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Original research

Keywords: quantitative imaging, molecular radiotherapy, SIMIND Monte Carlo code, quantitative activity estimation

Posted Date: July 1st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1756734/v1

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RESEARCH

Validation of SIMIND Monte Carlo for 99m Tc and 177 Lu

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Abstract

Purpose: Monte Carlo (MC) simulation in Nuclear Medicine is a powerful tool for modelling many physical phenomena which are difficult to track or to measure directly. MC simulation in SPECT/CT imaging is particularly suitable for optimizing the quantification of activity in a patient, and, consequently, the absorbed dose to each organ. To do so, it is mandatory validate MC results with real data acquired with gamma camera. The aim of this study was the validation of SIMIND Monte Carlo code for modelling a Siemens Symbia Intevo Excel SPECT-CT gamma camera both for 99m Tc and 177 Lu.

Methods: Phantom experiments using 99m Tc and 177 Lu have been performed with the purpose to measure spatial resolution, sensitivity and evaluate the calibration factor (CF) and recovery coefficients (RC) from acquired data. The geometries used for 2D planar imaging were (1) Petri dish and (2) capillary source while for 3D volumetric imaging were (3) a uniform filled cylinder phantom and (4) a Jaszczack phantom with spheres with different volumes. The experimental results have been compared with the results obtained from Monte Carlo simulations performed in the same geometries.

Results: Comparison shows good accordance between simulated and experimental data. The measured planar spatial resolution was 8.3 ± 0.8 mm for 99m Tc and 12.2 ± 0.7 mm for 177 Lu. The corresponding data obtained by SIMIND for 99m Tc was 7.4 ± 0.1 mm, while for 177 Lu was 11.7 ± 0.1 mm. The CF was 110.1 ± 5.5 cps/MBq for Technetium and 18.3 ± 1.0 cps/MBq for Lutetium. The corresponding CF obtained by SIMIND for 99m Tc was 100.1 ± 0.3 cps/MBq, while for 177 Lu 20.4 ± 0.7 cps/MBq. Moreover, a complete curve RCs vs Volume (ml) both for Technetium and Lutetium was determined to correct the PVE for all volumes of clinical interest. In none of the cases a RC factor equal to 100 was found.

Conclusions: The results of validation process show that SIMIND can be used for simulating both gamma camera planar and SPECT images of Siemens Symbia Intevo using $^{99m}{\rm Tc}$ and $^{177}{\rm Lu}$ radionuclides for different medical purposes and treatments.

Keywords: quantitative imaging; molecular radiotherapy; SIMIND Monte Carlo code; quantitative activity estimation

Background

In modern nuclear medicine, the absolute quantification of SPECT images is fundamental for providing an estimate of the activity uptake in various organs and tissues for the purpose of diagnostic assessments and therapeutic decisions. Monte

Carlo (MC) simulation is a tool widely used to model real life systems, including nuclear medicine devices [1]. Starting from the description of particles interaction with matter, by using probability density functions (pdfs) and with the help of random number generators and sampling techniques, MC provides the opportunity to analyze the phenomena of physics underlying the formation of images with the aim of optimizing the data acquisition and processing steps. Due to the approximation and the simplification used in the description of physics laws inside a MC code, a mandatory step is the validation of MC model (code) before using it to simulate real world systems, in particular as a clinical simulator for SPECT imaging. To validate a MC code, outputs of simulated experiments are compared against results obtained from experimental measurements on the physical system. The validation ensures that the simulated system truly is in fact the physical one.

The absolute activity quantification consists in several steps: the first one is to reconstruct projection images, taking into account photon attenuation, scatter and Collimator Detector Response (CDR). CDR is one of the most degrading factors in SPECT imaging [2]. It is caused by several factors: photons which pass through the holes' septa and photons which, despite the scattering with hole septa, have been detected. For modeling the scanner CDR one can use a capillary source placed at several source-to-detector distances while keeping the rotation angle fixed [3]. Usually, the Gaussian + exponential function fits the measurements, and the fit results are used to model the distance-dependent CDR. The second step is to convert the reconstructed counts per second into activity [in MBq] through a Calibration Factor (CF). Different camera calibration methods have been proposed for evaluating CF: some researchers use planar scans of a small source [4] or of a petri dish (following NEMA protocol for camera sensitivity test) [5], other ones use tomographic scans of a very simple phantom, such as a large cylindrical phantom (to avoid Partial Volume Effect, PVE), with a certain, known activity inside[6]. The CF unit is cps/MBq and it should be computed for every radionuclide and collimator used. The last step is to compute recovery coefficient (RC) factors in order to correct for the PVE: for small volumes, measured activity appears to be distributed among a larger volume respect to the actual one; this may lead to an underestimation of the activity in the real volume (and, then, of the measured absorbed dose) and to a wrong volume estimation. This is due to blurring effect, caused by a finite spatial resolution. PVE can be estimated through phantom studies, using Jaszczak phantom with known volume spheres. The RC factors are equal to the ratio between the measured activity in each sphere and the true one and it is expressed in percentage; they will be used to correct the final activity inside each sphere.

