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Original paper

Monte Carlo study of the eye lens exposure of medical staff administering Sc-47 and Cu-67 labelled radiopharmaceuticals

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ABSTRACT

Purpose: In the last decades, new technologies and new radiopharmaceuticals for diagnosis and therapy have continuously grown, and that growth was accompanied by an increasing use in clinical practice, but, as with any other application involving radiation, the extent to which they may contribute to increasing the radiation dose to the operator must be studied. For that reason, EURADOS (European Radiation Dosimetry Group) decided to evaluate the exposure of medical staff in nuclear medicine to new possible radiopharmaceuticals labelled with Sc-47 and Cu-67.

Methodology: Modified ICRP voxel model were employed to determine the exposure of the eye lens and of the thyroid of operators administrating radiopharmaceuticals in a typical Peptide Receptor Radionuclide Therapy scenario. The simulations were validated comparing Monte Carlo results with TLD measurements performed in hospital with Lu-177 labelled compounds.

Results: Doses to the eye lens and thyroid are derived from the photon emissions (the beta contribution is three order of magnitude lower). The agreement obtained for Lu-177 provides confidence that, notwithstanding the limits of the simulations, the robustness of the followed approach can be extended also to the evaluation performed for Sc-47 and Cu-67.

Conclusions: The dose to the lens of the eye is of the order of 2 μSv/GBq per patient for Lu-177 compounds and, due to the different energies and yields, about 8 μSv/GBq for both Sc-47 and Cu-67. These evaluations can be useful to optimize the radiation protection of medical staff in the nuclear medicine environment and assess the correct personnel workload in these kinds of practices.

1. Introduction

Peptide Receptor Radionuclide Therapy (PRRT) has become an effective tool in the treatment of neuroendocrine tumor (NET) [1–4] in the last thirty years. More recently, radiopharmaceuticals labelled with Lu-177 have been proven to be a promising means for castration-resistant prostate cancer management [5–7]. These two practices are part of the broader field of theragnostic in oncology, a methodology that combines therapy and diagnostics, exploiting the particular characteristic of a radionuclide (or of a pair of radioactive isotopes of the same

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element) of simultaneously emitting less penetrating radiation (suitable for treatment of malignant cells) and highly penetrating radiation (appropriate for imaging) [8]. These therapies undoubtedly represent a relevant advancement in cancer treatment; but as for any other application with radiation, their possible contribution to increasing the dose to the operator must be studied. New technology, new radiopharmaceuticals for diagnosis and therapy, and molecular imaging have continuously grown in the last decades [9–12], and that growth was accompanied by an increasing use in clinical practice [13]. A recent paper [14] analyzing the operators' exposures across several hospitals in France, in the period 2009–2019, shows a general decrease of the non-zero doses (i.e. doses recorded as above the reporting threshold of the dosimetric system) for all the hospital departments except nuclear medicine departments. This suggests that there is still a crucial need to optimize radiation protection in nuclear medicine. In such a context, radiation protection of personnel and proper evaluation of the expected doses in the case of new practice with new radionuclides are mandatory. For that reason, in the framework of the activities of Working Group 6 (Computational Dosimetry), Working Group 7 (Internal Dosimetry) and Working Group 12 (Dosimetry in Medical Imaging) of EURADOS (European Radiation Dosimetry Group) it was decided to evaluate the exposure of medical staff in nuclear medicine due to clinically emerging radionuclides with potential for use in theragnostic management of patients. Initially a comprehensive literature review identified the radionuclides of most interest to be investigated. Once the appropriate radionuclides were selected, Monte Carlo simulations, employing modified versions of ICRP voxel reference adult models [15], were implemented to evaluate the doses to the lens of the eye and to the thyroid for operators administering the radionuclides to the patient. In the following paragraphs the most relevant outcomes of those Monte Carlo simulations are presented.

2. Methodology

2.1. The investigated radionuclides and the exposure scenario

A comprehensive literature review was performed, encompassing about 100 papers, which identified Scandium-47 and Copper-67 as being the two most important radionuclides to study due to their emerging clinical potential and decay characteristics. The same radionuclides appeared in a recent IAEA publication 'Therapeutic Radiopharmaceuticals Labelled with New Emerging Radionuclides (2016–2020)', which focused on the production and quality control of radiopharmaceuticals labelled with Cu-67, Re-186 and Sc-47 [16].

Scandium-47 is a β^- emitter (average β^- energy 162 keV) with a $T_{1/2}$ of 3.35 days. Its beta emission is accompanied by a 159.4 keV gamma ray (68.3 % branching ratio). The method of production Sc-47, based on nuclear reactions such as Ti(n,x)^{47}Sc and V(n,x)^{47}Sc, limits its availability [17,18], but some interesting applications have been suggested for this radionuclide as the possibility of producing bone seeker radiopharmaceuticals [19]. Indeed, Sc-47-folate shows comparable results to Lu-177-folate in pre-clinical studies [20]. Considering that Scandium-44, a β^+ emitter with a $T_{1/2}$ of 3.97 h, has been proposed for PET imaging [21], the couple Sc-44/Sc-47 could be an interesting matched pair of radionuclides for theragnostic procedures [22].

