Materials and Methods: The average activity of ^{111}In-DTPA-Phe^{1}-Octreotide [Group A: 12 cases (63 liver i.a. catheterizations)] was 6.3±1.3 GBq per session whereas the activity of n.c.a. Lu-177 DOTA-TATE, [Group B: 9 cases (54 liver i.a. catheterizations)] was 7.3±2.3 GBq. Repetitions were performed in intervals of 5-8 weeks. Blood samples were collected 30 min, 2, 4, 8 and 24 hrs p.i. as well as 24 hrs urine samples for dosimetry. Tumour dosimetric calculations were performed using the OLINDA/EXM 1.1 code.

Results: Absorbed dose kidneys' (critical organ) difference for both tracers has been measured to be almost the same. The organ average dose in mGy / MBq of ^{111}In-DTPA-Phe^{1}-Octreotide was found as follows: (a) Liver tumour of 10 gr spherical mass was estimated to be 10.80 (b) Liver 0.14, (c) Kidneys 0.41 and (d) Bone marrow 0.0032 whereas those of n. c. a. 177Lu-[DOTA0,Tyr3] TATE were (a) Liver tumour of 10 gr spherical mass was estimated to be 33.0, (b) Liver 0.19, (c) Kidneys 0.46 and (d) Bone marrow 0.030.

Conclusion: Comparing the infusions of both tracers a statistically significant 2.53-fold higher dose in tumour was found, in favor of 177Lu-[DOTA0,Tyr3]-TATE. Analyzing the Auger and Internal Conversion Electron Emission –high-LET of ^{111}In-DTPA-Phe^{1}-Octreotide an advantageous 8.9-fold lower dose in bone marrow was observed.

ePoster session 1

Could post-infusion ^{177}Lu-PSMA dosimetry be an explanation for the therapeutic response of lesions? A feasibility study

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Keywords (3 max): 177Lu-PSMA, dosimetry, lesion

Abstract

a) Background and aim

^{177}Lu-PSMA treatment for metastatic prostate cancer is routine and validation of its efficacy is still being evaluated. Our study focuses on the assessment of the lesion response as a function of absorbed dose in association with pre-treatment PET imaging.

b) Methods

Eighteen patients underwent at least two cycles of ^{177}Lu-PSMA therapy. Pre-therapeutic imaging with both ^{68}Ga-PSMA and ^{18}F-FDG PET, as well as two post-therapeutic ^{177}Lu-PSMA SPECT/CT acquisitions were performed. Lesion volumes (>2 cm³) were manually segmented on first SPECT/CT without contrast enhancement using 3DSlicer software. For each lesion, each cycle, SUVmax in PSMA and FDG, size, were extracted. Absorbed doses were calculated with OpenDose3D dosimetry workflow, applying standard recovery factors to compensate for partial volume effect.

c) Results

The evolution of the lesions mass between two consecutive courses of treatment as a function of the absorbed dose reveals a threshold of 26.5 Gy from which a mass is reduced by more than 20%. Furthermore, a correlation is observed between the lesion absorbed dose and its 68Ga-PSMA PET SUVmax value (Pearson = 0.92, $p < 0.001$). On the other hand, there is no correlation between the lesion absorbed dose and its FDG SUVmax value.

d) Conclusion

This feasibility study demonstrated the interest of dosimetry after each treatment cycle to assess tumor response. A predictive approach with pre-treatment imaging remains to be confirmed. The study gains to be extended to different tumor response markers.

Comparison of tumour segmentation methods for dosimetry in [^{177}Lu]Lu-PSMA I&T treated patients with metastatic castration resistant prostate cancer

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Keywords (3 max): Lu-177, tumour dosimetry, PSMA

Abstract:

Background and aim.
Image-based tumour dosimetry following radionuclide therapy requires segmentation of tumours to determine the ^{177}Lu concentration in the tumours. This is challenging as tumours are often small, or ^{177}Lu is present in nearby organs or other tumours. Here we present a comparison between three commonly applied segmentation methods, based on a small number of patients with prostate cancer treated by [^{177}Lu]Lu-PSMA I&T. For application of each method specific criteria on tumour diameter and tumour-background ratio must be fulfilled.

Methods
Eighteen tumours in 9 patients were analyzed using the so-called Small Volume-of-Interest (VOI) method (spherical VOIs with diameter 10-15-20 mm), the Large VOI method (with two background correction methods) and the Isocontour method (with/without partial volume correction).
Criteria for inclusion of tumours were based on a phantom study (NEMA IEC body phantom) using different sphere-background ratios and reconstruction algorithms.

Results
The Small VOI method (with 20 mm diameter sphere), the Large VOI methods and the Isocontour methods were found to be in acceptable agreement for tumour dosimetry. Relative to the Isocontour method with partial volume correction as reference method, the relative percentage differences of ^{177}Lu concentration were in the range (-23)-26%, and (-16)-19% for the derived absorbed doses.

Conclusion
The agreement between the methods permits a comparison between dosimetry studies, where some of these methods are applied. As the application criteria are complementary, it is possible to include both small (>15 mm diameter) solitary tumours and larger (>30 mm diameter), possibly non-solitary, tumours in a dosimetry study.

References

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Comparison of absorbed dose using calculation algorithms and manual methods with patients treated with 177Lu-iPSMA, 177Lu-DOTATOC, 131I-NaI and Y-90 glass spheres

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Keywords (3 max): Calculation algorithms, MIRD organ formalism, Sphere method

Abstract

a) Background and aim: Absorbed dose calculation in molecular radiotherapy is influenced by calculation methods. Computational algorithms such as Monte Carlo (MC), dose kernel convolution (CONV), and local energy deposition (LED) are available in clinical or open-source software. Traditional methods like S values for organ pairs using the MIRD schema or the sphere model (SPH) are also used to estimate absorbed dose.

b) Methods: SPECT/CT patients images treated with ^{177}Lu-iPSMA, ^{177}Lu-DOTATOC, and ^{131}I-NaI were analyzed using MIM SurePlan with a convolution-based algorithm. Post-treatment ^{90}Y PET/CT images were evaluated using LED and MIRD methods. Corrections for reconstruction and quantification were applied. Accumulated activity and residence time were used to estimate dose via S values and the sphere model using IDAC-Dose. MC calculations with Open Dose (3D Slicer)-GATE were used as a reference. Percent differences in dose values and relative differences in 3D dose distributions were assessed.

c) Results: Dose differences between MC and CONV were under 5% for most tissues. Bone and lung tissues showed greater variability (up to 32%) with LED methods compared to MC and CONV, due to medium definition. Manual methods like MIRD and SPH tend to overestimate dose due to assumptions about geometry, activity homogeneity, and kernel definition. SPH are suitable for simple tumor dose estimates but not for organs at risk. 3D dose distribution comparisons confirmed these findings.

d) Conclusion: MC and CONV algorithms yield similar results for most tissues. Manual methods are appropriate for simplified dose estimations based on volume and geometry.

Comparison of Peripheral Blood and SPECT-Derived Aortic Activity Concentration in Patients Treated with [^{177}Lu]Lu-DOTATOC

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Keywords (3 max): ^{177}Lu, SPECT, quantification

Abstract

a) Background and aim

The aim of this methodological study was to compare the activity concentration of [^{177}Lu]Lu-DOTATOC in peripheral blood with the corresponding SPECT-derived activity concentration in the aorta. Here we describe the results of the first two patients.

b) Methods

For both patient, 8 mL blood was collected at 1, 24, 96, and 168 hours post injection (h p.i.). Blood samples were divided into two 4 mL samples, weighed and measured in a gamma counter (2480 Wizard, PerkinElmer). SPECT/CT scans were performed in conjunction with the blood sampling. The aorta was chosen to represent a pure blood compartment and was delineated on the CT using volume-of-interests (VOIs) of varying sizes.

c) Results

The highest similarity between the two measurements was found with the smallest VOI (4 mL). Larger VOIs overestimated the activity concentration in the SPECT scan, especially at later time points.

In patient one, gamma counter measurements were 1.8×10², 5.6, 1.4, and 0.81 kBq/mL at 1–168 h p.i. (Fig. 1A); SPECT-derived activity concentrations were higher at all time points but 96 h p.i.; 1.9×10², 9.4, 1.3, and 2.0 kBq/mL. In patient two, 1.4×10², 2.2, 0.027, 0.017 kBq/mL were measured by the gamma counter at 1–168 h p.i. (Fig. 1B), and 4.44, 3.73, and 1.15 kBq/mL by SPECT at 24–168 h p.i. (1 h p.i. SPECT missing).

d) Conclusion

These preliminary results show similar kinetics between the blood samples and SPECT-derived activity concentrations (Fig. 1), though SPECT values were generally higher. Whether the overestimation arises from a positive bias in low-count regions or from differences between aortic and peripheral blood remains to be investigated.

Supporting figure / Table

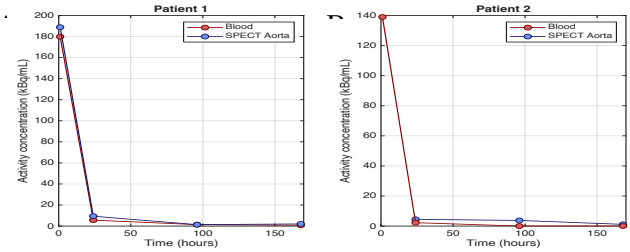

Figure 1

Correlations between blood count and absorbed dose in red bone marrow in [^{177}Lu]Lu-DOTA-TATE treatments

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Keywords (3 max): red marrow, blood based-method, SPECT based-method

Abstract

a) Background and aim
Correlation of red marrow-absorbed doses and haematological toxicity in treatments with [^{177}Lu]Lu-DOTA-TATE has been addressed within the last few years.
The objective of this study is to determine whether blood-based dosimetry or SPECT-based dosimetry of the red marrow correlates better with changes in blood count parameters.

b) Methods
37 patients treated with 4 cycles of [^{177}Lu]Lu-DOTA-TATE were included.
Leukocyte, lymphocyte, neutrophil, and platelet counts were measured before each cycle and one month after the end of treatment. In each cycle, bone marrow absorbed doses were determined using the blood sampling method and four SPECT imaging methods considering: 1)all bone cavities, 2)spheres in all visible vertebrae in the SPECT, 3)spheres in lumbar vertebrae and 4)spheres in thoracic vertebrae. The Spearman correlation test was used to search for correlations between the decrease in blood count of the parameters studied at their nadir and the accumulated absorbed doses at that point.

c) Results
Correlation of the decrease in blood counts with absorbed doses to red marrow for both blood and SPECT methods was weak or moderate ($\rho<0.60$), and significant ($p<0.05$) in most cases, especially for lymphocytes and platelets.
Except for lymphocytes, correlation was stronger for absorbed doses determined using SPECT imaging than for absorbed doses determined using the blood-based method. The SPECT imaging method that showed the stronger correlations was that using spheres in thoracic vertebrae.

d) Conclusion
SPECT-based dosimetry showed in most cases a greater correlation with haematological toxicity than blood-based dosimetry.

Table 1. Spearman's rank correlation ρ(p-value)

	Leukocytes	Neutrophiles	Lymphocites	Platelets
Blood-based	-0.27(0.11)	-0.24(0.15)	-0.50(<0.05)	-0.28(0.09)
SPECT-based, all bone cavities	-0.38(<0.05)	-0.36(<0.05)	-0.37(<0.05)	-0.41(<0.05)
SPECT-based, spheres all vertebrae	-0.36(<0.05)	-0.31(0.06)	-0.36(<0.05)	-0.44(<0.05)
SPECT-based, spheres lumbar vertebrae	-0.33(0.05)	-0.30(0.08)	-0.36(<0.05)	-0.45(<0.05)
SPECT-based, spheres thoracic vertebrae	-0.43(<0.05)	-0.40(<0.05)	-0.42(<0.05)	-0.53(<0.05)

Validation of ^{177}Lu-PSMA-617 parotid dosimetry using Monte Carlo simulations in a 3D-printed patient realistic phantom

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Keywords (3 max): Radiotheranostics, Dosimetry, Metastatic castration-resistant prostate cancer

Abstract

a) Background and aim: Pluvicto® (^{177}Lu-PSMA-617) is an FDA-approved radiotheranostic for metastatic castration-resistant prostate cancer (mCRPC). Voxel-based platforms for radiotheranostic dosimetry are emerging, but we lack a standard commissioning workflow to ensure accuracy. This study developed a quality assurance (QA) protocol for clinical radiotheranostic dosimetry and evaluated two commercial voxel-based dosimetry platforms.

b) Methods: We injected 83 MBq of Pluvicto® into 3D-printed organ-realistic parotid phantoms and acquired SPECT/CT images 96 hours post injection. Clinical voxel-based dosimetry used MIM SurePlan™ MRT (dose point kernel-based) and Voximetry TorchMC™ (accelerated MC). Independent MC (iMC) simulations with 50 billion histories in egs_mird (EGSnrc) and reDoseMC (Geant4 10.02.p02) used SPECT images and nominal mass densities and elemental compositions for bones, nasal air cavity, and water-equivalent materials identified on the CT images. Dose was scored in 1×1×3 mm^3 voxels and time-integrated, assuming physical decay only. We compared the mean parotid doses between the iMC algorithms, dose-volume histograms among all 4 algorithms, and the minimum voxel-wise difference among the most discrepant 2cc (ΔD_{2cc}) between the clinical and the averaged MC calculations.

c) Results: Mean doses in the parotids from the iMC calculations agreed within 2%. The ΔD_{2cc} from MIM SurePlan™ MRT and TorchMC™ were -32.8 and 13.3 Gy, respectively.

d) Conclusion: We developed and tested a QA workflow for standardized radiotheranostic dosimetry to enable accurate dosimetry for patients. Two independent MC calculations agreed but discrepancies with commercial platforms require further investigation.