Some authors have reported the comparison of measured and simulated gamma camera performances like spatial resolution, planar sensitivity, CF and RC for 99m Tc, 177 Lu or radionuclides with photons of energy higher than 140 keV [7, 8, 9, 10], both to investigate the influence a parameter has on systems' performances and to validate the MC codes' capability in modelling a specific gamma camera to use it later as a clinical simulator [11].

The aim of our work is to develop a tool able to accurately simulate the activity distribution inside the patient body, calibrating a gamma camera for absolute quantification in tomographic imaging and comparing the obtained results with MC

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simulation. To this aim, a Siemens Symbia Intevo Excel SPECT/CT scintillation camera has been modelled by using the SIMIND Monte Carlo Program (version 6.1) [12]. Planar and tomographic studies have been performed for two radioisotopes: 99m Tc the most used radionuclide in SPECT/CT imaging studies, and 177 Lu an attractive radionuclide used for peptide receptor radionuclide therapy (PRRT) using the theranostic approach [13]. Moreover, RC factors have been evaluated both for 99m Tc and 177 Lu.

Materials and methods

This study is composed of two parts: experimental data acquisition and Monte Carlo simulations. In each part both 99m Tc and 177 Lu radioisotopes are studied, for a total of 40 experimental scans and 140 simulation runs. The information about the isotopes' half-lives, their main gamma emissions and the maximum energy of their beta emission are summarized in Table 1.

The SPECT/CT scanner used for the experimental measurements is a Siemens Symbia Intevo Excel provided by Nuclear Medicine Unit, University Hospital of Ferrara (Italy). The system is equipped by two gamma camera heads with NaI scintillator crystals (FOV 53.3x38.7 cm). The gamma camera parameters are listed in Table 2. The so-called "step and shot" technique was used for the tomographic studies. The CT was performed after the SPECT acquisition, with a 110 kV voltage and Care Dose 4D. The Symbia Intevo Excel was equipped with a Low Energy High Resolution (SY-LEHR) collimator for ^{99m}Tc studies and with a Medium Energy Low Purpose collimator (SY-MELP) for ¹⁷⁷Lu studies. A Mec Murphil MP-DC-Chamber dose calibrator has been used for the activity measurement. Activities have been assessed by performing five measurements of the syringes containing the isotopes, subtracting the residual activity. The ^{99m}Tc radioisotope has been obtained as sodium perthecnetate ($Na[^{99m}Tc]O_4$) from ⁹⁹ $Mo/^{99m}Tc$ generator (Ultratechnekow, CURIUM, Netherlands), while the ¹⁷⁷Lu has been obtained as Lutetium chloride ([¹⁷⁷Lu]Cl₃) (EndoLucinBeta, ITM, Munich, Germany).

Phantom experiments for 99m Tc and 177 Lu: planar imaging

Planar measurements aim at the evaluation of the fundamental SPECT features: spatial resolution and sensitivity, which are defined by the scintillation crystal and the collimator. In order to characterize the main properties of the Symbia Intevo gamma camera's, one at a time the two heads have been exploited.

The gamma camera data were acquired with a 15% energy window centered on the 140.5 keV for the main photopeak of the 99m Tc, and with two 15% energy windows centered on the 113 keV and 208 keV photopeaks of the 177 Lu. All measurements have been repeated three times and performed with different distances between the source and the detector.

Extrinsic spatial resolution measurement

A capillary tube with an inner diameter of 1 mm was used to determine the system spatial resolution. The tube was filled with 30 \pm 1 MBq of a 99m Tc solution and with a 130 \pm 7 MBq of a 177 Lu solution.