Copper-64 has already shown its quality as a PET tracer [23,24]; Copper-67 is a β^- emitter (average β^- energy 141 keV) with a $T_{1/2}$ of 61.88 h, and its beta emission is accompanied by 91 keV (7 % branching ratio), 93 keV (16 % branching ratio) and 184 keV (48.7 % branching ratio) gamma emissions. It can be produced by irradiating Zn-67 in high neutron flux reactors or in cyclotrons by bombarding zinc, natural or enriched, with protons [25]. Cu-67 has been proven to be effective in treatment of NET [26], having good imaging and dosimetric characteristics [27] and the possibility of coupling Cu-64 with Cu-67 is promoted in various studies [28,29].

The characteristics of the simulated exposure scenario were based on Lu-177-DOTATATE administration to NET patients via intravenous infusion. The physician supervises the gravity infusion (Fig. 1a), which starts by allowing the saline solution to drip into the vial, thus forcing the radiopharmaceutical out to the patient intravenous port; this technique avoids the employment of a syringe and reduces the risk of vein rupture and extravascular injection. Typically, the duration of the infusion ranges between 10 min and 30 min, depending on clinical requirements and suggested protocols. During the administration, film badge and thermoluminescent dosimetry (TLD) ring dosimeters are provided to measure doses to the whole body and extremities respectively, and, in some centres, protective lead aprons are worn by operators [30,31]. The vial containing the radionuclide is generally shielded by polymethyl methacrylate (PMMA) thick enough to stop the beta radiation, and, possibly, by an additional lead shield to absorb the gamma radiation (Fig. 1b). Accordingly the main source of radiation exposure to the operator, excluding the patient, is the unshielded catheter that connects the vial to the patient and through which the radiopharmaceutical flows.

The scenarios analysed in this study assume the use of a lead apron, which protects the operator's abdomen and torso, as well as lead gloves. Hence this dosimetric study aimed to evaluate the dose to unshielded (and generally unmonitored) organs, namely the lens of eyes and the thyroid.

2.2. The Monte Carlo simulations

The investigated exposure scenario was modelled in Monte Carlo simulations considering only the unshielded part of the source, i.e. the

Fig. 1a. An operator wearing a lead apron and lead gloves during the administration phase.

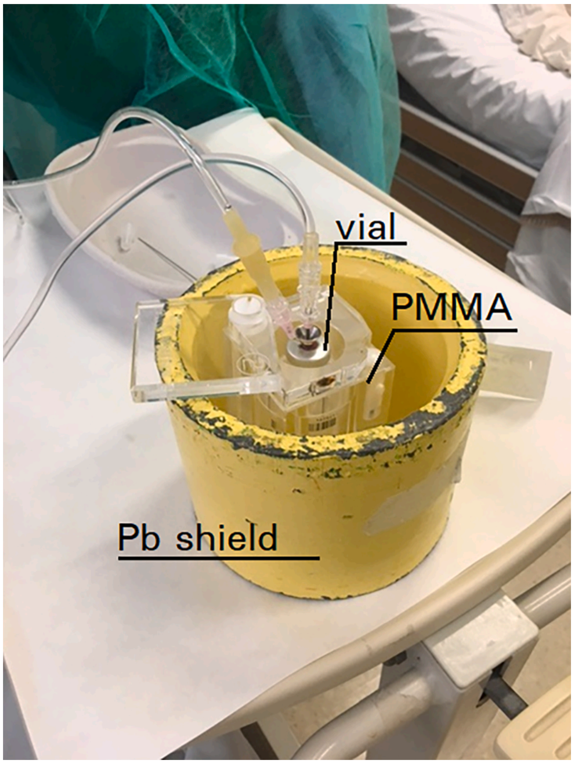

Fig. 1b. The vial and the shielding.

catheter, and the operator supervising the injection. To achieve this ICRP voxel reference adult models [15] were employed. These voxel phantoms were developed by ICRP on medical image data of real people and are consistent with the reference anatomical and physiological parameters representing the male and female western-caucasian population. The female model is 167 cm tall, weighs 60 kg and consists of 3.9 million voxels; the male model is 176 cm tall, weighs 73 kg, and consists of 1.9 million voxels. Both models have been segmented to identify 140 different tissues through their body. With the aim of determining the absorbed dose to the eye lens, the phantoms were modified by substituting the original eye voxel model with a mathematical model including a realistic lens [32] (Fig. 2). That was needed because the original description of the eye, and of its small internal structures, is not accurate due to the limited voxel resolution. In the adult male phantom the single voxel is $0.2 \times 0.2 \times 0.8$ cm^3, that means that the smallest structure that can be represented in that phantom is a parallelepiped corresponding to a single voxel element.

The source was simulated as a simple polyvinylchloride (PVC) catheter (density 1.3 g/cm^3), defined as a 50-cm-long cylinder of 0.3 cm internal diameter and 0.41 cm external diameter, containing water (Fig. 3). The radionuclide was assumed to be distributed uniformly in the bore of the catheter and emits radiation isotropically (4 π directions). The catheter is positioned parallel to the right – left shoulder direction of the anthropomorphic models representing the operator, at a distance of about 35 cm from the outer surface of the skin. Its axis is about 70 cm from the eye lenses. A sensitivity study was performed to estimate the influence of source-operator distance on the calculated doses, moving the catheter nearer of farer from operator external surface and head.

The simulation model was validated by comparing it to occupational exposure measurements recorded in clinical practice during a Lu-177 PRRT administration. Once validated, the simulations were then applied to the radionuclides of interest in this study, namely Sc-47 and Cu-67.