Supporting figure / Table (optional)

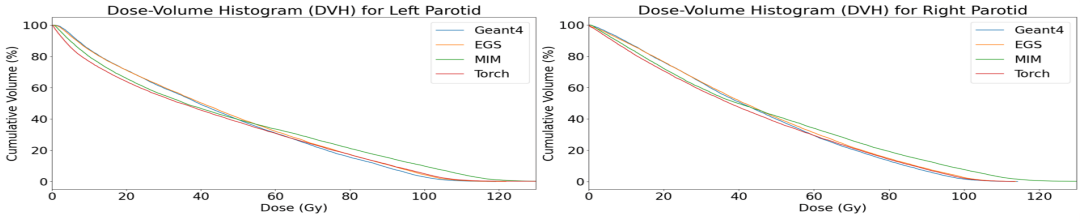

Figure 1: Dose-volume histograms for the left and right parotids.

Feasibility of a one-day protocol combining ^{166}Ho-PLLA simulation and ^{99m}Tc-BrIDA hepatobiliary scintigraphy, and predictive added-value of ^{99m}Tc-BrIDA hepatobiliary scintigraphy combined with personalized dosimetry in selective internal radiotherapy for hepatocellular carcinoma

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Keywords (3 max): SIRT, personalized dosimetry, hepatobiliary scintigraphy

Abstract:

a) Background and aim

The non-tumoral liver is often compromised, making functional assessment crucial in order to reduce risk of liver failure following selective internal radiotherapy (SIRT) for hepatocellular carcinoma (HCC). Hepatobiliary scintigraphy (HBS) can offer valuable insights in this context. This study aimed to assess the feasibility of a one-day protocol combining ^{166}Ho-PLLA simulation and ^{99m}Tc-BrIDA HBS, and evaluate the predictive added-value of functional imaging combined with personalized dosimetry for estimating future remnant liver function (FRLF).

b) Methods

Twenty-one patients underwent 24 simulations with ^{166}Ho-PLLA; 15 proceeded to treatment. HBS using ^{99m}Tc-BrIDA was performed at three time points: one week before ^{166}Ho-PLLA simulation (baseline HBS), on the day of ^{166}Ho-PLLA simulation (one-day HBS), and three months after ^{166}Ho-PLLA treatment (follow-up HBS). Comparisons included: whole liver function between baseline and one-day HBS, FRLF from baseline and one-day HBS vs. actual RLF from follow-up HBS, using 60 Gy isodose segmentation, and correlation of baseline and one-day HBS whole liver function with albumine-bilirubine (ALBI) score.

c) Results

Whole liver function: baseline vs. one-day HBS showed $R^2 = 0.58$ ($p = 0.65$); FRLF vs. RLF: one-day vs. follow-up HBS: $R^2 = 0.70$ ($p = 0.65$), baseline vs. follow-up HBS: $R^2 = 0.75$ ($p = 0.78$); Correlation with ALBI score: baseline HBS: $R^2 = 0.43$, one-day HBS: $R^2 = 0.17$.

d) Conclusion

A one-day protocol combining ^{166}Ho-PLLA simulation and ^{99m}Tc-BrIDA HBS is not feasible. However, baseline HBS, when integrated with personalized dosimetry, shows promis as a predictive tool for remnant liver function in HCC patients undergoing selective internal radiation therapy.

No References (optional) - **No Supporting figure / Table** (optional)

ePoster session 2

Establishing a scatter window correction technique for CZT gamma cameras for improved LSF accuracy

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Keywords (3 max):

Abstract:

a) **Background and aim:** Accurate lung shunt fraction (LSF) estimation is necessary for accurate lung and liver dose estimates in SIRT therapies**.** Scatter contributions affecting LSF accuracy can be accounted for through employment of a scatter energy window correction (SC), validated through Monte Carlo (MC) simulation. This technique has been demonstrated for analogue systems and has not yet been investigated for new cadmium-zinc-telluride (CZT) digital systems with improved spatial and energy resolution. The objective of this research was to firstly determine the accuracy of the LSF estimation for a CZT gamma camera and secondly to improve LSF accuracy through employment of a scatter correction.

b) **Methods:** The GE 870 CZT SPECT system was modelled in SIMIND MC software and validated through experimental ^{99m}Tc phantom work, with a SC established through analysis of the simulated spectra. Planar and SPECT-CT acquisitions of an anthropomorphic phantom with known LSFs were acquired to assess the impact of the SC on LSF estimation. The SC was tested on a series of 4D XCAT digital anatomical phantoms of varying BMIs replicative of the clinical patient cohort.

c) Results: A CZT SC window of 123-129 keV, accounting for scatter in the photopeak window, was established. Uncorrected planar LSF measurements overestimated the true LSF by up to 81% while use of scatter correction led to improved accuracy of within 27%. Data on SPECT-CT LSF estimations with incorporated SC will be presented.

d) **Conclusion:** A CZT specific SC for accurate LSF estimation was established using a combination of experimental investigations and MC simulations of voxel-based phantoms.

Development of a Partial Volume Effect (PVE) correction framework for incorporation into personalised dosimetry approaches towards improved SIRT dose planning

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Keywords (3 max):

Abstract:

a) **Background and aim:** The use of quantitative SPECT-CT with personalised dosimetry systems offers enhanced differentiation between tumour and non-tumour tissues, improved quantification and, hence, more individualised and optimised treatment planning. However, for smaller volumes, tumour uptake can be underestimated due to the partial volume effect (PVE). Inclusion of PVE correction improves the dosimetric accuracy, however, PVE correction is not included in all dosimetry software's. This research aimed to investigate PVEs in SIRT therapy planning, and to assess the impact of PVE correction inclusion on the dosimetry calculation using Simplicity^{90}Y dosimetry software.

b) **Methods:** SPECT-CT acquisitions of a NEMA phantom which included a 60-cc sphere, were performed using GE 870 DR and CZT systems for sphere-to-background ratios of 18:1, 11:1, 5:1 and cold background. Images were reconstructed with varying parameters (subsets, iterations, filter) to determine the optimal reconstruction for quantitation. Recovery coefficients were established and the impact of PVE correction on the target volume dosimetry was retrospectively investigated in patient studies using Simplicity^{90}Y.

c) **Results:** Optimal reconstruction parameters for quantitative pre-SIRT imaging were established. A PVE correction framework which accounts for tumour-to-background ratio, background variability, tumour volume and recovery coefficient was established for pre-SIRT SPECT imaging. The impact of this PVE correction framework on the patient dosimetry will be presented.

d) **Conclusion:** This work established a radionuclide therapy planning framework accounting for SPECT PVEs for improved quantitative dosimetric accuracy, towards delivering more targeted and effective treatments to patients.

Recovery coefficients for concentration-based ^{177}Lu dosimetry of small objects

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Keywords (3 max): ^{177}Lu dosimetry, concentration-based analysis, recovery coefficients

Abstract:

Background and aim: ^{177}Lu dosimetry requires accurate quantification of activity concentration in SPECT/CT images. Three image analysis methods can be adopted; (1) Delineation of targets [1], using recovery coefficients (RC) to correct for partial-volume effects; (2) Over-sized VOIs [2], using background VOIs to subtract contributions from surrounding tissue; (3) Small VOIs [3], applying concentration-based analysis, primarily intended for larger objects with homogeneous uptake.

This study investigates small-VOI analysis on smaller objects, using RCs to correct for partial-volume effects, like the delineation method.

Methods: Phantom measurements were performed on two GE Discovery 670 Pro SPECT/CT systems using: (i) NEMA with ^{177}Lu in six spheres with 10–37 mm diameter, and (ii) Jaszczak with ^{177}Lu in a central 60-mm sphere (cold background). Activity concentration ranges were 0.41–75 MBq/ml (Jaszczak, 14 concentrations) and 0.90–150 MBq/ml (NEMA, 13 concentrations). Clinical ^{177}Lu dosimetry protocols were used. Reconstructed images were analysed using a 7-voxel VOI (4.18 mm isometric voxels), placed in the centre of each sphere.

Results: Count profiles at equal ^{177}Lu concentrations illustrate how partial-volume effects cause lower voxel counts in the centre of smaller spheres (figure 1). However, small-VOI analysis provided highly repeatable results for the measured sensitivity of each sphere over the whole set of measurements for both SPECT/CT systems. Relative standard deviations were 2.2-7.3% (NEMA) and 1.3-2.2% (Jaszczak). Accordingly, adopting RCs may facilitate adequate quantification (figure 2).

Conclusion: Measured data indicate that RCs can be defined to make adequate partial-volume corrections for the small-VOI method, like the delineation method.

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[3] M. Sandström et.al., Eur J Nucl Med Mol Im (2010), DOI: 10.1007/s00259-009-1216-8

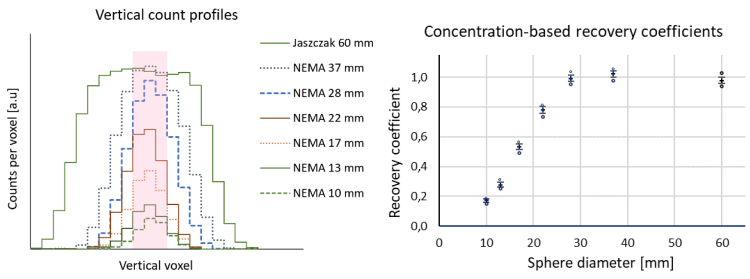

Figure 1. Reconstructed counts in one voxel column over the seven spheres under study. The shaded area covers the analysed 7-voxel VOI.

Figure 2. Calculated small-VOI RCs for the seven phantom spheres under study, presented as mean values with error bars at ±1 σ.

Including Multi-Stage Reconstructions to Improve Deep Learning-based Partial-Volume Correction in ^{177}Lu SPECT Imaging

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Keywords (3 max): partial-volume correction, ^{177}Lu SPECT/CT, deep learning

Abstract

a) Background and aim

Partial-volume effects lead to biased activity-concentration estimates, compromising the accuracy of quantitative SPECT/CT imaging and the reliability of voxel-based dosimetry. Many correction techniques operate post-reconstruction and therefore do not exploit all information contained in raw projections. This study explores enhancing deep learning-based partial-volume correction (DL-PVC [1]) by leveraging multiple reconstruction stages with varying iteration numbers.

b) Methods

DL-PVC was trained as previously described [1] (10,000 XCAT-based [2] attenuation maps, random-shape activity distributions, SPECT simulations using the SIMIND Monte Carlo program [3], reconstructions in PyTomography [4] with OSEM using 5/20/50 iterations (i), 4 subsets (s), attenuation correction, triple-energy-window scatter correction, and resolution modeling). Overlapping smaller structures were added in the activity distributions to model discontinuities and improve the performance of earlier implementations. Seven u-nets (50 epochs, L1 loss, 9,000/500/500 for training/validation/testing) were trained to predict ground-truth activity distributions from single-reconstructions (5i4s, 20i4s, 50i4s) or multi-reconstruction inputs (5i4s+20i4s, 5i4s+50i4s, 20i4s+50i4s, 5i4s+20i4s+50i4s). Performance was evaluated using SSIM, NRMSE, and voxel activity accuracy (VAA [1]).

c) Results

The boxplots show that all new models outperform previous DL-PVC implementations. The best performance was achieved by the u-net using all reconstruction convergence stages. No significant differences were observed between two-reconstruction and 50i4s inputs.

d) Conclusion

Combined reconstruction convergence stages and more realistic training data improve performance of DL-PVC. This highlights DL-PVC's potential to exploit complementary information from different reconstruction convergence stages.

e) References (optional)

[1] Leube, JNM(65(6):980,2024)
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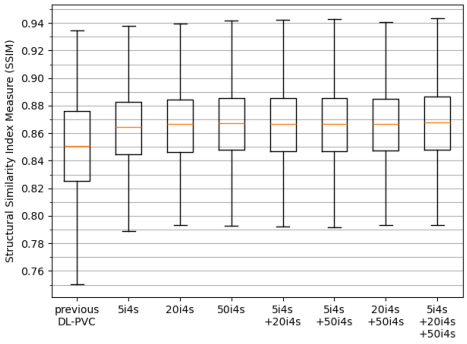
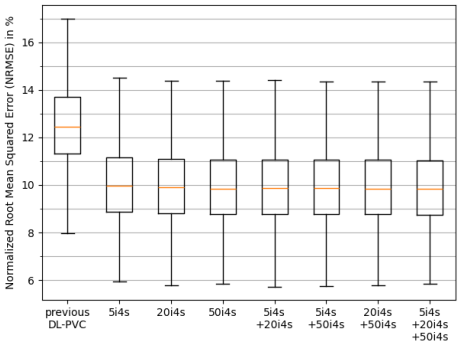
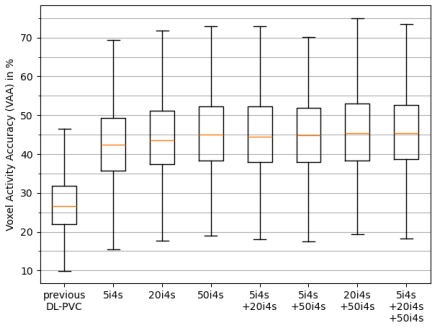
Supporting figure / Table (optional)







Quantitative discrepancies in dosimetry: A voxel-wise comparison of Monte Carlo and S-value–based radiopharmaceutical dose estimations

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Keywords (3 max): voxelized dosimetry, 177Lu-PSMA-617, normal tissue dose

Abstract

a) Background and aim: Radiopharmcaeutical therapy offers promise for challenging diseases, like metastatic castration-resistant prostate cancer. Although ^{177}Lu-PSMA-617 (Pluvicto®) was FDA-approved in 2022, patient-specific dosimetry is not yet standard clinical practice. This work evaluated two approaches to voxelized normal-tissue dosimetry among patients treated with Pluvicto® at our institution.

b) Methods: Patients received Pluvicto® per standard protocol (7400 MBq/cycle, 6 cycles, 6-week intervals). Quantitative SPECT/CT was acquired 72 hours post-injection after 1-3 cycles using a calibrated scanner (Siemens Symbia Intevo). We calculated committed absorbed dose via two approaches: S-value with Hanscheid time integration (MIM SurePlanMRT, v7.1.6) and Monte Carlo (Voximetry Torch, v1.7) with literature-based biokinetics[1]. We considered doses in the kidneys and parotids and compared the approaches using mean-organ and voxel-wise differences.

c) Results: We achieved comparative dosimetry (i.e., MIM and Torch) for 39 cycles across 29 patients. Average kidney dose per cycle was 1.0 ± 0.4 Gy (Torch) vs. 2.2 ± 0.8 Gy (MIM), with MIM exceeding Torch by up to 9.8 Gy (point dose). Parotid doses per cycle averaged 0.6 ± 0.4 Gy (Torch) and 1.6 ± 1.0 Gy (MIM), with MIM exceeding Torch by up to 2.6 Gy (point dose).

d) Conclusion: MIM consistently yielded higher dose estimates than did Torch. Our results highlight that patient-specific dosimetry is highly method-dependent. Ongoing work will evaluate dosimetry approaches compared to measurement and independent Monte Carlo calculations. Standardization of dosimetry approaches is essential for advancing personalized radiopharmaceutical therapy.

e) References (optional) 1. Schuchardt, C., et al., *Prostate-Specific Membrane Antigen Radioligand Therapy Using (177)Lu-PSMA I&T and (177)Lu-PSMA-617 in Patients with Metastatic Castration-Resistant Prostate Cancer: Comparison of Safety, Biodistribution, and Dosimetry.* J Nucl Med, 2022. **63**(8): p. 1199-1207.