In order to study the spatial resolution, the tube was placed at three different distances from the front face of collimator for the experimental measurements: $10.0 \pm 0.5 \text{ cm}$, $25.0 \pm 0.5 \text{ cm}$ and $35 \pm 0.5 \text{ cm}$.

The spatial resolution was measured by drawing a profile across the image of the capillary tube in three different positions in order to compensate for the possible non-uniformity in the tube filling. The line profile was fitted with a Gaussian function from whose full width at half maximum (FWHM) and the full width at tenth maximum (FWTM) were calculated. The reference value provided by SIEMENS for the extrinsic spatial resolution with a LEHR collimator and a capillary tube filled with a ^{99m}Tc source is 7.5 mm at 10 cm.

System sensitivity measurement

A Petri Dish with an inner diameter of 10 cm was filled with $25.0 \pm 1.3 \,\mathrm{MBq}$ of a $^{99m}\mathrm{Tc}$ solution and with a $30.0 \pm 1.5 \,\mathrm{MBq}$ of a $^{177}\mathrm{Lu}$ solution. The reference value provided by SIEMENS for the sensitivity with a LEHR collimator and a Petri dish filled with a $^{99m}\mathrm{Tc}$ source is $91.8 \,\mathrm{cps}/\mathrm{MBq}$ at $10 \,\mathrm{cm}$.

Phantom experiments for 99m Tc and 177 Lu: tomographic imaging

Calibration Factor measurement

A cylindrical Jaszczak SPECT Phantom (figure 1) deprived of the inner spheres has been employed to obtain the CF. The cylinder was filled with a 6800 ml solution of distilled water, 350 MBq of 99m Tc.

Similarly, the uniform Jaszczak phantom was filled with a 6800 ml solution of distilled water (6720 ml), 2810 MBq of 177 Lu from a certificated vial with an accuracy of $\pm 10\%$, 67ml of HCl (37%) added in order to make the solution the most homogeneous as possible and to avoid lutetium accumulation on phantom borders.

Both for 99m Tc and 177 Lu, the SPECT/CT acquisitions were performed via the Siemens Symbia Intevo Excel with the step-and-shoot technique. Each tomographic acquisition consisted in 64 projections performed maintaining a constant distance of 25 cm between the center of the cylinder and the lower part of the detector head. The acquisition time was of 10 s or 20 s for 99m Tc, while it was of 30 s for 177 Lu.

The reconstruction of the projected images was performed with the built-in software from the vendor, Siemens Flash3D. The OSEM 3D was the iteration reconstruction technique chosen, with 10 iterations and 8 subsets. The Flash3D is capable of applying attenuation, scatter and CDR corrections.

The scatter correction for Technetium was performed via the DEW (Double Energy Windows) technique with the use of the PW (Peak Window) and the LSW (Lower Scatter Window).

The scatter correction for Lutetium was performed via the TEW (Triple Energy Windows) method for the 113 keV peak and the DEW method for 208 keV peak; the widths of each photopeak window are reported in Table 3.

Recovery coefficients measurement

In order to obtain the RC factors, the absolute quantification of 99m Tc was performed via a Jaszczak SPECT Phantom with six hot spheres.

The phantom was placed in the center of the field of view. Acquisitions were performed with the same settings as those of the uniformly filled Jaszczack phantom

previously described and conducted with 64 projections of 10 s or 20 s scan time. The energy windows are the same as those set for the CF evaluation and are listed in Table 3. The spheres volume and the background activity are listed in Table 4. Each activity value reported in Table 4 is the mean of five different measurements. For the evaluation of the RC factors of ¹⁷⁷Lu a NEMA image quality PET phantom with five spheres of different diameters was used. Spheres diameters, volumes, injected and background activities are listed in the Table 5. Measurement settings are the same as those used for the CF evaluation and are listed in Table 2 and Table 3. The number of projections was 64, each of 30 s duration.

The ratio between activity concentration in the background and the activity concentration in the spheres is 1:45. Each value reported in this Table 5 is the mean of five different measurements, with an associated standard deviation of less than 1%. The process of activity measurement is the same as that described for the 99m Tc. CT data has been used for the delineation of volume of interest (VOI) of each sphere in Symbia SPECT studies.