For the three investigated radionuclides, the beta and gamma emissions were considered separately. That means, beside the calculation for the beta spectrum, two additional simulations of 113 keV (emission probability of 6.4 %) and 210 keV (emission probability of 11 %) photons were performed for Lu-177; for Sc-47, only the 159 keV (68.1 %) photons were considered; and for Cu-67, the 91 keV (7 %), 93 keV (16 %) and 185 keV (49 %) photon emissions were simulated. Beta spectra were interpolated from the data published in [33] for Sc-47 and [34] for Cu-67. All simulations were repeated for the female and male reference models. Moreover, for the Lu-177 simulation with the female phantom, the impact of the location of the source was also investigated. This was achieved by positioning the catheter closer to or farther from the relevant organs of interest (eye, thyroid).

The absorbed dose in the lens of the eyes (sensitive and unsensitive parts of the lens [32]), and the absorbed dose in the thyroid were evaluated and averaged between the female and male phantoms. A 0.5-cm-radius air sphere was also defined on the forehead, just between the eyes. In that "ideal detector" the dose equivalent at 3 mm, $H_p(3)$ [35], and the ICRU95 personal absorbed dose in the lens of the eyes, D_{lens} [36], were calculated by tallying the fluence through its small volume and folding it with the corresponding conversion coefficients.

Once the exposure scenarios were defined, simulation models were then implemented in two different multi-purpose Monte Carlo codes, MCNP, 2.7 and 6 [37] and PHITS [38]. MCNP and PHITS are two well-validated Monte Carlo code families employed in different fields of radiation protection and radiation dosimetry in a number of applications including medical field [39,40,41]. They are multipurpose codes that

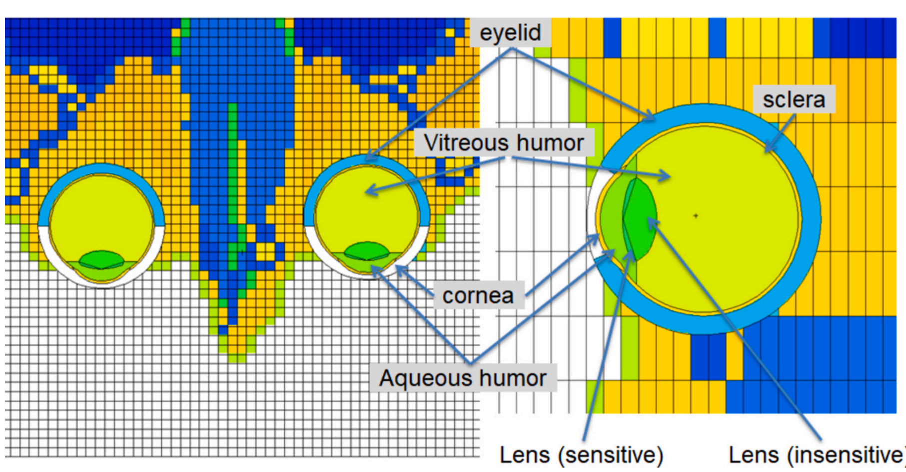

Fig. 2. A 2-D image (axial cut on the left, sagittal cut on the right) of part of the head of the ICRP reference adult voxel model (voxel elements are clearly visible) with the detailed mathematical eye lens model inserted in.

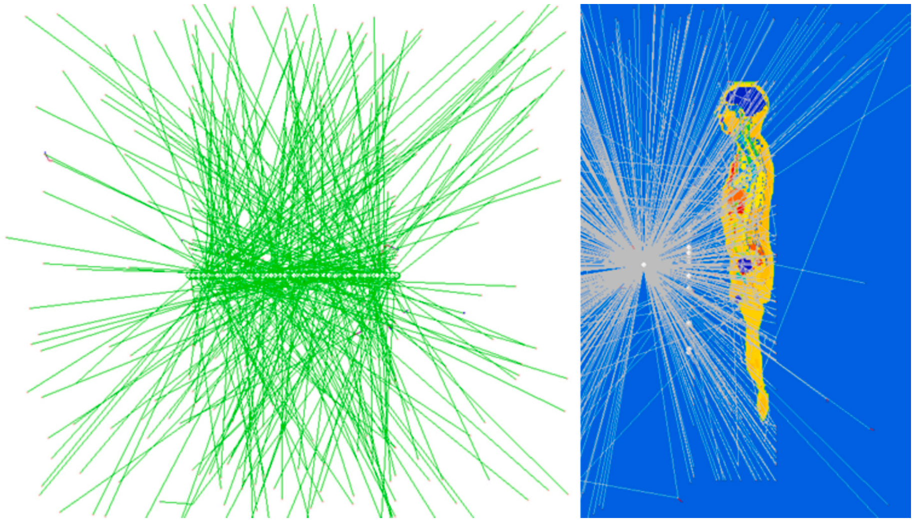

Fig. 3. A 2-D image of the source and of the operator (sagittal cut).

model the transport of different kind of particles, including neutrons, protons, heavy ions, photons, and electrons, over wide energy ranges using various nuclear reaction models and data libraries. They describe complex 3-dimensional geometries employing simple volumes (as cones, cubes, spheres…) and repeated structures (as voxel models). The execution time was tailored to achieve a general relative uncertainty lower than 10 % (at one standard deviation, i.e. k = 1 [42]). No variation reduction technique was applied except for the electrons, for which an energy cut-off of 250 keV was applied, i.e., beta rays with energy lower than that value were not transported. This is due to the assumption that betas with energies below the threshold applied are unable to pass through the PVC catheter walls (range calculated using the stopping power published in the NIST database [43]). The results shown in the following paragraphs and tables are the averages between the simulations with those two codes.