Supporting figure / Table (optional)

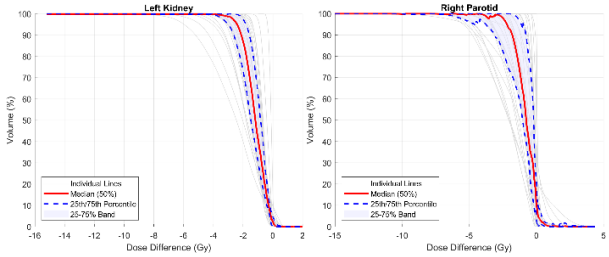

Figure 2. Representative population dose-difference–volume histograms (ΔDVHs) showing voxel-wise dose differences between Torch and MIM. Negative values indicate higher doses calculated by MIM.

A pilot study on absolute quantification of SPECT/CT imaging for Actinium-225 at low count rates

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Keywords (3 max): Quantitative Imaging, SPECT/CT, Actinium-225

Abstract

Background and aim: Absolute quantification of SPECT imaging is required for accurate image-based dosimetry in radiopharmaceutical therapy. High-energy alpha emitters like Ac225 pose challenges due to their low count rate. This pilot study aims to demonstrate the feasibility of absolute quantification in SPECT imaging using a phantom at low activity levels and calculates planar sensitivity for potential application in planar imaging.

Methods: A Jaszczak phantom containing Ac-225 in cylindrical sources was scanned using the Siemens Intevo Bold SPECT/CT with a high-energy collimator, 60 projections per head, 30 seconds per projection, and a 128x128 pixel matrix. Three primary photopeaks were used: 78 keV (20%), 218 keV (10%), and 440 keV (10%) lower scatter windows of 10%, 5%, and 5%. Attenuation correction employed the manufacturer's default CT settings. The image calibration factor (ICF) was calculated, followed by the recovery coefficient (RC) for partial volume correction. Planar sensitivity was measured using an Ac-225 petri dish solution. Standard uncertainties for ICF, RC(V), and planar sensitivity were also calculated.

Results: The ICF for low counts rates of quantified Jaszczak phantom image was 8.43 cps/MBq. The RC(V) model used was $RC(V) = 0.0090 \cdot V^2 - 0.00584 \cdot V + 1.00826$ with R^2=1. Planar sensitivity was 29.3 cps/MBq. Standard uncertainties for ICF, RC(V) and planar sensitivity were 4.74 cps/MBq, 1.12 (2.08 ml), 2.68(4.43ml) and 5.79(7.89ml), 0.29cps/MBq, respectively.

Conclusion: This pilot study demonstrates the feasibility of absolute quantification in low-count-rate SPECT imaging for Ac-225. The high uncertainty observed in the ICF highlights the need for further optimization. These findings will guide future studies in refining quantification methods for Ac-225 imaging.

References (optional)

1. Tulik, M., Kuliński, R., Tabor, Z., Brzozowska, B., Łaba, P., Bruchertseifer, F., Morgenstern, A., Królicki, L., & Kunikowska, J. (2024). Quantitative SPECT/CT imaging of actinium-225 for targeted alpha therapy of glioblastomas. *EJNMMI Phys*, *11*(1), 41. https://doi.org/10.1186/s40658-024-00635-1

Correlation Between SPECT/CT-Derived TMTV Metrics and Biological Response in 177Lu-PSMA Therapy: Insights from a Multicentric Study

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Abstract

a) Background and aim: Radiopharmaceutical therapy with ^{177}Lu-PSMA is an established treatment for metastatic castration-resistant prostate cancer (mCRPC). While PET/CT is the standard for disease evaluation, post-treatment SPECT/CT is gaining recognition for its prognostic value. This study investigates the predictive potential of Total Metabolic Tumor Volume (TMTV) derived from whole-body 360° SPECT/CT performed 24 hours after the first therapy cycle.

b) Methods: A retrospective analysis was conducted on 204 patients treated across four European centers using a 360° CZT SPECT/CT system (VERITON-CT). Patients underwent imaging 24 hours post-treatment. Two reconstruction protocols were used: diagnostic (n=74) and quantitative (n=130), the latter incorporating scatter correction and advanced iterations. TMTV was calculated via automated segmentation excluding physiological uptake in organs at risk, followed by patient-specific thresholding. First-order statistics (min, mean, stdev, max SUV, and TMTV volume) were extracted. PSA nadir was used to assess biological response via the PSA50 criterion. Statistical correlations were evaluated using the Welch test.

c) Results :Significant differences were observed in TMTV SUV max ($p<0.001$) and SUV mean ($p=0.001$) between responders and non-responders, indicating strong predictive value. TMTV volume showed no significant correlation ($p=0.953$). Stratification by reconstruction type revealed superior predictive power in the quantitative group ($p<0.001$ vs. $p=0.067$).

d) Conclusion: This multicentric study supports the prognostic utility of SPECT/CT-derived TMTV metrics post-first ^{177}Lu-PSMA cycle. It underscores the importance of quantitative reconstruction protocols for early response assessment.

Supporting figure / Table (optional)

	Threshold	AUC	Sensitivity	Specificity	Accuracy	NPV	PPV	F1 Score	p-value	Adj. p-value
TMTV SUV mean	6.11	0.702	0.611	0.789	0.715	0.741	0.673	0.641	< 0.001	0.001
TMTV SUV stdev	6.06	0.761	0.611	0.842	0.746	0.753	0.733	0.667	< 0.001	< 0.001
TMT SUV max	69.53	0.731	0.537	0.816	0.700	0.713	0.674	0.598	< 0.001	< 0.001
TMTV SUV min	1.84	0.462	0.500	0.553	0.531	0.609	0.443	0.470	0.431	0.517
TMTV sum	203148.94	0.582	0.685	0.513	0.585	0.696	0.500	0.578	0.138	0.207
TMTV Volume (cc)	558.96	0.518	0.667	0.434	0.531	0.647	0.456	0.541	0.953	0.953

Performance metrics for different TMTV features across all the 130 patients (quantitative reconstruction)

Fast Enough to Matter: Shortened SPECT Protocols for Accurate Dosimetry in Lu-177 PSMA Therapy

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Keywords:

Abstract

a) Background and aim

The recent approval of ^{177}Lu-PSMA-617 has sparked growing interest in adopting this therapy for prostate cancer in Canada. However, widespread implementation of post-treatment SPECT imaging remains limited by scanner availability and lengthy acquisition protocols.
This study evaluates the impact of reduced acquisition times and fewer projections on organ dosimetry accuracy, using multiple reconstruction algorithms.

b) Methods

^{177}Lu-PSMA-617 projection data (96 projections, 15 seconds-per-projection) from 100 PR.21 (NCT04663997) trial patients were utilized. We simulated shortened protocols by reducing projection counts and time per projection via binomial thinning. Data were reconstructed using OSEM and BSREM algorithms with PyTomography[1], and time-integrated activities (TIA) were computed using PyTheranostics[2]. Differences in TIA estimates between standard and shortened protocols were assessed for organs at risk.

c) Results

In a preliminary cohort (n=44), reducing projections to 24 (15 seconds each), resulted in a median TIA underestimation of -3.1% ([-8.1%, +4.8%]) (OSEM) and -2.4% ([-7.7%, +3.5%]) (BSREM) in kidneys, and -6.2% ([-16.8%, +6.2%]) (OSEM) and -3.5% ([-11.5%, +7.4%]) (BSREM) in parotid glands. Using all 96 projections with reduced time per projection (as low as 3.75 s/projection) yielded a TIA deviation of -1.0% ([-5.6%, +1.9%]) in kidneys and -0.2% ([-7.2%, +4.1%]) in parotid glands for OSEM, while BSREM slightly overestimated TIA, especially in parotids +1.0 ([-5.8%, +37.5%]).

d) Conclusion

Our findings suggest that acquisition time per projection can be reduced by up to a factor of 4 using OSEM without significantly compromising organ-at-risk dosimetry. Ongoing work includes evaluating lesion-level impacts and the potential benefits of Monte-Carlo-based reconstruction.

e) References

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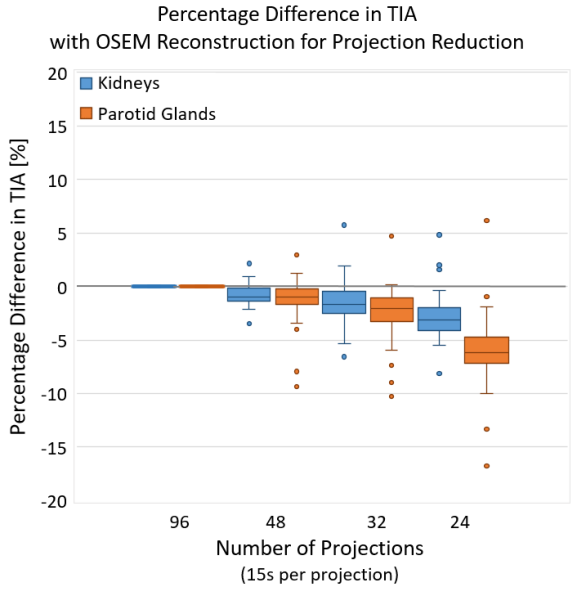
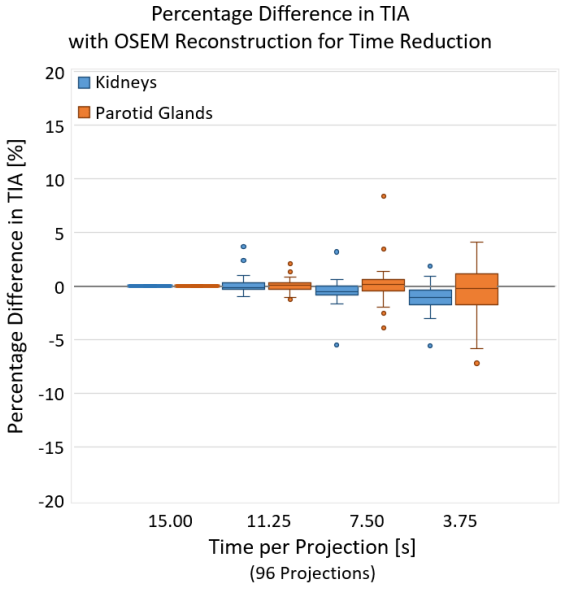
[2] Kurkowska, S., Brosch-Lenz, J., Esquinas Fernandez, P., Toosi, A., Polson, L., Rahmim, A., Benard, F., & Uribe, C. (2024). PyTheranostics: A novel software tool to accelerate research in personalized theranostics with preclinical and clinical dosimetry. *Journal of Nuclear Medicine*, 65(supplement 2), 242469. GitHub: https://github.com/qurit/PyTheranostics.git

Supporting figures

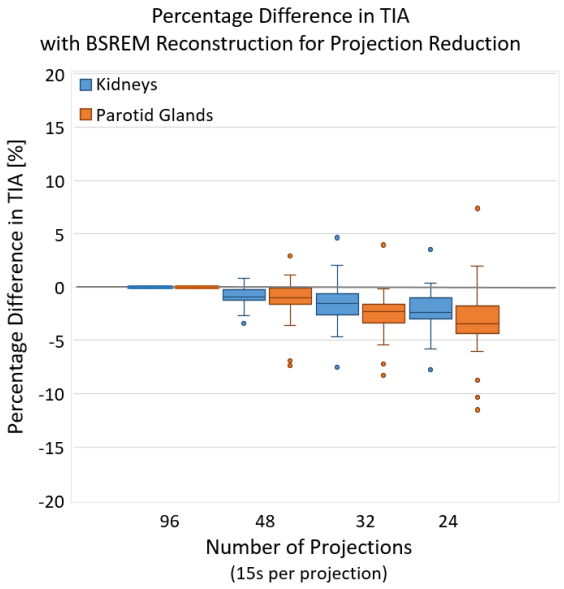


(I)

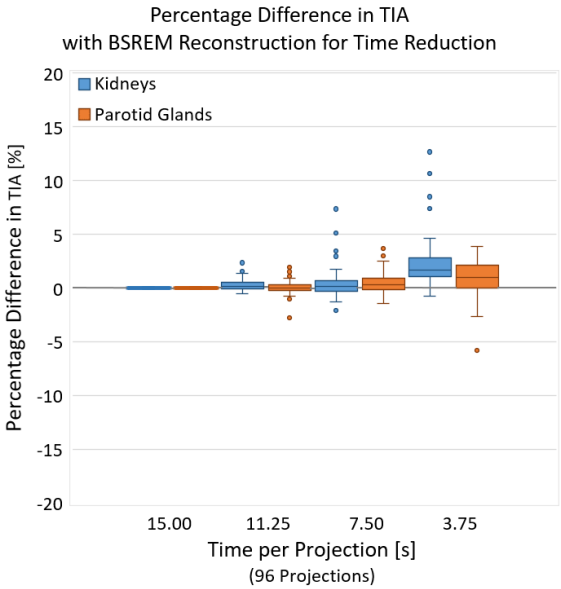


(II)