The exponential curve fitting the RC values was performed using the Igor software [Igor Pro, version 4.01, Wavemetrics, Inc, 1988-2000, Oregon, USA]. RC data errors were evaluated by taking into account the Poisson distribution of the SPECT acquired counts and the errors in activity measurement, volume and time interval estimation.

Monte Carlo simulation for $^{99m}\mathrm{Tc}$ and $^{177}\mathrm{Lu}$

Monte Carlo simulations of the experiments performed with 99m Tc and 177 Lu have been performed via SIMIND v6.1.

The Monte Carlo simulation code SIMIND is a photon-tracking program developed by Professor Michael Ljungberg (Medical Radiation Physics, Department of Clinical Sciences, Lund, Lund University, Sweden). SIMIND describes a standard clinical SPECT camera and provides projected images from user defined attenuation map and activity distribution.

Both 99m Tc and 177 Lu were studied via SIMIND: the main parameters set for the Monte Carlo simulations are listed in Table 6.

In order to obtain the three-dimensional studies, the projected images produced via SIMIND were reconstructed using CASToR (Customizable and Advanced Software for Tomographic Reconstruction [14]), an open-source toolkit for tomographic reconstruction for both emission and transmission exams. CASToR applies an iterative reconstruction technique, in particular an OSEM-3D with 10 iterations and 8 subsets was used including scatter and attenuation correction with a stationary PSF modelled as a 3D isotropic Gaussian.

Results

As preliminary step, we compared the profiles of a uniform filled cylinder with the radionuclides used in this study, 99m Tc or 177 Lu, measured experimentally with the Monte Carlo calculated ones. Figure 2 (top) shows the result for 99m Tc, while the figure 2 (bottom) shows the results for 177 Lu. The error bar associated with each position of the measured profile has been calculated as the square root of the counts associated with the position.

Planar Spatial Resolution and Sensitivity

Figure 3 (top) shows the comparison between the experimentally measured and Monte Carlo calculated spatial resolution plotted as function of the source-detector distance for 99m Tc while the figure 3 (bottom) shows the comparison between the experimentally measured and Monte Carlo calculated sensitivity plotted as function of the source-detector distance for 99m Tc. Experimental results are in good agreement with the results obtained from SIMIND simulation.

Figure 4 shows the data about the spatial resolution for the peaks 113 keV and 208 keV of ¹⁷⁷Lu as function of source detector distance, while the figure 5 shows the experimentally measured and Monte Carlo calculated sensitivity as function of source detector distance for the two peaks of ¹⁷⁷Lu. Even in this case, the experimental results are in good agreement with the simulated ones, apart from the 208 keV sensitivity: the experimental values are nearly 14% lower than those obtained with SIMIND. Ramonaheng et al. [9] have reported for 208 keV peak of ¹⁷⁷Lu the experimental and MC (SIMIND) simulated data of $10.0 \pm 0.3 \text{ cps/MBq}$ and 10.3 cps/MBq, respectively.

In table 7, the measured and the simulated sensitivity at a distance of sourcedetector of 10 cm both for 99m Tc and 177 Lu are reported.

CF and RC for $^{99m}\mathrm{Tc}$ and $^{177}\mathrm{Lu}$

Symbia Intevo CF has been evaluated for all the uniformity phantom acquisitions performed. Two cylindrical ROIs were used for CF evaluation: the type 1 ROI had a volume 30% larger than the volume of Jaszczak phantom but with the same geometrical center, while the type 2 ROI had a volume 30% smaller than the volume of Jaszczak phantom but with the same geometrical center. The errors associated with experimental results take into account:

- the Poisson distribution of the counts;
- errors in the evaluation of phantom volume;
- error in activity evaluation through the calibrator (standard deviation of the measurement of the syringe samples, but also the systematic error of the calibrator itself);
- the standard deviation of the VOIs volume values;
- error in time interval evaluation.

The 99m Tc calculated CF value for the type 1 ROI was $110.1 \pm 5.5 \text{ cps/MBq}$ for experimental data while for SIMIND data the calculated value was $100.1 \pm 0.3 \text{ cps/MBq}$. The CF value calculated by using the type 2 ROI were $111.8 \pm 5.6 \text{ cps/MBq}$ and $101.7 \pm 0.3 \text{ cps/MBq}$ respectively for experimental and simulated data.