All phantom's tissues elemental composition and densities were taken from ICRP report [15], for the remaining materials the NIST database was used [44].

A 2D image of the simulated geometry with the source and the voxel phantom representing the operator (sagittal cut) is shown in Fig. 3. On the left pane only the cylindrical source is visible, i.e. the PVC catheter containing the radionuclide, which emits gamma radiation isotropically; on the right pane the same source is positioned in front of the operator. In that case the source cylinder main axis is parallel to the right – left shoulder direction of the operator. The tracks of the emitted gammas are shown in the air surrounding the models.

2.3. Validation of the simulations

Validation of the simulations was achieved by comparing the simulated $H_p(3)$ results against measurements performed in Reggio Emilia Hospital, Italy, during Lu-177 radiopharmaceutical administration to NET patients. In that case, the physicians wore protective aprons, and whole body and extremity dosemeters. Three additional TLDs, calibrated in terms of $H_p(0.07)$, were supplied to the physicians to evaluate the possible eye lens exposure, and were placed outside the safety goggles (standard safety goggles not protecting from X-rays) on their left side, right side and centrally between the eyes ([45] and F. Fioroni, Reggio Emilia Hospital, personal communications). When the measurements were performed, $H_p(3)$ calibrated dosemeters were not available at the hospital. However the dosemeters used are able to provide a satisfactory approximation of Hp(3), at least for the penetrating gamma emissions [46], which is the main contribution to the dose to the eye lens. Considering the energy spectrum of the beta emitters of Lu-177 (mean energy 149 keV), the electrons' expected range is about 0.025 cm in PVC and 25.5 cm in air (data calculated with ESTAR from NIST database [39]); the doses deposited by primary electrons at the depth of $H_p(3)$ are therefore expected to be very small.

The results of the measurements are given in terms of dose per GBq per patient. In order to compare these data to the simulations a further step is necessary. Monte Carlo code outcomes are 'per source particle', but can be renormalized using Equation (1) to obtain the dose per GBq per patient:

$$D' = d_{MC} \times y \times \frac{1}{GBq} \times t \quad (1)$$

where d_{MC} is the dose calculated with Monte Carlo in Gy (or Sv) per source particle per second, y is the yield of the gamma emission and t is the duration of the exposure (s). The D' calculated for each gamma emissions of a given radionuclide are then summed together to get the total dose per GBq per patient for that radionuclide.

3. Results

3.1. Lu-177 simulation and measurements

Simulations were performed using both the female and the male models. For each model, three simulations were performed for the Lu-177 source: modelling the beta spectrum, the 113 keV gamma (yield 0.064) and the 201 keV gamma energy (yield 0.11). The resultant doses to the eye lens, the $H_p(3)$, and the D_{lens} are reported in Tables 1 and 2. Only the data for the gamma contribution is reported, as the data for the beta emission were found to be about three orders of magnitude lower and were therefore considered negligible. The values presented are the averages of the female and male models. In general, the values for the female model were around 30 % higher than those calculated for the male model mainly due to the different height of the phantoms [47]. $H_p(3)$ and D_{lens} were evaluated in the air sphere placed over the models' skin surface between the eyes. Statistical uncertainties were below 5 %.

Values for the sensitive and unsensitive part of the lens of the eye were found to be identical considering the range of the uncertainties; and as such only the results for the sensitive part of the lens are presented here.

Due to the symmetry of the simulated scenario, there was very little difference in the measured dose for the right or left eye. Both $H_p(3)$ and D_{lens} are considered to represent a satisfactory estimate of the dose to the lens of the eye.

A selection of the doses to the eye lens, measured during Lu-177

Table 1
Absorbed dose in the eye-lens. Results of the simulations for Lu-177: gamma contribution (MC k = 1 uncertainties in brackets).

Mean values between female and male models	Right eye lens absorbed dose	Left eye lens absorbed dose
113 keV gamma (6.4 % yield) contribution (μGy/GBq.s)	5.88×10^{-4}	5.56×10^{-4}
210 keV gamma (11 % yield) contribution (μGy/GBq.s)	1.92×10^{-3}	1.87×10^{-3}
Total dose (μGy/GBq.s)	2.51×10^{-3}	2.43×10^{-3}
Total dose for 15-minutes exposure (μGy/GBq)	2.26 (8 %)	2.19 (8 %)

Table 2
$H_p(3)$ detector and D_{lens} in the detector between the eyes. Results of the simulations for Lu-177: gamma contribution (MC k = 1 uncertainties in brackets).

Mean values between female and male models	$H_p(3)$ in the center of forehead	D_{lens} in the center of the forehead
113 keV gamma (6.4 % yield) contribution	7.03×10^{-4} (μSv/GBq.s)	6.72×10^{-4} (μGy/GBq.s)
210 keV gamma (11 % yield) contribution	2.16×10^{-3} (μSv/GBq.s)	2.09×10^{-3} (μGy/GBq.s)
Total dose	2.86×10^{-3} (μSv/GBq.s)	2.76×10^{-3} (μGy/GBq.s)
Total dose for 15-minutes exposure	2.57 (3 %) (μSv/GBq)	2.49 (3 %) (μGy/GBq)

DOTATOC and Lu-177 DOTATATE administrations, is reported in Table 3. Doses are given for the dosemeters worn on the right (RDD), in the center (CDD) and on the left (LDD) of the safety goggles (standard safety goggles not protecting from X-rays). The RDD, CDD and LDD results are normalized by considering a 15-minute injection (F. Fioroni, Reggio Emilia Hospital, personal communications and [48]). The doses are expressed in terms of μSv per GBq per patient and the uncertainty associated is around 35 %. There is a variability among operators that is a result of their different distance from the catheter; whilst the inhomogeneity between left and right dosemeters estimated value (as in case I and J) can be related to the orientation of the head of the operator with respect the catheter.