OSEM reconstruction algorithm used to determine the percentage difference in time integrated activity (TIA) of the kidneys (blue) and parotid glands (orange) for (III) reduced number of projections (96, 48, 32, 24) and for (IV) reduced time per projection (15.00s, 11.25s, 7.50s, 3.75s)



(III)



(IV)

BSREM reconstruction algorithm used to determine the percentage difference in time integrated activity (TIA) of the kidneys (blue) and parotid glands (orange) for (III) reduced number of projections (96, 48, 32, 24) and for (IV) reduced time per projection (15.00s, 11.25s, 7.50s, 3.75s)

PSMA-PET based dose planning for Lu-177-PSMA therapy: speculation in retrospect

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Keywords (3 max): dose planning, Lu-177-PSMA, quantitative imaging

Abstract

a) Background and aim

Peters *at al* [1] studied the potential of pre-treatment Ga-68-PSMA-PET/CT to predict dose distribution in Lu-177-PSMA-617 therapy with promising results. Our aim is to similarly handle, in retrospect, a group of patients imaged, treated and analyzed with our local clinical protocol.

b) Methods

Six patients were imaged with F-18-PSMA-1007 (3 MBq/kg) and treated with Lu-177-PSMA-I&T (7.4 GBq) for the first cycle. Firstly, we compared projected activity distributions between the pre-treatment PET/CT (single time-point at 2 h) and post-treatment SPECT/CT scans acquired at an early (4 h) and late (144 h) time-point. For each patient, one representative lesion ("tumor") was analyzed in more detail. Dose estimates were calculated based on the PET/CT and literature values [2] for effective half-lives and compared against the dosimetry results from the treatment.

c) Results

We observed high variations in the PET/SPECT absorbed dose ratios, which were not improved by applying patient-specific effective half-lives or resolution recovery correction methods. Although the projected kidney PET uptakes appeared higher, no consistent scaling factor, as proposed in [1], was seen in our cohort. The projected PET/SPECT$_{4h}$ activity concentration ratio ranges were 0.96-2.4 for kidneys, 0.31-4.1 for tumor, and 0.15-2.2 for lumbar spine (lesions subtracted), and the absorbed dose ratio ranges were 1.05-2.88, 0.70-1.65, and 0.10-2.33, respectively.

d) Conclusion

Our findings suggest that the predictive value of F-18-PSMA-1007 PET/CT for Lu-177-PSMA-I&T dosimetry varies substantially across patients, highlighting the need for further investigation. With closer inspection of the analysis steps and inter-patient variations, some hypotheses for explanations can be formed – we plan to further discuss these speculations.

e) References (optional)

1. Peters SMB, *et al*. Eur J Nucl Med Mol Imaging. 2022 Mar;49(4):1101-1112. doi: 10.1007/s00259-021-05538-2.
2. Schuchardt C, *et al*. J Nucl Med. 2022 Aug;63(8):1199-1207. doi: 10.2967/jnumed.121.262713.

Supporting figure / Table (optional)

ePoster session 3

Integration of experimental and inter-user uncertainties in the quantification of ^{177}Lu in SPECT/CT images for molecular radiotherapy absorbed dose calculation

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Keywords (3 max): Experimental uncertainty, ^{177}Lu quantification, SPECT/CT imaging

Abstract

a) Background and aim

Accurate activity quantification is essential for personalized dosimetry. This study aims to refine the estimation of uncertainty proposed by EANM, by integrating experiment-related and inter-user components when determining the calibration factor (CF) and the recovery coefficient (RC).

b) Methods

The experimental uncertainty was quantified from repeated phantom acquisitions. The CF was assessed under varying phantom position and activity concentrations (224 to 12 kBq/mL). The RC values were derived using a Jaszczak phantom with filled spheres (0.5 cc to 106 cc), different contrasts (7:1, 10:1), activity concentrations in the spheres (832 to 551 kBq/mL) and phantom positions. The impact of sphere volume definition was studied. The uncertainties calculated using this approach were compared to the standard EANM model.

c) Results

The experimental CF uncertainty was equal to 0,87 % and was a minor component of the global CF uncertainty equal to 10,87%. It was found for the smaller sphere, an experimental RC uncertainty equal to 4% and equal to 1,1% for the largest. The uncertainty associated to the volume definition was equal to 4,49% When estimating the activity of ^{177}Lu in a volume of 30 cc, the total uncertainty is found to be 65,54% with the proposed model in comparison to 58% with the standard EANM model.

d) Conclusion

The proposed model provided more realistic uncertainty in activity estimates compared to the standard EANM model. A work is ongoing to evaluate activity quantification accuracy on SPECT/CT images of an anthropomorphic phantom mimicking ^{177}Lu-PSMA patient uptake.

Feasibility and Safety of 90Y Radioembolization (TARE) Retreatment Guided by Voxel-Based Dosimetry and Post-Therapy Imaging: a Case Study

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Keywords (3 max): Radioembolization; Voxel-based Dosimetry; Retreatment

Abstract:

Background and aim:
90Y TARE is an effective and safe treatment for hepatocellular carcinoma (HCC), inducing tumor necrosis and delaying progression. In selected cases of recurrence, repeat TARE may be indicated, although concerns persist regarding cumulative liver dose and risk of radiation-induced liver disease. Evidence on safety and efficacy of repeated treatments in the same hepatic region remains limited. This study aims to assess the feasibility and safety of repeat 90Y TARE using voxel-based dosimetry.

Methods:
A patient with unresectable HCC underwent two TARE procedures with TheraSphere® glass microspheres, 19 months apart, targeting the same hepatic arterial territory. Voxel-based dosimetry with MIM software was conducted using 99mTc-MAA SPECT to determine administered activity. Post-treatment Y90 PET-CT verified microsphere distribution and absorbed doses. Tumor segmentation was performed on MAA-SPECT, registered to diagnostic CT. Safety was evaluated through assessment of abdominal toxicities; efficacy was based on imaging response.

Results:
Cumulative administered activity was 4.9 GBq (2.8 GBq and 2.1 GBq respectively). Lung shunt was <6% in both procedures. Calculated mean whole liver doses were 71Gy and 63Gy respectively (below the recommended value of 90Gy for single treatments). Mean tumor doses were 297Gy and 222Gy. Post-treatment imaging confirmed activity distribution and pre-treatment dosimetry. Tumor control was achieved after both treatments without observed toxicity. Follow-up is ongoing.

Conclusion:
Repeated TARE to the same hepatic territory seems feasible, with an acceptable safety profile and evidence of objective tumor response. Voxel-based dosimetry supported by post-therapy imaging provides critical support to guide re-treatment decision.

Supporting Table

	Whole Liver Volume	Tumor Volume	Whole Liver Mean Dose	Tumor Mean Dose	Normal Liver Mean Dose
1st treat	1615 cc	357 cc	71 Gy	297 Gy	17 Gy
2nd treat	1613 cc	169 cc	63 Gy	222 Gy	44 Gy

Standardisation and development of dosimetric approaches for trials sponsored by the French Urogenital Tumour Study Group (GETUG) for external beam radiotherapy and molecular radionuclide therapy

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Keywords (3 max):, Dosimetry standardization, Molecular radionuclide therapy, External beam radiotherapy

Abstract :

a) Background and aim

The French GETUG group develops research programs for urogenital cancers and collaborates with a large number of French and international centres. A group of medical physicists was recently set up with the objective of standardising the practices regarding dosimetric methods for external beam radiotherapy (EBRT) and molecular radionuclide therapy (MRT).

b) Methods

The following objectives has been identified:
- Collection of practices, imaging systems, linear accelerators, dosimetry software in the GETUG network.
- Proposal for a standardised dosimetric protocol with associated budget, to be incorporated in GETUG trials when MRT treatment is planned.
- Development of methods and tools to calculate cumulative absorbed doses when association of Stereotactic Body Radiation Therapy and ^{177}Lu-PSMA are considered.
- Communication on dosimetry methods and challenges to medical specialists.

c) Results

The group comprises 38 physicists from 23 French hospitals, 18 of whom specialise in nuclear medicine. A collection of practices was conducted for 12 centres with various levels of experience in MRT dosimetry.
A standardised protocol for MRT dosimetric studies is currently being developed, which includes the qualification and calibration of the systems based on ^{177}Lu SPECT EARL accreditation and the images acquisition protocols for various systems. The proposed workflow integrates the procurement of anonymised quantitative images for the purpose of centralised dosimetric calculations.

d) Conclusion

A group of medical physicists was established within the French GETUG group with the aim of proposing standardised dosimetric protocols for EBRT and MRT trials involving urogenital tumours.

A Radiobiological Model for Studying Tumor Control Probability in Targeted Radionuclide Therapies

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Keywords (3 max): targeted radionuclide therapy, tumor control probability, simulation
Abstract:

a) Background and aim
Targeted radionuclide therapy (TRT) has emerged as a promising treatment for various cancer types. However, traditional TRT efficacy analysis often overlooks key factors like dose-rate dynamics and tumor repopulation. This study presents a radiobiological model for tumor control probability (TCP) that incorporates these factors, aiming to offer a more comprehensive framework for optimizing TRT treatment schedules and improving therapeutic efficacy.

b) Methods
The model integrates the lethal-potentially lethal model with the Zaider–Minerbo model for TCP. It incorporates factors such as dose-rate patterns over multiple treatment cycles, tumor cell repopulation, and repair kinetics, which are often neglected in traditional absorbed dose-based evaluations. Originally applied to analyze TRT efficacy in advanced prostate cancer (Galler et al., 2024), we now focus on its general applicability to various cancer types treated with TRT.

c) Results
The model demonstrated that variations in the dose-rate pattern significantly affected TCP outcomes, even when the absorbed dose remained constant. It showed that dose-rate dynamics and tumor repair kinetics can substantially influence TRT efficacy, highlighting the importance of considering these factors in treatment planning. This result was consistent across multiple parameter settings reflecting diverse tumor biological profiles, suggesting broad applicability in optimizing TRT across diverse clinical contexts.

d) Conclusion
This model provides a more detailed framework for studying TCP in TRT. By incorporating dose-rate effects and cellular repair processes, it refines treatment planning, offering significant potential for improving TRT efficacy. Although initially applied to advanced prostate cancer, the model can be adapted for other cancer types, supporting more personalized and optimized therapeutic strategies.

e) References (optional)
Galler M, Chibolela C, Thiele F, Rogasch JMM, Amthauer H. Dose-rate effects and tumor control probability in 177Lu-based targeted radionuclide therapy: a theoretical analysis. Phys Med Biol. 2024 Oct 1;69(20). doi: 10.1088/1361-6560/ad7cbe. PMID: 39293493.

Quantification of cellular damage using advanced computational techniques

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Keywords (3 max): theragnostics, dosimetry, Monte Carlo simulations

Abstract

Background and Aim: Understanding radiation-induced DNA damage at the cellular level is critical for optimizing targeted radionuclide therapy (TRT) and Boron Neutron Capture Therapy (BNCT). The "molecularDNA" application, part of the Geant4-DNA toolkit, enables detailed Monte Carlo simulations of DNA damage and repair, offering insights into accurate dosimetry and cellular damage quantification for these therapies. This study aims to evaluate the efficacy of "molecularDNA" in simulating early DNA damage for TRT and BNCT applications.

Methods: Using the Geant4-DNA toolkit, the "molecularDNA" example was employed to simulate both physical and chemical radiation interactions in a human fibroblast cell model with a fractal-based DNA geometry (~6.4 Gbp). Simulations included radionuclides (e.g., Lu-177, Ac-225) for TRT and neutron-induced reactions for BNCT. Direct and indirect DNA damage, including single-strand breaks (SSBs), double-strand breaks (DSBs) as well as more complex damage, were quantified. The independent reaction time (IRT-sync) approach modeled chemical stages, and results were validated against literature data.

Results: The "molecularDNA" application accurately predicted SSB and DSB yields, aligning with literature data lithium inelastic cross-section data. Fragment length distributions and repair kinetics were consistent with published radiobiological studies, demonstrating reliable dosimetry at the nanoscale.

Conclusion: The "molecularDNA" application provides a robust platform for quantifying radiation-induced DNA damage in TRT and BNCT, supporting precise dosimetry and improved therapeutic outcomes. Future enhancements in DNA geometries will further refine its predictive capabilities.