In figure 6, the RC experimental values for 99m Tc are compared with the RC values obtained by using Monte Carlo simulation and reconstructed by CASTOR software. For partially compensating the CDR function, a 2D gaussian distribution has been used in the reconstruction process, and in figure 6 we reported the results for three standard deviations corresponding to the gamma camera spatial resolution at the mimimum, maximum and central distance between Jaszczak SPECT phantom and collimator.

In order to obtain the CF factor for Lutetium, the previous procedure has been

repeated, except that the starting activity used to fill the phantom, $2818 \pm 70 \text{ MBq}$ was so high that gamma camera dead-time had effect on the calculated CF value. Hence, starting from dead-time response of modern gamma camera, typically described by the paralyzable model, it is possible to derive the measured calibration factor CF_m as function of the true calibration factor CF_t , the source activity A and the gamma camera apparent dead-time τ_a (the ratio between the true dead-time τ and the fraction of detected events occurring within the selected energy window $w_f)[15]$

$$CF_m = CF_t \cdot e^{-CF_t \cdot A \cdot \tau_a} \tag{1}$$

In figure 7 is shown the CF values obtained as function of phantom activity: a curve fitting procedure by using the eq. 1 allowed us to calculate the $CF_t = 18.3 \pm 1.0 \text{ cps/MBq}$ for type 1 ROI, while the $CF_t = 18.6 \pm 1.0 \text{ cps/MBq}$ for type 2 ROI. The estimated value for apparent dead-time $\tau_a = 2.3 \pm 1.6 \,\mu\text{s}$ is compatible with the result reported by Frezza et al. [16]. The results of CF for type 1 ROI are reported in Table 8.

The same uniformity phantom acquisitions have been repeated with SIMIND, in order to find CF for Lutetium; it is important to underline that CASToR can reconstruct studies taking into account only one peak at time. So, two different values for CF (one for the peak at 113 keV and one for the peak at 208 keV) have been obtained. Results are in Table 8. The "right peak" for dosimetry tasks is the second one, because of the less scattering/down scattering and the major abundance. RC factors have been evaluated from 1.4 ml to 1000 ml, using pockets filled with Lutetium. The final fit is shown in figure 8 weighted for the errors.

Discussion

The results obtained for the parameters acquired in planar imaging show an excellent agreement with the simulated data except for the sensitivity of the gamma camera for the 208 keV photons of 177 Lu, in this case the value calculated with the MC simulation is 10% higher than the experimentally measured value.

A critical element in the experimental evaluation of sensitivity is the accuracy with which the activity used in the experimental tests is measured. The certified activity of the ¹⁷⁷Lu sample provided by the ITM is known with an error of 10%, and this sample is used to determine the conversion factor k between the current measured by the dose calibrator and the activity of ¹⁷⁷Lu, assuming that the activity meter behaves in a linear manner over the entire measurement range of the activities we use. This assumption introduces at least 10% error in the calculation of experimental sensitivity.

The parameters acquired in tomographic mode, CF and RC, require a further step to be calculated: tomographic reconstruction using appropriate software. Usually, for SPECT tomographic reconstruction it is used an iterative reconstruction algorithm that allows to include in the projection operator the following three contributions: the response function of the collimator, the contribution of scatter and the contribution of tissue attenuation of radiation. Thus, the parameters calculated from the reconstructed images depend on how correct the estimate of the three contributions is. For this reason, we checked the effects of these three contributions both in the calculation of the CF and the RC curve.

In the calculation of the CF using the simulated data with SIMIND we have noticed as it was critical the estimation of the contribution of the scatter, in particular for the 99m Tc using the dual energy window (DEW) method and a weight factor w for the calculation of the scatter contribution in each projection. By changing the weight factor w starting from 0.5, theoretical weight of DEW method, to 0.87, value estimated by the 99m Tc simulated energy spectrum with fitting procedure, we have obtained values between $107.3 \pm 0.3 \text{ cps/Mbq}$ and $93 \pm 0.3 \text{ cps/Mbq}$. The value shown in Table 8 is the one obtained with the value of w=0.667 used by the Symbia Intevo software.