Table 3
Results of the measurements during Lu-177 DOTATOC and Lu-177 DOTATE administration (RDD: right dosemeter dose; CDD: central dosemeter dose; LDD: left dosemeter dose).

operator	RDD per patient (μSv/GBq)	CDD per patient (μSv/GBq)	LDD per patient (μSv/GBq)
A	1.35	9.63	4.59
B	4.89	3.85	4.21
C	2.03	2.91	2.50
D	0.29	0.29	0.29
E	0.28	0.09	0.28
F	0.40	0.23	0.27
G	0.15	0.19	0.10
H	0.31	0.04	0.38
I	0.27	0.43	1.77
J	0.04	0.11	0.14
K	8.09	9.29	9.14
L	0.22	0.13	0.17
Min	0.04	0.04	0.10
Max	8.09	9.63	9.14
Mean	1.53	2.27	1.99

A good agreement can be found when comparing the mean values the Monte Carlo results in Tables 1 and 2 and the measurements outcomes of Table 3 considering the uncertainty and the variability of the data. That consistency can be considered a validation of the adopted methodology.

3.2. Sc-47 and Cu-67 eye dose results

Similar to the ^{177}Lu simulations, the doses due to emitted beta of Sc-47 and Cu-67 were found to be three orders of magnitude lower than the doses derived from their gamma emissions. For that reason, only the gamma simulations results are presented here. The Monte Carlo results for the Sc-47 (159-keV-gamma emission, yield 68 %) are presented in Table 4.

In Table 5 the Monte Carlo results for Cu-67 are shown for the three main gamma emissions: 91.3 keV (yield 7 %), 93.3 keV (yield 16 %) and 184.6 keV (yield 49 %).

3.3. Dose to the thyroid

In Table 6 the absorbed dose to the thyroid is reported for the investigated radionuclides. For the same reason reported above, the values correspond to the total dose produced by the gamma emissions. Doses are normalized to 'per GBq' considering 15-minute exposures.

4. Discussion

This study employed a combination of experimental measurements and Monte Carlo simulations to estimate the dose to the lens of the eye and thyroid from occupational exposures during therapeutic radiopharmaceutical administration for a range of clinically relevant radionuclides.

In the case of Lu-177, the simulated eye lens absorbed doses and the evaluated $H_p(3)$ and D_{lens} were in good agreement with both the measurements performed here, and in the study reported by Riveira-Martin et al. [49]. In the cited paper the mean (range) measured eye lens doses in terms of $H_p(3)$ was found to be 1.94 [1.36–2.83] μSv/GBq for the left eye and 1.76 [0.63–2.15] μSv/GBq for the right eye, for an infusion duration of 15–20 min per patient.

Considering the particular position of the thyroid, in the frontal part of the body, and the limited shielding offered by the surrounding (soft) tissue, the absorbed dose evaluated in the thyroid can be compared with the whole body exposure during Lu-177 radiopharmaceutical administration, at least as an order of magnitude. In a paper by Abuqbeitah et al. [50], the exposure of medical staff during practices with Lu-177

Table 4
Results of the simulations for Sc-47: gamma contribution (MC k = 1 uncertainties in brackets). All results are reported in μGy/GBq.s or μGy/GBq, but $H_p(3)$ in μSv/GBq.s or μSv/GBq.

Mean values of female and male models	Right eye lens absorbed dose	Left eye lens absorbed dose	D_{lens} in the center of the forehead	$H_p(3)$ in the center of the forehead
159 keV gamma (68 % yield) dose (μGy/GBq.s)	8.80×10^{-3}	8.56×10^{-3}	9.87×10^{-3}	1.03×10^{-2}
Dose for 15-minutes exposure (μGy/GBq)	7.92 (2 %)	7.70 (2 %)	8.88 (1 %)	9.23 (1 %)

Table 5
Results of the simulations for Cu-67: gamma contribution (MC k = 1 uncertainties in brackets). All results are reported in μGy/GBq.s or μGy/GBq, but $H_p(3)$ in μSv/GBq.s or μSv/GBq.

Mean values of female and male models	Right eye lens absorbed dose	Left eye lens absorbed dose	D_{lens} in the center of the forehead	$H_p(3)$ in the center of the forehead
91.3 keV gamma (7 % yield) dose (μGy/GBq.s)	5.05×10^{-4}	4.93×10^{-4}	6.23×10^{-4}	6.55×10^{-4}
93.3 keV gamma (16 % yield) dose (μGy/GBq.s)	1.18×10^{-3}	1.16×10^{-3}	1.67×10^{-3}	1.52×10^{-3}
184.6 keV gamma (49 % yield) (μGy/GBq.s)	7.50×10^{-3}	7.29×10^{-3}	8.23×10^{-3}	8.52×10^{-3}
Dose for 15-minutes exposure (μGy/GBq)	8.26 (2 %)	8.04 (2 %)	9.47 (1 %)	9.62 (1 %)