Avidination for RadionuclideTHerapy in Nonpalpable Breast Cancer (ARTHE): Dosimetry of a New Locoregional Approach

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Keywords (3 max): non-palpable breast cancer, Biotin-DOTA-90Y, dosimetry

Abstract

a) Background and aim

The "Avidination for Radionuclide Therapy in Nonpalpable Breast Cancer (ARTHE)" is a novel nuclear medicine approach for early breast cancer management. After a Vacuum Assisted Breast Biopsy (VABB), avidin is injected into the VABB cavity, followed by Biotin-DOTA-90Y. The goal is to deliver 200 Gy to the residual microscopic disease in the target volume surrounding the VABB cavity. This phase I study investigates three activity levels of 90Y Dota-biotin and evaluates the side effects of biodistribution of avidin-biotin-DOTA-90Y after loco-regional injection.

b) Methods

A radioactive solution is injected in the cavity resulting from a VABB procedure, with three activity levels investigated: 28, 57, and 126 MBq. For each patient a standard scintigrafic whole-body image and PET image are acquired at 1-3 h p.i. A Monte Carlo (MC) simulation is performed to evaluate the dose in tissues surrounding the cavity, where residual microscopic disease is generally present. Different cavity geometries and volumes are simulated. he dose profiles outside the cavity was fitted and an analytic approach was implemented in order to estimate the absorbed dose for several injected activities. The model also considers a possible diffusion in the shell surrounding the VABB cavity.

c) Results

The dose was estimated at 1-3 mm of distance from the edge of cavity, with and without the diffusion. The diffusion increases the dose in the layers surroundings the cavity.

d) Conclusion

The dose strongly depends on the assumption made on the cavity volume and on the distance from the injection site. The small volume of interest represents a challenge for an accurate dosimetry also for a MC approach.

e) References (optional)

Supporting figure / Table (optional)

^{212}Pb Human dosimetry estimates derived from ^{203}Pb SPECT imaging of an integrin-targeting peptide and the impact of ^{212}Bi disassociation on kidney dose

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Keywords (3 max): ^{212}Pb, Preclinical Dosimetry, ^{212}Bi disassociation

Abstract:

a) Background and aim:

^{212}Pb is a promising radionuclide for receptor targeted alpha therapy with ^{203}Pb as an imaging surrogate. If not mitigated, disassociation of decay product ^{212}Bi results in accumulated dose in the kidneys. Here we focus on the impact of kidney dose due to release of ^{212}Bi utilizing preclinical imaging of ^{203}Pb translated to ^{212}Pb.

b) Methods

^{203}Pb was obtained from Arronax (France) through the PRISMAP EU program (N#10100857). Female mice (n=4) were injected with ^{203}Pb labelled integrin targeting peptide and imaged at 0.08, 0.66, 5, 18, and 24 hours post injection. Brain, salivary glands, heart, kidneys, liver, gut, bladder, and whole-body were segmented. Time activity curves were translated to ^{212}Pb and scaled to human ICRP 89 adult female. Time integrated activity coefficients were calculated with estimation of bladder using the voiding bladder model. Dosimetry estimates were calculated in OLINDA 2.2.3 both with the assumption of equivalent biodistribution for all decays and with the assumption of ^{212}Bi disassociation with 40% accumulating in the kidneys, both runs used RBE=5.

c) Results

The greatest dose from both runs was to the kidneys, with the no disassociation run estimating 89.1 mSv/MBq and the ^{212}Bi disassociation estimating 93.5 mSv/MBq. The dose to other tissues was similar for both runs (0.25-11.8 mSv/MBq).

d) Conclusion

^{212}Pb has great potential for treatment in clinical practice. It is evident that the kidneys are likely to limit dose, and it is necessary to have an understanding of mitigation and impact of released ^{212}Bi to properly plan dosing.

Can [^{64}Cu]Cu-PSMA-I&T improve diagnosis and pre-therapeutic dosimetry in prostate cancer?

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Keywords (3 max): PSMA, Dosimetry, Theranostic

Abstract

Background and aim: Prostate cancer remains a leading cause of cancer-related death. PET/CT imaging using [^{68}Ga]Ga-PSMA-11 and radiopharmaceutical therapy using [^{177}Lu]Lu-PSMA-617 have become standard-of-care for patients with mCRPC. However, [^{177}Lu]Lu-PSMA-617 is typically administered at a fixed dose without individualized dosimetric planning, as pre-therapeutic imaging with ^{68}Ga-tracers does not account for differences in pharmacokinetics or radionuclide properties. This study proposes the use of [$^{64/67}$Cu]Cu-PSMA-I&T as a more accurate theranostic pair to better demonstrate the predictive value of PET imaging when using isotopically matched diagnostic and therapeutic agents.

Methods: An isotropic 0.5mm resolution small-animal RPC-PET system developed by LIP-Coimbra was used for image acquisition, following administration of [^{64}Cu]Cu-PSMA-I&T (482.64±110.16MBq). PET images were acquired at multiple time points to derive time-integrated activity coefficients (TIACs). Absorbed doses to tumors and critical organs were calculated according to MIRD schema using OLINDA/EXM (version 2.3). The method was validated using ex vivo biodistribution data.

Results: PET/MR imaging showed high and specific uptake in PSMA-positive tumors (5.36±2.34%ID/g), with minimal uptake in PSMA-negative controls (0.37±0.34%ID/g) at 12h p.i. Except for the anticipated renal clearance, no significant off-target accumulation was observed, highlighting the potential of [^{64}Cu]Cu-PSMA-I&T for pre-therapeutic imaging and dosimetry, and subsequent treatment with its ^{67}Cu-based therapeutic counterpart. Tumor absorbed doses were determined to range from 2.24 to 0.0133 Gy/MBq, depending on tumor mass.

Conclusion: These findings support the feasibility of [^{64}Cu]Cu-PSMA-I&T PET imaging as a tool to guide personalized treatment, enabling optimized dosing and improved efficacy of radioligand therapy.

References (optional): A. Blanco et al., «An RPC-PET prototype with high spatial resolution», Nucl. Instrum. Methods Phys. Res. Sect. Accel. Spectrometers Detect. Assoc. Equip., vol. 533, n.o 1–2, pp. 139–143, nov. 2004, doi: 10.1016/j.nima.2004.07.016.

Supporting figure / Table (optional)

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Cure Rate of Dosimetry-based 131I Therapy in Hyperthyroidism Management

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Keywords (3 max): Radioiodine therapy, Dosimetry, Cure Rate

Abstract

a) Aim: This study aims to evaluate the effectiveness and cure rate of individualized radioiodine therapy in patients diagnosed with Graves' disease and toxic adenoma.

b) Methods: A total of 11 patients with toxic adenoma and 20 patients with Graves' disease were enrolled in the study. Radioiodine activities were individually calculated using patient-specific data and a mathematical model to deliver target absorbed doses of 300 Gy for toxic adenoma and 200 Gy for Graves' disease. The mean administered RAI activity was 826 ± 124 MBq for patients with toxic adenoma and 541 ± 215 MBq for those with Graves' disease.

c) Results: At the 3-month follow-up, 35% of patients with Graves' disease and 54.6% of those with toxic adenoma reached a euthyroid state. Hypothyroidism occurred in 65% of Graves' patients and 45.4% of toxic adenoma patients; all began thyroid hormone replacement therapy and achieved euthyroid status by the 6-month follow-up.

d) Conclusion: Dosimetry-based RAI therapy achieved complete remission within three months following a single administration of ^{131}I, with no patients requiring a second course of RAI therapy. In contrast to empirical treatment protocols, individualized therapy enhances safety, minimizes risk, and improves clinical outcomes.

Assessment of uncertainty in kidney concentration at multiple time points following PRRT with ^{177}Lu-DOTATATE

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Keywords (3 max): **^{177}Lu-DOTATATE, uncertainty in concentration, dosimetry**

Abstract

Background and aim

During peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE, the absorbed dose to the kidneys is determined by fitting an exponential curve to the concentration in the kidneys during three timepoints p.i. The aim om this study was to estimate the uncertainty in the concentration in the kidneys at the three different timepoints.

Methods

1154 patients with metastatic neuroendocrine tumours were included in the study. SPECT images were acquired at 24, 96 and 168 h post infusion of 3.7-7.4 GBq ^{177}Lu-DOTATATE and the concentration to the kidneys was calculated by delineating the kidneys using small VOI (4 cm^3). The uncertainty in the concentration was calculated using error propagation of the concentration equation. In 15 patients the right kidney, and in 20 patients the left kidney was excluded from the calculations because of missing organ.

Results

The median uncertainty in the absorbed dose for the kidneys during 24, 96 and 168 h p.i. was 5.04 (IQR:5.03-5.04), 5.1 (IQR:5.08-5.12) and 7.17 (IQR:7.13-7.22) % respectively. For the left kidney the corresponding uncertainty was 5.04 (IQR:5.03-5.05), 5.1 (IQR:5.08-5.13) and 7.18 (IQR:7.14-7.23) % respectively. The highest uncertainty was seen for the latest timepoint, which is highly affected by the uncertainty in the placement of the 4 mL VOI. There was no significant difference in the uncertainty between right and left kidney at the different timepoints.

Conclusion

The uncertainty in the concentration during 24 and 96 h p.i. are lower than during 168 h p.i.

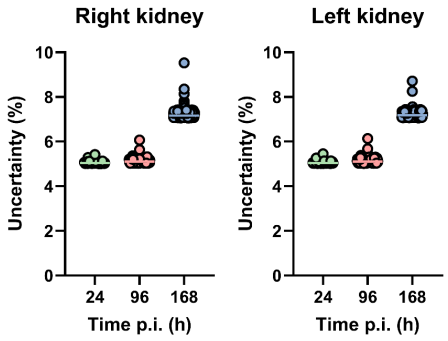

Figure: Uncertainty in kidney concentration in right and left kidney during 24, 96 and 168 h p.i. of ^{177}Lu-DOTATATE. Solid line represents median value.

Red marrow dosimetry with imaging method: a new approach for ^{131}I and ^{177}Lu dose-toxicity correlations

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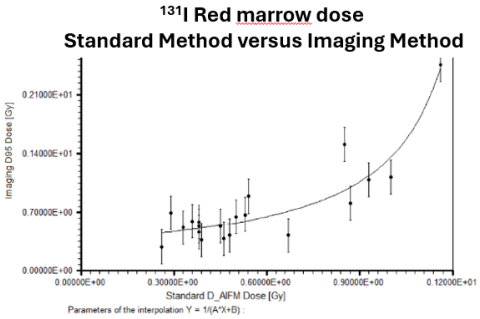
Keywords (3 max): red marrow dosimetry, imaging, toxicity

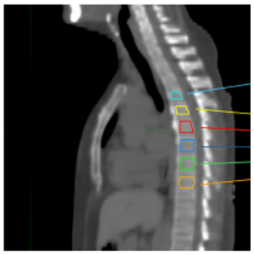
Background and aim
Red marrow dosimetry is mandatory in radionuclide therapies but often not implemented. Aim of this work was to investigate imaging dosimetry compared to standard method for toxicity dose correlations.

Methods
After the therapeutic administration (^{177}Lu®Lutathera 7400 MBq or Na^{131}I 3700÷7473 MBq) blood samples (0-2,24,48,96 h), whole-body (WB) measurements (∀ 2 h) and 2 SPECT-CT (24-48,96 h) were acquired. Red marrow doses were calculated with standard (blood/WB) method (SM). With imaging method (IM) vertebras were contoured both for 36 ^{177}Lu patients (L2-L4 and spleen) and for 20 ^{131}I patients (T4-T9) with the 3D-voxel dosimetry software (MIMSureplanMRT). Correlations and paired t-test analysis as well as ROC curve analysis were performed.

Results
For ^{177}Lu red marrow doses were (1.31±0.31) Gy (IM) and (0.83±0.58) Gy (SM) respectively. No correlation between IM and SM was obtained (R^2_{D95} = 0.39) as well as nor statistical agreement (paired t-test $p > 0.05$). No correlation of red marrow dose to hematological toxicity was found (AUC_{IM} = 0.56, AUC_{SD} = 0.62), while total spleen mean dose demonstrate a better predictive power (AUC_{IM} = 0.71). Conversely ^{131}I red marrow dose showed a good correlation between IM and SM method (R^2_{D95} = 0.82) with P −value < 0.0001. Mean doses were (0.75±0.50) Gy (IM) and (0.56±0.26) Gy (SD) respectively. For these patients, correlation with hematological toxicity, well known by literature, was not investigated. Dose variability within different contoured vertebras was evaluated < 1% both for ^{177}Lu and ^{131}I.

Conclusions
Red marrow dosimetry with imaging method demonstrated his effectiveness both for ^{131}I and ^{177}Lu.





Automation of clinical reporting of dosimetry calculations and uncertainties for MRT

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Uncertainty Quantification, Clinical Dosimetry, Interface Automatization Reporting

Abstract:

Personalized dosimetry in molecular radiotherapy (MRT) is essential to optimize the balance between therapeutic efficacy and toxicity. Despite technical advances, most clinical reports omit the quantitative analysis of uncertainties, compromising clinical accuracy. This work presents an automated interface to quantify, propagate, and report dosimetric uncertainties in accordance with the guidelines of the EANM Dosimetry Committee.

A systematic analysis was performed on the main sources of uncertainty in the MRT workflow: functional volume, count rate, recovery coefficient, calibration factor, time-activity curves (TAC), accumulated activity, S value, and absorbed dose. Empirical models and error propagation were applied using a matrix-based formalism that incorporates covariance matrices. The interface was developed in Python and MATLAB, using statistical libraries (NumPy, SciPy) and graphical integration for clinical analysis. Validation was carried out through retrospective analysis of patients treated with ^{177}Lu-PSMA, Na^{131}I, and ^{90}Y.

The tool enables patient-specific dosimetric analysis and automatic generation of standardized reports compatible with dosimetry software (such as MIM SurePlan MRT). Absorbed dose, D95%, and maximum dose were estimated for tumors and organs at risk, including expanded uncertainties. The dominant sources of uncertainty were identified as the recovery coefficient and volume in small structures.

This solution improves reproducibility and quality control, promotes the standardization of dosimetry with uncertainty, and strengthens dosimetric auditing processes and the design of prospective studies in nuclear medicine, fostering safer and more precise MRT worldwide.

Reference : Gear, et. al. (2018). EANM practical guidance on uncertainty analysis for molecular radiotherapy absorbed dose calculations. European Journal of Nuclear Medicine and Molecular Imaging.

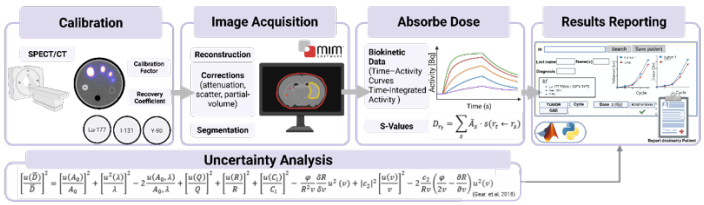

Figure 1: Workflow for absorbed dose quantification and uncertainty propagation in MRT.