For the estimation of the RC curve using the simulated data with SIMIND we noticed that the correction for the collimator response function was critical. The software CASTOR at the moment allows to include a Gaussian collimator response function not dependent on the distance. For this reason, we have used Gaussian distributions with FWHM values ranging from the minimum value to the maximum value which depends on the distance of the activity from the collimator. For 99m Tc the minimum FWHM is 9.18 mm and the maximum FHWM 13.5 mm values obtained from the figure 2 and taking into account the minimum and maximum distance of the activity present in the cylindrical phantom from the collimator. The same was done for 177 Lu. So, in figure 6 we reported the values of the RC curve for 99m Tc that matches better with the experimental data is the one obtained with the Gaussian distribution with FWHM corresponding to the distance of the center of the cylindrical phantom from the collimator. In figure 8 we reported the RC curve for 177 Lu.

Conclusions

In this study the best parameters for reconstruction and correction of SPECT-CT analysis have been found, in order to standardize successive study and at the same guaranteeing the best achievable image quality and a correct activity evaluation. Moreover, it has be proven that SIMIND is a useful tool to simulate gamma cameras, using several radionuclides for different purpose both in diagnostic and therapeutic fields. In particular, in the nuclear medical therapeutic field, the role of targeted therapies is emerging for the treatment of neuroendocrine tumors, prostate cancer and other solid neoplasms. These treatment modalities, which can also be defined as endoradiotherapy, aim to concentrate ionizing radiation on the lesions and, at the same time, limit as much as possible the irradiation of healthy tissues and potential organs at risk (kidney, bone marrow, glands salivary ...). A predictive or peri-therapeutic dosimetry evaluation is therefore mandatory to optimize therapeutic efficacy and reduce the risk of toxicity, especially in those therapeutic models that have not yet achieved complete standardization. At the same time, the EURATOM 59 directive (implemented in the Italian state by legislative decree 101) indicates the need to carry out a dosimetric evaluation in all therapeutic practices including the use of ionizing radiation. Hence the need to develop friendly dosimetric models based on increasingly precise and accurate calculation algorithms.

Declarations

Ethics approval and consent to participate Not applicable

Consent for publication Not applicable

Availability of data and materials Not applicable

Competing interests

The authors declare that they have no competing interests.

Funding

This research has been partially supported by the Regione Emilia Romagna grant funded on "Programma operativo Fondo sociale europeo 2014/2020".

Authors' contributions

SDB was responsible for the tomographic acquisitions, tomographic image data analysis and she wrote the first draft of manuscript. LL was responsible for the planar acquisitions and planar image data analysis. GDD was responsible for the MC simulations, the MC data reconstruction, the MC data analysis and he wrote the manuscript. AT, ET, MCL were involved in the experimental design of this study, LU was involved in the chemistry management of Lu-177, MB supervised the project. All authors were involved in reviewing the manuscript, and they all read and approved the final manuscript.