Table 6
Dose to the thyroid due to gamma emissions of the radionuclide for a 15 min exposure (MC k = 1 uncertainties in brackets).

radionuclide	Total absorbed dose in thyroid for 15 min exposure (μGy/GBq)
Lu-177	2.30 (1 %)
Sc-47	8.27 (1 %)
Cu-67	8.77 (1 %)

DOTATATE and Lu-177 PSMA was estimated by employing electronic personal dosemeters, obtaining a mean effective dose of 2.0 ± 0.9 μSv for DOTATATE and 2.0 ± 0.5 μSv for PSMA per patient per unit administered activity. These values are in fair agreement with the 2.3 μGy evaluated in our simulations for the Lu-177 case. Similar values were estimated by Calais and Turner [48], who estimated a mean physician exposure during a Lu-177 octreotate therapy day of 7.6 μSv (4 patients a day), i.e. about 1.9 μSv per patient.

The good agreement obtained for Lu-177 compared to measurements performed here and in the literature provides confidence that, notwithstanding the limits of the simulations, reasonable estimations of occupational exposure for Sc-47 and Cu-67 can be obtained with the simulation model developed here.

It is generally accepted that once appropriate shielding and good radiation practices are adhered to, the occupational exposure due to ^{177}Lu therapies is low [40,51], this finding is further confirmed here. While extremity exposure in terms of dose to the skin of the hands has been previously studied [40,51,52], there is very little published information available on the dose to the thyroid or eyes for ^{177}Lu procedures. The simulation models developed and validated here for ^{177}Lu provide baseline occupational exposures that other centres may benchmark their data against.

Comparing the simulated eye exposure across the three radionuclides, assuming the same administration scenario, indicates an increased occupational dose when Cu-67 and Sc-47 are used (Fig. 4). Similarly, the two emerging radionuclides result in a 4-fould increase in thyroid exposure compared to Lu177. Eye lens and thyroid monitoring and additional protection for these organs may be required for these radionuclides; this is an area that requires further investigation.

The limitations of the present investigation are mainly dominated by the employed geometry, where the source is simulated as a line at a fixed distance from the operator body, and by the duration of the exposure, related to the flowing of the radiopharmaceutical through the catheter, which was fixed to 15 min. To investigate the impact of the source position a sensitivity study was performed using the female phantom. Specifically, the source was moved 10 cm closer or farther from the operator's body and her eyes (moving the source toward the feet or the head) for the two gamma emissions of the Lu-177 source. The simulations were then rerun, and the resulting eye doses compared. The outcomes showed a variability ranging from about −20 % when the source was shifted 10 cm towards the feet and −10 % when the source was moved 10 cm away from the torso, to + 10 % when the source was drawn 10 cm nearer to the operator and + 20 % when the source was shifted toward the operator's head.

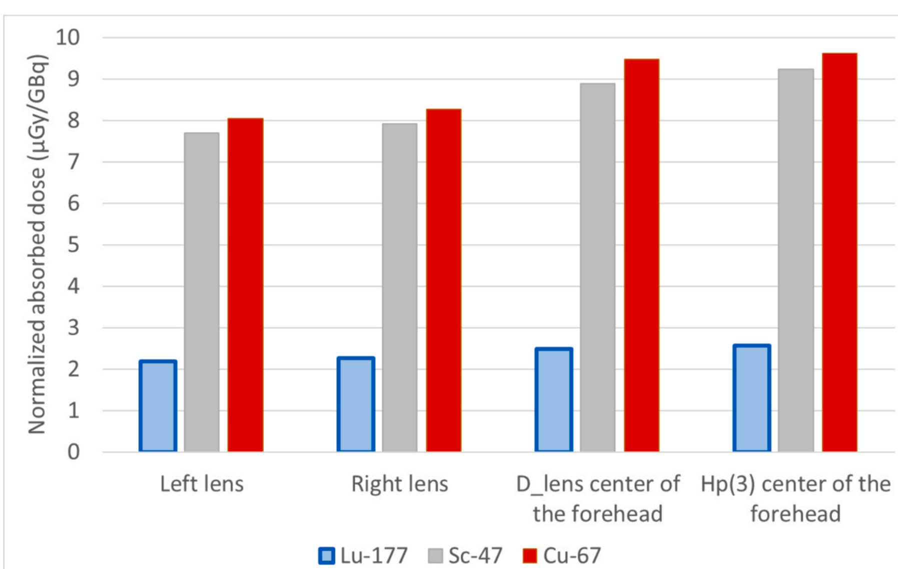

Fig. 4. Simulated normalized absorbed eye dose for a 15 min practice.