Clinical Implementation and Voxel Dosimetry of ^{161}Tb-PSMA Therapy in mCRPC: First Experience in Southeast Asia

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Keywords (3 max):

Abstract

a) Background and aim

Prostate-specific membrane antigen (PSMA)-targeted radioligand therapy is an established treatment for metastatic castration-resistant prostate cancer (mCRPC). While Lutetium-177 (^{177}Lu) PSMA therapy is widely used, Terbium-161 (^{161}Tb) PSMA presents a promising alternative due to its emission of both beta and Auger electrons, potentially enhancing efficacy, particularly in micrometastatic disease. In this work, we report the first clinical application of ^{161}Tb-PSMA in Thailand and Southeast Asia for a patient with progressive mCRPC following 13 cycles of ^{177}Lu-PSMA. Radiopharmaceutical preparation, quantitative SPECT/CT imaging, and voxel-based absorbed dose estimation were integrated to guide personalised treatment.

b) Methods

Due to the absence of ^{161}Tb in commercial SPECT systems, a custom calibration protocol was implemented. Post-therapy SPECT/CT was acquired at 2 h, 24 h, and 96 h, with reconstruction tailored for voxel-level dosimetry.

c) Results

The mean kidney absorbed dose following ^{161}Tb-PSMA was 1.83 Gy, comparable to the 1.84 Gy observed in a previous ^{177}Lu-PSMA cycle. However, the dose-per-activity was higher for ^{161}Tb (0.29 mGy/MBq vs. 0.22 mGy/MBq), reflecting different clearance kinetics. Tumour-absorbed doses were highest in skeletal lesions, with up to 6.51 Gy.

d) Conclusion

The study demonstrates the feasibility of multi-timepoint voxel-based dosimetry for ^{161}Tb-PSMA and highlights the importance of quantitative imaging in evaluating emerging theranostic agents.

e) References (optional)

Clinical and Dosimetrical Analysis of Furosemide Use in [^{177}Lu]Lu-PSMA Therapy: A Case Report from SQCCCRC, Oman

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Keywords (3 max):

Abstract

a) **Background and aim**: This case study evaluates the dosimetric impact of furosemide administration on off-target organ radiation exposure following [^{177}Lu]Lu-PSMA-617 radioligand therapy.

b) **Methods**: Dosimetric analyses compared absorbed doses between two consecutive treatment cycles: the first cycle included intravenous administration of furosemide to induce forced diuresis, while the second cycle did not.

c) **Results**: Contrary to anticipated outcomes, absorbed doses to kidneys and salivary glands increased notably with furosemide administration (kidneys: 6–27%, salivary glands: >37%), except for the right parotid gland, which remained consistent. Bladder wall doses showed no significant difference between cycles.

d) **Conclusion**: The increased renal absorbed doses during forced diuresis may result from altered renal pharmacokinetics induced by furosemide and differences in baseline renal function, indicated by higher estimated glomerular filtration rate (eGFR) prior to the second cycle. These findings highlight the importance of careful assessment of renal function and suggest further investigation into furosemide use in [^{177}Lu]Lu-PSMA therapy protocols.

e) **Supporting figure / Table** (optional)

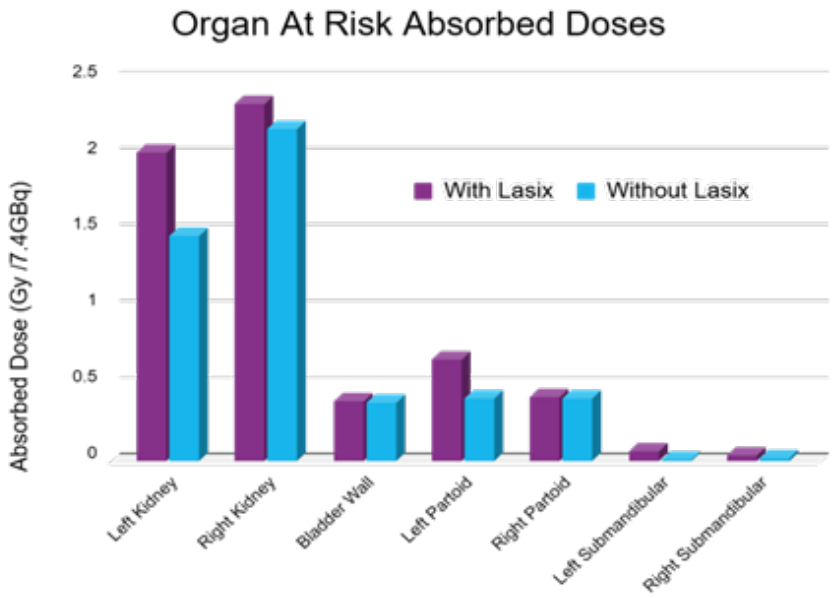

Figure 1: Absorbed Doses to Organs at Risk per Administered Standard Activity

Dosimetry Analysis in [^{177}Lu]Lu-PSMA Therapy with Different Dialysis Timings and Its Impact on Non-Target Organs: A Case report from SQCCCRC, OMAN

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Keywords (3 max):

Abstract:

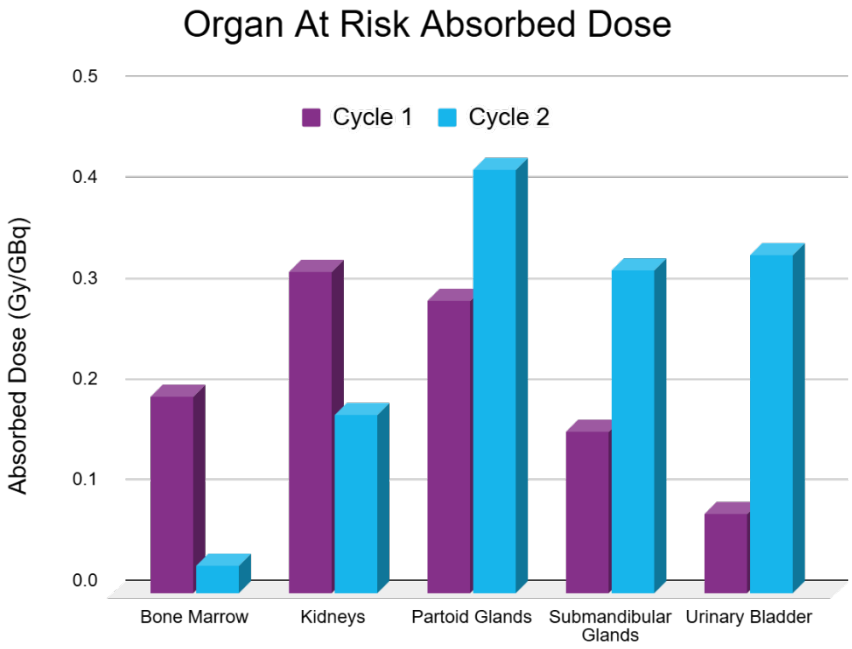
a) Background and aim: To evaluate the impact of different dialysis timings—next-day (24 hours) and same-day (3–4 hours) post-injection—on dosimetry and radiation exposure to non-target organs in patients undergoing [^{177}Lu]Lu-PSMA therapy.

b) Methods: A 72-year-old man with mCRPC undergoing regular hemodialysis (HD), received two cycles of [^{177}Lu]Lu-PSMA- 617, 6 weeks apart. During his first cycle he received his first HD 18 hours post radionuclide injection and second HD 48 hours later. During his second round of therapy, he received HD 3 hours post injection and second HD 72 hours after. Organ dosimetry, radiation safety parameters, and patient outcomes were compared between the two dialysis regimens.

c) Results: Mean absorbed doses to organs at risk from the first to the second treatment cycle ranged as follows: 0.19–0.03 Gy/GBq for red bone marrow, 0.32–0.18 Gy/GBq for kidneys, 0.29–0.42 Gy/GBq for parotid glands, 0.16–0.32 Gy/GBq for submandibular glands, and 0.08–0.34 Gy/GBq for the urinary bladder. Same-day dialysis reduced absorbed doses by 86% for bone marrow and 45% for kidneys. Conversely, absorbed doses for salivary glands and the urinary bladder increased by at least 30%, attributable to the significant decrease in tumor load observed during the second cycle.

d) Conclusion: Same-day dialysis reduces organs at risk radiation exposure more effectively, providing insights for optimizing therapy protocols in dialysis-dependent patients. Both HD regimens resulted in exposures below the known limits for all non-target organs. Hence our current recommendation is same day hemodialysis for patients undergoing [^{177}Lu]Lu-PSMA therapy.

Supporting figure / Table (optional)



Reproducibility and Feasibility of Dosimetry in Multi-Centre Studies: Inter-Operator Variability

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Keywords (3 max): Dosimetry, Radioiodine, Thyroid

Abstract

Background: INSPIRE is a multi-centre, investigator-led study evaluating the range of absorbed doses to thyroid remnants and non-target organs following radioiodine therapy for thyroid cancer. To ensure consistency, dosimetry was centralised at the sponsor site. This study investigates inter-operator variability in absorbed dose calculations and explores the feasibility of decentralised dosimetry for larger multi-centre trials.

Methods: SPECT and SPECT/CT imaging data, acquired between 6 and 168 hours post-therapy for 10 patients, were independently analysed by five technologists and physicists across three INSPIRE sites using Hermes software. Absorbed doses for the thyroid remnant, parotid, and submandibular glands were derived from dose maps, recorded, and compared. Parotid and submandibular gland volumes obtained through CT segmentation were assessed. Users recorded perceived difficulty during scan alignment and time required to perform the dosimetry steps.

Results: Inter-operator variability in absorbed dose calculations was low, supporting the feasibility of decentralised dosimetry. The largest observed variation in absorbed doses were 5.7 Gy for the thyroid remnant, 1.1 Gy for the parotid glands, and 0.2 Gy for the submandibular glands. Volume discrepancies reached 272% for the parotid glands and 137% for the submandibular glands. Dosimetry processing time was longest if patient position was not reproducible between scans.

Conclusions: This study demonstrates that absorbed dose calculations show low inter-operator variability, supporting the potential for decentralised dosimetry in multi-centre trials. Nevertheless, discrepancies in dose and volume highlight the need for enhanced training and standardisation. Future studies will assess the impact of patient positioning on dosimetry accuracy and potential time saving.

Characterization and commissioning of a dosimetry clinical software for molecular radiotherapy

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Keywords (3 max): clinical dosimetry, commissioning, molecular radiotherapy software

Abstract

Background and aim: Performing internal dosimetry at clinical centres not only requires characterizing medical equipment, but also clinical softwares must be commissioned. The commissioning and characterizing consists of a series of measurements to verify workflows and tools that the software has to offer.

Methods: According to EANM recommendations with Lu-177 and I-131 dosimetry, calibration factors, recovery coefficients and density curves were determined. These results were compared with the software OpenDose3D. Also, the dosimetry approaches (Multiple SPECT/CT´s, Prior information, etc.), filters, registration, and the time activity fitting models available in the clinical software were evaluated in order to analyse their impact on the dosimetry.

Results: Calibration factors, determined using both volumetric and point sources, showed percentual differences below 5%. Density curves pre-loaded into the clinical software (fitted to the experimental data) had determination coefficients greater than 0.98. Recovery coefficients for volumes above 100 mL were greater than 0.87. Filtering (both 2D pre-reconstruction and 3D post-reconstruction) showed a decrease in the recovery coefficients, worsening the activity quantification for small volumes. In TAC fitting, the number of timepoints should be greater than the fitter parameters.

Conclusion: With the purpose of performing reliable dosimetry, the commissioning of the software must be based on protocols recommended by international organizations, as well as the performance and specifications of the SPECT/CT corresponding to the medical centre. Characterization of the software tools allows a better understanding of their impact on the dosimetry.

Regulatory Challenges in Theragnostics: A competent authority's perspective

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Keywords (3 max): regulatory framework, radiation safety, competent authority

Abstract:

Background and aim: The rapid integration of theragnostics in molecular radiotherapy presents challenges for the regulatory control of the related practices. This study aims to assess the effectiveness of the current national regulatory framework in addressing emerging safety issues and outlining actions for potential improvements.

Methods: The Greek Atomic Energy Commission (EEAE) conducted a SWOT-analysis to evaluate the national regulatory framework for the control of practices with theragnostics. Key factors included the relevant legislative provisions and outcomes from the core regulatory processes. Comparative benchmarking against other European and international competent authorities was also considered.

Results: The current national regulatory framework efficiently covers nuclear medicine practices. However, gaps were identified regarding provisions for the joint use of diagnostic and therapeutic radiopharmaceuticals and the availability of specialized training. Dedicated regulatory guidance could facilitate the implementation of necessary safety measures and ensure regulatory compliance. Moreover, active participation in the European and international relevant initiatives could further enhance regulatory alignment with the best practices. However, advances in theragnostics may develop faster than regulatory updates leading to potential insufficient control or safety gaps. In addition, variations in the practices or adverse events could affect public trust and increase scrutiny of regulatory authorities.

Conclusion: The study highlights the need for adaptive, evidence-informed regulatory strategies. Competent authorities should prioritize embedding appropriate provisions in the regulatory frameworks to ensure their alignment with clinical innovation. By addressing regulatory needs emerged from innovative medical applications like theragnostics, EEAE strengthens its capacity to regulate other evolving uses of nuclear technology.

Monte Carlo investigation of red bone marrow dosimetry in ^{177}Lu therapy of metastatic prostate cancer patients

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Abstract

Rationale:

Red bone marrow (RBM) dosimetry is valuable for optimizing radiotheranostics. We applied Monte-Carlo (MC) methods to study RBM dosimetry in metastatic prostate cancer (mPC) patients treated with ^{177}Lu-PSMA.

Methods:

Step 1: We evaluated lesion-to-RBM irradiation from diffuse bone metastases using Geant4 MC simulations with the ICRP-110 adult male voxel phantom and literature-based time-integrated activity coefficients (TIACs) for source organs. Two cases were simulated with equivalent lesion volume (100 mL) and specific TIAC/mL: case A (n=10) and case B (n=20), using cortical bone or spongiosa compositions.