Acknowledgements

Not applicable

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References

- 1. Zaidi H. Relevance of accurate Monte Carlo modeling in nuclear medical imaging. Med Phys. 1999;26:574-608.
- Liu S, Famcombe TH. Collimator-detector response compensation in quantitative SPECT reconstruction. In: 2007 IEEE Nuclear Science Symposium Conference Record: 27 October - 3 November 2007; Hawaii. IEEE Nuclear Science; 2007. p. M19–327.
- Chun SY, Fessler JA, Dewaraja YK. Correction for Collimator-Detector Response in SPECT Using Point Spread Function Template. IEEE Trans Med Imaging. 2013;32:295–305.
- Willowson K, Bailey DL, Baldock C. Quantitative SPECT reconstruction using CT-derived corrections. Phys Med Biol. 2008;53:3099–3112.
- Pacilio M, Cassano B, Pellegrini R, Di Castro E, Zorzi A, De Vincentis G, et al. Gamma camera calibrations for the Italian multicentre study for lesion dosimetry in 223Ra therapy of bone metastases. Phys Medica. 2017;41:117–23.
- Zeintl J, Vija AH, Yahil A, Hornegger J, Kuwert T. Quantitative accuracy of clinical 99mTc SPECT/CT using ordered-subset expectation maximization with 3-dimensional resolution recovery, attenuation, and scatter correction. J Nucl Med. 2010;51:921–8.
- Dong X, Saripan MI, Mahmud R, Mashohor S, Wang A. Characterization of SIEMENS Symbia T SPECT camera in Monte Carlo simulation environment. Pakistan Journal of Nuclear Medicine. 2019;8(1):18–26.
- Toossi MTb, Islamian PJ, Momennezhad M, Ljungberg M, Naseri SH. SIMIND Monte Carlo simulation of a single photon emission CT. Journal of Medical Physics. 2010;35(1):42–47.
- Ramonaheng K, van Staden JA, du Raan H. Validation of a Monte Carlo modelled gamma camera for Lutetium-177 imaging. Appl Radiat Isot. 2020;163:109200.
- Ejeh JE, van Staden JA, du Raan H. Validation of SIMIND Monte Carlo Simulation Software for Modelling a Siemens Symbia T SPECT Scintillation Camera. In: World Congress on Medical Physics and Biomedical Engineering 2018. IFMBE Proceedings, vol 68/1. Springer, Singapore. IUPESM; 2018. p. 573–576.
- Morphis M, van Staden JA, du Raan H, Ljungberg M. Validation of a SIMIND Monte Carlo modelled gamma camera for lodine-123 and lodine-131 imaging. Heliyon. 2021;7(6):e07196.
- Ljungberg M. The SIMIND Monte Carlo program. In: M Ljungberg MAK S E Strand, editor. Monte Carlo calculations in nuclear medicine: Applications in diagnostic imaging. 2nd ed. Boca Raton: CRC Press; 2012. p. 111–128.
- Ljungberg M, Celler A, Konijnenberg MW, Eckerman KF, Dewaraja YK, Sjögreen-Gleisner K. MIRD Pamphlet No. 26: Joint EANM/MIRD Guidelines for Quantitative 177Lu SPECT Applied for Dosimetry of Radiopharmaceutical Therapy. J Nucl Med. 2016;57:151–162.
- 14. Merlin T, Stute S, Benoit D, Bert J, Carlier T, Comtat C, et al. CASTOR: a generic data organization and processing code framework for multi-modal and multi-dimensional tomographic reconstruction. Phys Med Bio. 2018;63:151–162.
- 15. S R Cherry MEP J A Sorenson. Physics in Nuclear Medicine. Philadelphia: Elsevier Saunders; 2012.
- Frezza A, Desport C, Uribe C, Zhao W, Celler A, Després P, et al. Comprehensive SPECT/CT system characterization and calibration for 177_L u quantitative SPECT (QSPECT) with dead-time correction. Eur J Nucl Med Mol Imaging. 2020;7(10):1–22.

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 Bé MM, Duchemin B, Lamé J, Morillon C, Piton F, Browne E, et al. Table de Radionucléides. vol. 1. DAMRI/LPRI BP 52, F-91193 Gif-sur-Yvette Cedex, France: Commissariat à l'Énergie Atomique; 1999.

 Uccelli L, Boschi A, Cittanti C, Martini P, Panareo S, Tonini E, et al. 90Y/177Lu-DOTATOC: From Preclinical Studies to Application in Humans. Pharmaceutics. 2021;13:1463.

Figures

Figure 1 Experimental Setup Example of experimental configuration: on the left, the uniform phantom is shown; on the right, the acquisition moment for Tc-99m.

Figure 2 Comparison of experimental and simulated projection profiles. (top) Plot of experimentally measured and Monte Carlo simulated profile of uniform cylinder filled with 99m Tc. (bottom) Plot of experimentally measured and Monte Carlo simulated profile of uniform cylinder filled with 177 Lu.

Figure 3 Spatial resolution and sensitivity for 99mTc. (top) Plot of spatial resolution as function of distance between source and detector for 99mTc. (bottom) Plot of sensitivity as function of distance between source and detector for 99mTc.

Figure 4 Spatial resolution for ¹⁷⁷Lu. Plot of spatial resolution as function of distance between source and detector for ¹⁷⁷Lu: 113 keV peak (top), 208 keV peak (bottom).

Figure 5 Sensitivity for ¹⁷⁷Lu. Plot of sensitivity as function of distance between source and detector for ¹⁷⁷Lu: 113 keV peak (top), 208 keV peak (bottom).

Figure 6 RC for 99m Tc. Plot of measured and calculated by MC data recovery coefficients (RC) for 99m Tc as function of sphere volumes.

Figure 7 CF for 177 Lu. Plot of calibration factor coefficients (CF) for 177 Lu as function of activity in the phantom.

Figure 8 RC for 177 Lu. Plot of measured and calculated by MC data recovery coefficients (RC) for 177 Lu as function of sphere volumes.