5. Conclusions

In the present work, the potential exposure to the thyroid and eyes of operators performing PRRT administrations has been evaluated using Monte Carlo simulations and occupational exposure measurements obtained in clinical practice. Three radionuclides were considered in the simulation model; Lu-177, Sc-47 and Cu-67. The model was validated against Lu-177 occupational exposure measurements obtained in clinical practice. While Lu-177 is currently widely used in PRRT, Sc-47 and Cu-67 are promising radionuclides with potential clinical applications. As expected, the dose to the lens of the eye is mainly due to the gamma radiation and is of the order of 2 μSv/GBq per patient for Lu-177 compounds and, due to the different energies and yields, about 8 μSv/GBq for both Sc-47 and Cu-67. The contribution to dose from the beta components of the decays is three orders of magnitude lower for all radionuclides studied. Similarly, the dose to the thyroid is dominated by the gamma emissions and was found to be a factor of 4 times higher for Sc-47 and Cu-67 than Lu-177. The simulations performed and validated here provide novel information for the clinically emerging radionuclides of interest and may be useful when deciding what radiation protection measures to implement.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Nicolas GP, Morgenstern A, Schottelius M, Fani M. New developments in peptide receptor radionuclide therapy. J Nuclear Med 2019;60(2):169–71.
[2] Basu S, Parghane RV, Chakrabarty S. Peptide receptor radionuclide therapy of neuroendocrine Tumors. Sem Nuclear Med 2020:447–64. https://doi.org/10.1053/j.semnuclmed.2020.05.004.
[3] Lu X, Lu C, Yang Y, Shi Z, Wang H, Yang N, Yang K, Zhang X. Receptor radionuclide therapy in the past 20 years (2000–2019): a bibliometric study. Front Pharmacol 2021;12:1–13.
[4] Santo G, Di Santo G, Virgolini I. Peptide receptor radionuclide therapy of neuroendocrine tumors: agonist, antagonist and alternatives. Sem Nuclear Med 2024;54:557–69. https://doi.org/10.1053/j.semnuclmed.2024.02.002.
[5] O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L. T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W. J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer The New England J Med 385;12 nejm.org 16, 2021 1091 – 1103.
[6] Kratochwil C, et al. Joint EANM/SNMMI procedure guideline for the use of 177Lu-labeled PSMA-targeted radioligand-therapy (177Lu-PSMA-RLT). Eur J Nucl Med Mol Imaging 2023;50:2830–45.
[7] Ahmadzadehfar H, Seifert R, Afshar-Oromieh A, Kratochwill C, Rahbar K. Prostate cancer theranostics with 177Lu-PSMA. Sem Nucl Med 2024;54(4):581–90. https://doi.org/10.1053/j.semnuclmed.2024.02.007.
[8] J Harvey Turner theranostics and precision medicine special feature: review article - an introduction to the clinical practice of theranostics in oncology Br J Radiol 2018; 91: 20180440. doi: 10.1259/bjr.20180440.
[9] Uccelli L, Martini P, Cittanti C, Carnevale A, Missiroli L, Giganti M, Bartolomei M, Boschi A. Therapeutic radiometals: worldwide scientific literature trend analysis (2008–2018). Molecules 2019;24:640. https://doi.org/10.3390/molecules24030640.
[10] Mikolajczak R, van der Meulen N, Lapi ES. Radiometals for imaging and theranostics, current production, and future perspectives. J Label Compd Radiopharm 2019;62:615–34.
[11] Djekidel M. The changing landscape of nuclear medicine and a new era: the "NEW (Nu) CLEAR Medicine": a framework for the future. Front Nucl Med 2023;27. https://doi.org/10.3389/fnume.2023.1213714.
[12] Weber WA, et al. The future of nuclear medicine, molecular imaging, and theranostics. J Nucl Med 2020;61(12 Suppl. 2). https://doi.org/10.2967/jnumed.120.254532.
[13] S.C. Vaz, F. Oliveira, K. Hermann and P. Veit-Heibach Nuclear medicine and molecular imaging advances in 21st century. Br J Radiol 93 pp. 20200095 10.1259/bjr.20200095.
[14] Baudin C, et al. Occupational exposure to ionizing radiation in medical staff: trends during the 2009–2019 period in a multicentric study. Eur Radiol 2023;33:5675–84.
[15] ICRP, 2009. Adult Reference Computational Phantoms. ICRP Publication 110. Ann. ICRP 39 (2).
[16] Therapeutic radiopharmaceuticals labelled with copper-67, rhenium-186 and scandium-47 / International Atomic Energy Agency. International Atomic Energy Agency, 2021. | Series: IAEA TECDOC series, ISSN 1011–4289 ; no. 1945 Vienna (2021).
[17] Mamtimin M, Harmon D, Stariviutiva VN. Sc-47 production from titanium targets using electron linacs. Appl Radiation Isotopes 2015;102:1–4.
[18] De Nardo L, Pupillo G, Mou L, Furlanetto D, Rosato A, Esposito J, Melendez-Alafort L. Preliminary dosimetric analysis of DOTA-folate radiopharmaceutical radiolabelled with 47Sc produced through $^{nat}V(p,x)^{47}Sc$ cyclotron irradiation. Phys Med Biol 2021;66:025003. https://doi.org/10.1088/1361-6560/abc811.