Step 2: MC-based RBM dosimetry was performed in a real patient. Quantitative 42 hours post-injection SPECT/CT (8.0 GBq ^{177}Lu-PSMA) provided source activity and tissue data. TIACs for lesions and rest-of-body compartments were estimated from single-time-point dosimetry using effective half-lives ($T_{eff,lesions}$ = 69 h; $T_{eff,rob}$ = 39 h). Lesion (20% and 40% threshold of the maximum local SPECT signal) and spongiosa volumes were segmented in SPECT/CT using 3DSlicer. A threshold-based method for spill-out correction was applied. Mean absorbed dose (AD) to spongiosa was used as a surrogate for RBM.

Results:

Step 1: RBM AD was ~3.5× higher in case B vs. A, showing the importance of lesion distribution. Lesions with spongiosa composition yielded ~1.5× higher RBM AD than cortical.

Step 2: RBM ADs were 0.02 vs. 0.05 Gy/GBq (with correction) and 0.3 vs. 0.7 Gy/GBq (without correction) for 20% vs. 40% thresholds.

Conclusion:

MC simulations underscore the importance of tumor burden geometry and spill-out correction in accurate RBM dosimetry for mPC patients receiving ^{177}Lu-PSMA.

^{177}Lu-PSMA administration using large volume infusion pump, radiopharmaceutical multidose injector and gravity method: comparative analysis

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Keywords (3 max): ^{177}Lu-PSMA, administration of radiopharmaceuticals, efficiency.

Abstract:

The rapidly escalating number of prostate cancer cases on a global scale has led to the emergence of ^{177}Lu-PSMA therapy as a significant treatment approach. The radiopharmaceutical exhibits a high degree of receptor-antigen binding affinity, which is overexpressed on the metastatic prostate carcinomas. This molecular interaction allows particles with a radioisotope to reach the target and eradicate cancerous cells. However, the administration techniques along with the radiation protection concerns of ^{177}Lu-PSMA remain challenging for nuclear medicine personnel. The primary method for the infusion of ^{177}Lu-PSMA remains the gravity method. Nevertheless, there are further options that have the potential to enhance the safety and efficiency of the administration process, including the use of a syringe pump, a large-volume infusion pump, or a radiopharmaceutical multidose injector. In this research, the B. Braun Spaceplus Infusomat large-volume infusion pump and the Lemer Pax Posijet multidose injector were tested and compared with the reference gravity method in terms of cost, preparation time, radiation exposure duration for the nuclear medicine technician, residual activity and potential risk of contamination. In order to minimize radiation exposure to medical personnel, the short-half-life radionuclide ^{99m}Tc was deliberately selected for injection simulations over ^{177}Lu-PSMA. Potential sources of contamination during the administration of radiopharmaceutical were investigated by dye method. The findings suggest that the optimal infusion technique varies according to the factors that have been investigated. However, it is acknowledged that the insights gathered could be applied according to the specific needs of the facility.

Rekindling I-131 Dosimetry for Hyperthyroidism in the UK: A Case Series

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Keywords (3 max): thyroid, benign, case-series

Abstract

Background and aim

In the UK, I-131 therapy for hyperthyroidism is typically prescribed at fixed activities, often resulting in hypothyroidism. Absorbed dose–based prescribing remains common in many European centres. With growing interest in theragnostics, we explore the feasibility of reintroducing dosimetry-guided I-131 therapy in a UK setting.

Methods

Three patients underwent pre-therapy I-131 tracer-studies to calculate the activity required for planned thyroid absorbed doses to achieve euthyroidism in two cases of Graves' disease and provide a definitive treatment for a heavily symptomatic patient with toxic nodular goitre (TNG).

Thyroid volume was measured pre-therapy using ultrasound and Tc99m SPECT/CT. Iodine uptake was tracked over time with serial gamma-camera imaging and SPECT/CT to calculate time-integrated activity and effective half-life with associated uncertainties.

Results

Ultrasound and SPECT/CT volumes agreed to with 15% across studies. Effective half-lives ranged from 6.7 to 8.0 days, exceeding the 5.5 day value typically cited in literature. 24h uptake ranged from 20 to 50%. Patient-1 (Graves') received 83.7MBq for a delivered absorbed dose of 62±4 Gy. Relapse required a second cycle at 30 Gy and the patient is now euthyroid without medication 24 months post-treatment. Patient-2 (TNG) sought definitive treatment and received 820MBq for a delivered absorbed dose of 220±11 Gy. Despite a lower-than-expected dose, hypothyroidism was achieved. Patient-3 (Graves') is scheduled to receive 150MBq.

Conclusion

The range of observed uptake and retention values supports individualized dosimetry planning and verification for a specific treatment aim.

Single-time-point dosimetry in vertebrae for 177Lu therapies: does using dose-rate maps improve accuracy?

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Keywords (3 max):

Abstract

Background and aim

In radiopharmaceutical therapy, dosimetry usually requires multiple post-injection SPECT/CT acquisitions, limiting clinical use. Single-Time-Point (STP) methods have been proposed, relying on the MIRD formalism with non-patient-specific S-values, often considering only self-dose. This study evaluates whether using voxel-based Monte Carlo dose-rate maps (MoCaDoRa) with cross-dose can improve absorbed dose estimation.

Methods

Three published STP dosimetry methods [1–3] (STP1-3) were adapted to use MoCaDoRa and compared against a multi-time-point (MTP) reference method [4]. Reference doses were estimated from a cohort of 16 patients treated with ^{177}Lu-PSMA at Centre Léon Bérard, each with three post-injection SPECT/CT acquisitions (after 4h, 24h, between 96h and 168h) after the first treatment cycle. Healthy thoracic and lumbar vertebrae were selected for analysis due to their potential active bone marrow content, low physiological uptake, and proximity to high-uptake lesions that may cause cross-dose. Vertebral contours were refined by subtracting the Total Metabolic Tumor Volume [5] from anatomical contours [6]. Statistical analyses were conducted to compare original and adapted STP doses with reference.

Results

Dose differences (%) across volumes were calculated between STP methods and the reference method:

- 49.1 ± 56.4% (original) vs 11.4 ± 27.2% (MoCaDoRa) for STP1 (medians ± interquartile ranges, on average),

- –42.0 ± 20.8% vs –18.2 ± 18.6% for STP2,
- –20.9 ± 30.2% vs 11.4 ± 26.7% for STP3

Adapted methods showed significant differences from the reference in most cases, but errors were much smaller than with the original ones.

Conclusion

Adapted STP methods using MoCaDoRa provide more accurate dose estimates closer to the reference by accounting for cross-dose, and enable lesion-level dosimetry independently of patient-specific S-values.

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Supporting figure / Table (optional)

Tandem Surgery and PRRT with 177Lu-DOTA-NOC Efficacy after Intra-arterial Implementation in Liver Metastasized Vipoma NETs

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Introduction: We report on the efficacy of peptide receptor radionuclide therapy (PRRT) in a rare tiny cohort of liver-metastasized VIPomas followed by surgical lesion excision, aiming to optimize PRRT for longer-term survival and quality of life.

Patients and Methods: From 1997-2015 only four patients (m=3, f=1, age range 49 - 69 years) presented with bilobar liver-metastasized pancreatic VIPomas by biopsy confirmed. All four had ^{111}In-DTPA-Octreotide-avid disease (visual score IV) and underwent curative-intent surgical resection, followed intra-arterial PRRT with n.c.a. ^{177}Lu-DOTA-NOC, in an average activity of 7.3±2.3 GBq per patient/per session, consecutively. Response assessment was classified according to RECIST 1.1 criteria. Dosimetry was performed according to OLINDA/EXM 1.0 program. CT/MRI was done before and after the end of treatment and monthly US images for follow-up. Median OS and PFS were estimated using the Kaplan-Meier method.

Results: None of four patients resulted in CR, PR was assessed in two and SD in another two. Median PFS and OS were 36 and 48 months, respectively. Dosimetry was estimated as follows: liver-tumor 35.0, liver 0.03-0.1, kidneys 0.02-0.5, spleen 0.02-1.2 and bone-marrow 0.008-0.04 mGy/MBq. A WHO toxicity grade 1-2 erythro-, leuko-, thrombo-cytopenia occurred in 3 (75 %) cases, after the 4th session.

Conclusion: In liver metastasized VIPomas, scheduled for radiopeptide therapy, complementary surgical exeresis slows down the tumor aggressiveness and accelerates the efficacy with n.c.a. ^{177}Lutetium-DOTA-TOC. Kidneys and bone-marrow consist the critical organs. Thus, dosimetry should be a necessary appendage.

S-value based dosimetry for in-vitro assays: Effects of geometry, cell distribution, Monte Carlo code and radionuclide selection

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Keywords (3 max):

Abstract

Background and aim: Realistic S-value (Gy/Bq·s) modelling is essential for calculating absorbed dose in targeted radionuclide therapy (TRT) and establishing dose-effect relationships for cell lines during in-vitro studies. This work investigates the influence of geometry, spatial cell distribution, and Monte Carlo code selection on absorbed dose calculations for radionuclides in 96-well plates.

Methods: Monte Carlo simulations with GEANT4 (v.11.3) and MCNP6.2 modeled radionuclide decays in 100 µL water-equivalent medium in a well (6.35 mm diameter). Two geometries were considered: a simplified monolayer, and a Gaussian or uniform distribution of 15 µm-spherical cells at the well bottom. Absorbed energy was scored using the F8 tally in MCNP and electron tracking with the Livermore physics list in GEANT4. S-values were obtained by dividing absorbed energy by target mass: whole-cell or nuclei in the cell model, and full monolayer or nuclear layer for the monolayer model.

Results: For Lu-177 in the monolayer, S-values from GEANT4 and MCNP agreed within 5%, with differences attributed to cross-section data. The realistic geometry yielded higher absorbed doses, with monolayer S-values lower by 22% in MCNP and 8% in GEANT4. In the individual cell model, MCNP predicted S-values higher than GEANT4 by 11% (whole cell) and 8% (nucleus). Spatial arrangement effects were minor (~3%). Ongoing work will assess whether these differences arise from dose variations or model assumptions.

Conclusion: Geometry definition had the largest impact on S-values, followed by code selection, highlighting the importance of standardized models for reliable, reproducible dosimetry in preclinical TRT.

Development of a dosimetry protocol using Hermes software and a CZT-based gamma camera

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Keywords (3 max): calibration, CZT system, voxel dosimetry

Abstract:

Background and aim: Aim of the work was to validate a dosimetry protocol for SPECT/CT imaging with ^{177}Lu-labelled radiopharmaceuticals from calibration to quantification and dose assessment using a CZT-system (Veriton-CT, Spectrum Dynamics Medical) and Hermes software (Hermes Medical Solutions).

Methods: Quantitative SPECT/CT images of ^{177}Lu-filled phantoms were acquired on Veriton-CT. Reconstruction protocol consisted into a 3D-OSEM algorithm with TEW scatter correction and CT-based attenuation correction. A uniform cylindrical phantom (6820 mL) was prepared for camera sensitivity testing. A NEMA IEC Body phantom with 6 spheres and cylindrical phantoms (0.55-150 mL) were used to estimate Recovery Coefficients (RCs) on small volumes. An anthropomorphic phantom (1300 mL) was acquired for verification. In addition, mean absorbed dose calculations were performed on the six spheres of NEMA IEC Body phantom image considering Lu-177 physical half-life. MIRD formalism was applied considering both nominal and measured activity concentration values; voxel-wise dose distribution was computed through a fast semi-Monte Carlo algorithm.

Results: Measured SUV_{mean}=0.98 for sensitivity testing. RCs on spheres ranged from 0.14 to 0.56 and on cylinders from 0.97 to 1.00. Deviation on quantification on large volumes was into ±10%. Absorbed doses (mean ± standard deviation) calculated with MIRD formalism were 408±4 and 444±5 mGy/MBq for nominal and measured activity concentrations respectively. Voxel dosimetry led to 380±3 and 140±60 mGy/MBq whether RCs were included in computation or not.

Conclusion: Sensitivity calibration of gamma cameras and RC curve determination are essential steps for accurate quantification. Combination of CZT systems with dedicated software resulted in measured mean absorbed doses into ±10% of nominal values.

Comparison of dosimetric versus fixed-dose approaches for I-131 therapy in the treatment of Grave's Disease

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Keywords (3 max): I-131, Grave's Disease, dosimetry

Abstract:

Background and aim: Radioiodine therapy with I-131 is an established treatment for benign thyroid conditions such as Graves' disease (GD). Therapy planning methods are heterogeneous in Europe, spanning dosimetry to fixed activity approaches. We evaluated key dosimetric parameters like effective half-life (Teff) and activity-per-dose (ApD) pre and in therapy using the Marinelli (MAR), Hänscheid (HAN) methods [1,2] and fixed-dose approach [3].

Methods: Data from 70 patients with GD undergoing I-131 treatment between 2022-2025 was analysed using JMP (Student Edition 18). Each received 0.8-4.4MBq I-131 pre-therapy, with uptake measured at 4h, 24h, and 7d using a gamma probe (NUVIA Instruments GmbH). During therapy, uptake was additionally measured at 48h. Teff and ApD were calculated via MAR and HAN. Achieved post-therapeutic dose values from dosimetry and common fixed activities (555MBq for <30gr thyroid mass or 740MBq if >30gr) were compared with the prescribed dose.

Results: Significant differences for dosimetric approaches were observed in pre-therapy Teff (MAR+0.34d), ApD (MAR+0.29MBq/Gy) and in-therapy ApD (MAR+0.28MBq/Gy). Teff was larger pre-therapy (MAR by 0.81d, HAN by 0.47d) and ApD was underestimated by 0.2MBq/Gy for both methods. Deviations in resulting dose using HAN were at +4.33% on avg. (2.64% median, 22.95% standard deviation (SD)). MAR resulted in -8.16% avg. (-8.39% median, 21.94% SD). Fixed 555MBq lead to +17.00% avg. (6.04% median, 44.70% SD) and 740MBq resulted in -12.26 % avg. (-10.97% median, 24.10% SD).

Conclusion: Intrinsic variability of HAN and MAR methods is similar with MAR overestimating achieved dose by a greater margin. Fixed activities tend to result in higher deviations and uncertainties.