Tables

lsotope	Half-life	Strongest γ emission E $_{\gamma}$ [keV] (I $_{\gamma}$ [%])	$\begin{array}{l}Max\;\beta\;energy\\E_{max}\;[keV]\end{array}$
Tc-99m	6.01 h	140.5 (88.5)	436.2
Lu-177	6.65 d	112.9 (6.2) 208.4 (10.4)	498.3

Table 1 Decay characteristics of both Tc-99m and Lu-177; data from [17, 18]

Table 2 Main Symbia parameters, taken from Symbia Intevo data sheet

Crystal size	59.1 x 44.5 cm
Crystal thickness	9.5 mm
PMT total number	59
PMT array	Hexagonal
System resolution at 10 cm, 140 keV	7.5 mm
Energy resolution at 140 keV	9.9%
Sensitivity at 10 cm, 140 keV	91 cps/MBq
SPECT reconstruction matrix size	128×128

 Table 3 The lower and upper scatter windows for technetium and lutetium main peaks are listed.

Radionuclide	Main peak [keV]	PW range [keV]	LSW range [keV]	USW range [keV]
Tc-99m	140.5	123.9-151.4	103.2 - 123.9	not used
Lu-177	113	102.7-119.4	86.1-102.7	119.4 - 128.2
Lu-177	208	189.3-220.0	168.8-189.3	not used

Table 4 The six spheres of the Jaszczack phantom with their respective activity and the background are shown. Each of the value reported in this Table is the mean value of five different measurements, with a standard deviation less than 1%. These errors must be added to the 10% error on the Activity (certified by the producer).

Sphere Volume [ml]	Sphere Diameter [mm]	Activity [MBq]
0.5	9.8	4.8
1.0	12.4	4.4
2.0	15.6	4.5
4.0	18.9	4.7
8.0	24.8	4.7
16.0	31.2	4.6
Phantom Volume [ml]		Activity [MBq]
6800		131.7

Table 5 The five spheres of the NEMA PET phantom with their respective activity and background are shown. Each of the value reported in this Table is the mean value of five different measurements, with an associated error of less than 11%.

Sphere Volume [ml]	Sphere Diameter [mm]	Activity [MBq]
1.4	13.0	8.3
2.5	17.0	8.4
5.0	22.0	8.6
11.0	28.0	8.7
26.0	37.0	7.5
Phantom Volume [ml]		Activity [MBq]
9600		201.0

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	Tc-99m	Lu-177
Photon energy	140 keV	113 keV and 208 keV
Source type	Horizontal cylinder	Horizontal cylinder
Energy resolution	9.9% @140.5keV	9.9% @140.5keV
Intrinsic Resolution	0.38 mm	0.38 mm
Photons per projection	10^{7}	107
Distance to detector (circular orbit)	25 cm	25 cm
Matrix Size	128×128	128×128
Acceptance angle	45°	45°
Rotation mode	CW	CW
Rotation angle step	5.625°	5.625°
Number of projection	64	64
Collimator	Sy-LEHR	Sy-ME

Table 7	Comparison	of measured	planar System	Sensitivity	with	Monte	Carlo	results.	All	parameters
have bee	en measured	at distance o	f 10 cm from o	collimator.						

Parameter	Radioisotope	Main peak [keV]	Experimental	Simulated
Sensitivity [cps/MBq]	Tc-99m	140.5	88.0 ± 4.4	89.4 ± 0.5
Sensitivity [cps/MBq]	Lu-177	113.0	9.9 ± 0.5	9.7 ± 0.1
Sensitivity [cps/MBq]	Lu-177	208.0	9.6 ± 0.5	10.9 ± 0.2

 Table 8 CF evaluation study for Tc-99m with Isocontour and Ellipsoid contouring with Symbia NET workflow. CF evaluation study for Tc99m with Isocontour and Ellipsoid contouring with Monte Carlo Code SIMIND.

Parameter	Method	Radioisotope	Main peak [keV]	Experimental	Simulated
CF [cps/MBq]	Ellipsoid	Tc-99m	140.5	110.1 ± 5.5	100.1 ±0.3
CF [cps/MBq]	Ellipsoid	Lu-177	113.0 + 208.0	18.3 ± 1.0	20.4 ± 0.7



Left

Right



Profile position [mm]

Counts

Counts



Source to Detector Distance [cm]











Recovery Coefficient [%]



CF [cps/MBq]



Sphere Volume [ml]

Recovery Coefficient [%]