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Implementation of Quantitative SPECT/CT in Clinical Practice: Protocol Optimization and Validation for Dosimetric Applications

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Keywords (3 max): Quantitative SPECT, Image Reconstruction Algorithms, Dosimetry

Abstract:

Background and aim: In view of implementing patient-specific 177Lu-PSMA dosimetry in our department, this study aimed to establish a methodological framework and analysis tools for obtaining optimized quantitative SPECT/CT imaging. To facilitate protocol development, 99mTc was used as a practical substitute for 177Lu in phantom experiments.

Methods: After the calibration of our gamma camera (Pro.SpectaX3, Siemens), acquisitions were performed with the NEMA-IEC phantom considering three sphere-to-background ratios (∞, 5:1, and 9:1) to evaluate recovery coefficients (RC), FWHM derived from the RC [1], and background noise (COV) under different reconstruction settings, for both available algorithms (Flash3D, xSPECT). An optimal protocol was defined for each algorithm by identifying RC convergence while keeping COV as low as possible. Accuracy of quantification was finally validated using an anthropomorphic TORSO® phantom.

Results: xSPECT reached RC convergence with 32 updates (COV ≈ 10%), while Flash3D did so with 72 (COV ≈ 9%). Increasing the number of subsets in xSPECT led to a significant increase in noise (from 10% with 1 subset to 30% with 6 subsets). Using the TORSO® phantom, where lesions of different volumes and organs at risk were simulated, activity quantification (with partial volume effect (PVE) correction) was achieved with an error below 13.4% using xSPECT and 4.8% with Flash3D for a 6.08 mL lesion. PVE correction was most effective with an SBR of 9:1, significantly reducing quantification errors (up to 41% in xSPECT and 23% in Flash3D).

Conclusion: A methodological framework is provided to implement and validate quantitative SPECT/CT protocols for clinical dosimetry. Application to Lu-177 is ongoing using the same validation framework.

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Comparative assessment of modern dosimetry tools for the most reliable personalised organ-level dosimetry in 177Lu-based molecular radiotherapy

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Keywords (3 max): molecular radiotherapy, organ dosimetry

Abstract

Background and Aim: Personalised dosimetry is crucial for managing oncology patients undergoing radionuclide therapy (RNT). With recent advancements in dosimetric software, comparing tools is essential to evaluate variability and ensure reliability. This study compares five dosimetry software programs against a gold-standard method for quantifying absorbed dose in ^{177}Lu RNT.

Materials and Methods: Dosimetry was performed for one PRRT patient (7.4 GBq ^{177}Lu-DOTATATE), focusing on the kidneys and liver, and a NEMA IEC body phantom simulating tumour lesions (1.99 MBq/ml 177Lu). SPECT/CT images were acquired at 3, 24, and 120 hours post-injection and reconstructed quantitatively. Five software tools—ST-1: Voximetry, ST-2: OLINDA, ST-3: MIRDSoft, ST-4: Q Dose, and ST-5: MIM were used to estimate doses. Results were compared with gold-standard dosimetry based on co-registered images, voxel-level time-integrated activity (TIA) maps, and Geant4 Monte Carlo dose simulations.

Results: In the patient, gold-standard absorbed doses (mGy/MBq) were 0.34 (liver), 0.44 (spleen), and 0.37 (kidneys). In the phantom, tumour doses (113 ml and 26 ml) were 116.76 and 76.62 mGy/MBq. Maximum variation among software tools was 34.48% (liver, ST-2) and 94.57% (tumour 1, ST-3). Detailed values are in Table 1.

Conclusion: ST-1, ST-4, and ST-5 produced absorbed dose estimates closest to the gold standard. Larger cohort studies are needed to further validate and optimise ^{177}Lu dosimetry. Improved tools will support more accurate, personalised RNT planning in clinical practice.

Disclosure: This study was supported by Telix Pharmaceuticals and Voximetry. The authors declare no conflicts of interest.

Supporting Table 1

	Patient (mGy/MBq)					
Organs	Gold standard	ST1	ST2	ST3	ST4	ST5
Liver	0.34	0.35	0.24	0.38	0.35	0.32
Spleen	0.44	0.45	0.54	0.50	0.44	0.42
Kidneys	0.37	0.36	0.43	0.40	0.35	0.36
% difference from standard						
Organs		ST1	ST2	ST3	ST4	ST5
Liver		2.89	34.48	11	2.89	6

Spleen		2.24	20.40	12.76	0	4.65
Kidneys		2.73	15	7.79	5.55	2.73

	Phantom (mGy/MBq)					
Tumour	Gold standard	ST1	ST2	ST3	ST4	ST5
Tumour 1(113 ml)	116.76	118.19	319.00	326.22	112.42	120.91
Tumour 2(26 ml)	76.62	79.51	123.00	115.10	73.63	103.24
	% difference from standard					
Tumour		ST1	ST2	ST3	ST4	ST5
Tumour 1(113 ml)		1.21	92.82	94.57	3.78	3.50
Tumour 2(26 ml)		3.70	46.47	40.14	3.98	29.60

Framework for Theranostic Digital Twins Generation and Virtual Theranostic Trials

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Abstract

Background and aim: Theranostic Digital Twins (TDTs) are computational representations of individual patients that integrate personalized data, such as medical imaging and clinical information, with advanced modeling techniques like physiologically based pharmacokinetics (PBPK), enabling personalized radiopharmaceutical therapies (RPTs) to improve therapeutic precision and outcomes. Validating TDTs remains a significant challenge due to the limited availability of comprehensive datasets that include both pre- and post-treatment imaging, clinical data, dosimetry, and ground truth information such as treatment response.

Methods: To address this limitation, we present an enhanced publicly-shared simulation framework to generate synthetic datasets for benchmarking, validation, and optimization of TDT models. Extending our previous pipeline (Fedrigo et al., 2023), which supported XCAT phantoms with Monte-Carlo-based SPECT and analytical PET simulations, followed by image reconstruction, our improved framework now incorporates patient-specific CT phantoms, Monte-Carlo-based PET simulators, and Monte-Carlo-based dosimetry. Within this framework, PBPK modeling simulates realistic biodistribution of diagnostic and therapeutic radiopharmaceuticals to produce time-activity curves (TACs), which are assigned to these voxelized phantoms for generating realistic imaging and dosimetry datasets.

Results and Conclusion: Validation studies will compare simulated images and TACs against real patient data. Initial applications of generated datasets include evaluating AI-assisted SPECT lesion detection and segmentation and benchmarking longitudinal lesion tracking techniques, and AI-based predictive modeling of absorbed doses in RPTs from pre-therapy PET scans. Importantly, these datasets will enable systematic pursuit of what we refer to as “virtual theranostic trials” (VTTs), enabling optimization of imaging as well as RPT protocols, e.g. towards more accurate PBPK parameter estimation and improved predictive dosimetry for personalized treatment planning.

References

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Release Criteria for Therapies with ^{177}Lu-labeled Radiopharmaceuticals

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Keywords: ^{177}Lu, release criteria, dose rate

Abstract:

Background and aim: In recent years, the number of patients treated with 177Lu-labeled radiopharmaceuticals was on the increase. This trend is set to continue, as further radiopharmaceuticals targeting additional tumour entities like breast cancer are due to enter the market in the future.

Therefore, radiation protection for the public is becoming increasingly important. The 2007 recommendations of the ICRP and the Directive 2013/59/EURATOM establishes the effective dose to the public may not exceed 1 mSv/year [1, 2]. It is vital that practical release criteria for the discharge of patients treated with 177Lu-labeled radiopharmaceuticals are in use. However, the European Commission's final report on the SAMIRA study criticises the lack of uniform release criteria [3]. This work aims to investigate practical release criteria for 177Lu-therapies.

Methods: Whole-body dose rates were measured at a distance of 1 m from the patient's surface at different time points after administration. Data fitting was performed using R. To compare various release criteria with each other a standard observer was introduced. Published literature was studied with respect to practical release criteria.

Results: Release criteria should be simple, uniform and conservative for their implementation in terms of radiation protection. One criterion that meets all of these requirements can be directly derived from the dose integral. It depends largely on the number of cycles of the therapy. For six cycles per year, for example, the conservative discharge dose rate at a distance of 1 m is 2.9 µSv/h.

Conclusion: Practical release criteria are necessary to ensure that the dose constraint of 1 mSv/year is safely met. This work defines requirements for release criteria and compares and evaluates existing criteria on the basis of dose rate measurements.

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Feasibility analysis of dosimetric planning for [Lu^{177}]PSMA radionuclide therapies using whole-body PET/CT

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Keywords (3 max): RLT Planning. -dosimetry, -verification

Abstract:

Background and aim: The aim of this work is to assess the predictability of therapeutic absorbed doses is organs and lesions based on the distribution and time-activity behaviour (TAC) of the PET-tracer [Ga^{68}]PSMA617/[F^{18}]PSMA1007 in a theranostic setting for [Lu^{177}]PSMA treatment of mCRPC patients.

Methods: The imaging protocol includes a pre-therapeutic PET/CT scan (0 - about 60 min p.i. list-mode) and a late scan at about 3h p.i. (~15min static) on a LAFOV-PET/CT system (SIEMENS Biograph Vision Quadra) after application of ~100MBq [Ga68]PSMA617 or [F^{18}]PSMA1007. List-mode-data was reconstructed into decay corrected 3min-frames at 1.5, 11.5, 21.5, 31.5, 41.5, 51.5, 61.5 min p.i. Organs and lesions were manually segmented, activity concentrations measured over time and dose distribution is predicted voxel-wise based on the TACs as determined by PET/CT assuming the actual therapy activity being ~7400MBq [Lu177]PSMA (HERMES Affinity, VoxelDosimetry). After the first fraction, the actual dose distribution is determined employing a hybrid 2.5D method using one quantitative SPECT/CT (~24h p.i.) and four planar whole-body scans at about 1, 24, 48h and 7d p.i. (Discovery 670, GE; QDose, Telix Pharmaceuticals). The predicted and actual dose distributions are compared.

Results: As shown in the table below for 5 (out of 12) subjects who fully complied with the protocol, the predicted doses in lesions and OARs generally largely differ from each other, with deviations being highly individual.

Conclusion: The protocol is complicated for patients to fully comply with. Moreover, particularly large deviations are found – most likely not only due to co-registration errors and partial volume effects but also due to chemical and kinetic differences between diagnostic and therapeutic agent. So far, it seems to be challenging to use just standard available tools to predict therapeutic absorbed doses from pre-therapeutic PET-investigations.

Supporting table

mGy/MBq / Volume	subject 1			subject 2			subject 3			subject 4			subject 5		
	pre-th.	post-th.		pre-th.	post-th.		pre-th.	post-th.		pre-th.	post-th.		pre-th.	post-th.	
Spleen	0,172	0,006	3,7%	0,226	0,008	3,5%	0,090	0,019	20,7%	0,886	0,262	29,5%	0,132	0,024	18,1%
Liver	0,230	0,013	5,7%	0,178	0,016	9,1%	0,181	0,025	13,9%	3,616	0,275	7,6%	0,090	0,023	25,5%
Kidney r.	2,595	0,353	13,6%	4,888	0,460	9,4%	1,580	0,109	6,9%	3,234	0,457	14,1%	5,753	0,274	4,8%
Kidney l.	2,668	0,385	14,4%	5,263	0,450	8,6%	1,622	0,103	6,4%	2,771	0,459	16,6%	5,790	0,201	3,5%
Gl. Parotis r.	2,903	0,158	5,5%	data not (yet) available			1,809	0,256	14,1%	1,443	0,218	15,1%	data not (yet) available		
Gl. Parotis l.	2,599	0,175	6,7%				2,732	0,216	7,9%	1,381	0,147	10,7%			
Gl. Sublingualis r.	2,529	0,115	4,5%				2,132	0,166	7,8%	2,038	0,166	8,2%			
Gl. Sublingualis l.	2,323	0,077	3,3%				2,534	0,134	5,3%	1,601	0,168	10,5%			
Lesion 1	6,648	0,924	13,9%	0,305	0,032	10,4%	5,264	5,103	97,0%	4,037	1,950	48,3%	7,433	0,791	10,6%
Lesion 2	2,502	0,189	7,6%	0,626	0,080	12,7%	3,570	0,599	16,8%	2,915	2,025	69,5%			
Lesion 3				0,297	0,091	30,6%				4,083	2,208	54,1%			

Table 1: PET-predicted vs. actual doses

Intaking therapeutic Radioisotopes prior to the patient's connection to the dialyzer: does radioprotection needed?

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Keywords: radioisotopic therapy, aimodialysis

Abstract:
Background and aim: Our aim was clinically determine by measurements the radioactivity levels in the nephrologic unit, the exposure level of the staff and the hemodialysis residues, when a patient needs radioisotopic treatment while undergoes hemodialysis.

Methods: Three sessions needed per week and each session lasts 4 hours. Measurements were made in for 4 patients from 1 to 4 consecutive sessions. Three patients had been administered I-131 ≈ 70mCi, one had 208 mCi Lu-177. Calibrated ionization champer Inovision 451P, survey meter Polymaster pm1405 were used for the measurements and a nurse brought a personal TLD dosimeter. Hemodialysis was performed 2 or 4 days after treatment. The radiation exposure nursing staff was calculated and radioactivity of the filters was measured.

Results: Staff's exposure level was calculated 128 μSv/ session for Lu-177.

TLD's result while used for 2 sessions for I-131 was zeroing. At machine connections to the sewer was recorded: 4.45 μSv/h. Around patient the dose rate was 270 μSv/h, while a nurse stays there even for 40 min. Offices, corridors nearby the patient's room were measured to be 630nSv/h.
Conclusion: Increased levels of radiation exposure occur. DRLs of 300 μSv/y are not expected to be exceeded, mainly due to the small number of patients handled by each unit. Filters, etc remaining after give dose rates of 250 – 500 nSv/h and can be discarded. It is recommended that the unit should be supported from a Nuclear Medicine dpt.

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