[19] Deilami-nezhad L, Moghaddam-Banaem L. Sadeghi Mahdi Development of bone seeker radiopharmaceuticals by Scandium-47 and estimation of human absorbed dose. Appl Radiat Isot 2017;129:108–16.
[20] Siwowska K, et al. Therapeutic potential of ^{47}Sc in comparison to ^{177}Lu and ^{90}Y. Preclinical Investigations Pharmaceutics 2019;11:424. https://doi.org/10.3390/pharmaceutics11080424.
[21] Ferguson S, Jans HS, Wuest M, Riauka T, Wuest F. Comparison of scandium-44 g with other PET radionuclides in pre-clinical PET phantom imaging. EJNMMI Phys 2019;6:23. https://doi.org/10.1186/s40658-019-0260-0.
[22] Mueller C, Bunka M, Haller S, Koester U, Groehn V, Bernhardt P, van der Meulen N, Tuerler A, Schibli R. Promising prospects for 44Sc-/47Sc-based theragnostics: application of 47Sc for radionuclide tumor therapy in mice. J Nucl Med 2014;55 (10).
[23] Anderson C, Ferdani R. Copper-64 radiopharmaceuticals for PET imaging of cancer: advances in preclinical and clinical research. Cancer Biother Radiopharm 2009;24(4):379–93. https://doi.org/10.1089/cbr.2009.0674.
[24] C. B. Johnbeck, U. Knigge, A. Loft, A. K. Berthelsen, J. Mortensen, P. Oturai, S. W. Langer, D. R. Elema and A. Kjaer Head-to-Head Comparison of 64Cu-DOTATATE and 68Ga-DOTATOC PET/CT: A Prospective Study of 59 Patients with Neuroendocrine, Tumors J Nucl Med 58(3).
[25] Hosseini SF, Aboudzadeh M, Sadeghi M, Teymourlouy AA, Rostampour M. Assessment and estimation of 67Cu production yield via deuteron induced reactions on natZn and 70Zn. Appl Radiation Isotopes 2017;127:137–41. https://doi.org/10.1016/j.apradiso.2017.05.024.
[26] Cullinane C, et al. Peptide receptor radionuclide therapy with 67Cu-CuSarTATE is highly efficacious against a somatostatin-positive neuroendocrine tumor model. J Nucl Med 2020;61(12).
[27] Merrick MJ, Rotsch DA, Tiwari A, Nolen J, Brossard T, Song J, Wadas TJ, Sunderland JJ, Graves SA. Graves Imaging and dosimetric characteristics of 67 Cu. Phys Med Biol 2021;66:035002. https://doi.org/10.1088/1361-6560/abca52.
[28] Keinanen O, Fung K, Brennan JM, Zia N, Harris M, van Dam E, Biggin C, Hedt A, Stoner J, Donnelly PS, Lewis JS, Zeglis BM. Harnessing 64Cu/67Cu for a theranostic approach to pretargeted radioimmunotherapy. PNAS 2020;117(45). www.pnas.org/cgi/doi/10.1073/pnas.2009960117 10.
[29] Chhabra A, Thakur ML. Theragnostic radionuclide pairs for prostate cancer management, can be a budding hot duo. Biomedicines 2022;10:2787. https://doi.org/10.3390/biomedicines10112787.
[30] Cremonesi M, Ferrari M, Paganelli G, Rossi A, Chinol M, Bartolomei M, et al. Tosi Radiation protection in radionuclide therapies with 90Y-conjugates: risks and *safety*. Eur J Nucl Med Mol Imaging 2006;33(11):1322–7.
[31] Sghedoni R, Grassi E, Fioroni F, Asti M, Piccagli V, Versari A, Iori M. Personnel exposure in labelling and administration of 177Lu-DOTA-D-Phe1-Tyr3-octreotide. Nucl Med Commun 2011;32(10):947–53. https://doi.org/10.1097/MNM.0b013e328349fd60.
[32] Behrens R, Dietze G, Zankl M. Dose conversion coefficients for electron exposure of the human eye lens. Phys Med Biol 2009;54:4069–87.
[33] Cross WG, Ing H, Freedman N. A short atlas of beta-ray spectra. Phys Medi Bio 1983;28(11):1251.
[34] Syme AM, Kirkby C, Riauka TA, Fallone BG, McQuarrie SA. Monte Carlo investigation of single cell beta dosimetry for intraperitoneal radionuclide therapy. Phys Med Biol 2004;49:1959–72.
[35] ICRP Publication 60 1990 Recommendations of the International Commission on Radiological Protection.
[36] ICRU Report 95, Operational Quantities for External Radiation Exposure (ICRU 2020).
[37] D. B. Pelowitz (editor) MCNP6 User's Manual. Los Alamos National Laboratory Tech. Rep. LA-CP-13-00634. Los Alamos, NM, USA. May 2013.
[38] T. Sato et al., "Particle and Heavy Ion Transport code System, PHITS, version 2.52", J Nucl Sci Technol 50, 913-923 (2013) PHITS.
[39] Keith T Griffin , Yeon Soo Yeom , Matthew M Mille , Choonik Lee, Jae Won Jung, Nolan E Hertel, Choonsik Lee Comparison of out-of-field normal tissue dose estimates for pencil beam scanning proton therapy: MCNP6, PHITS, and TOPAS Biomed Phys Eng Express. 2022 23;9(1):10.1088/2057-1976.
[40] Solberg TD, DeMarco JJ, Chetty IJ, Mesa AV, Cagnon CH, Li AN, Mather KK, Medin PM, Arellano AR, Smathers JB. A review of radiation dosimetry applications using the MCNP Monte Carlo code. Radiochimica Acta 2001;89(4–5):337–55. ISSN: 0033-8230.

[41] Takuya Furuta, Tatsuhiko Sato Medical application of particle and heavy ion transport code system PHITS Vol.: (0123456789)1 3Radiological Physics and Technology (2021) 14:215–225.
[42] ISO/IEC Guide 98-1:2024 Guide to the expression of uncertainty in measurement.
[43] https://physics.nist.gov/PhysRefData/Star/Text/ESTAR.html (site checked on 29th October 2024).
[44] https://www.nist.gov/pml/x-ray-mass-attenuation-coefficients (last checked on 24 June 2025).
[45] Fioroni F, Ferrari P, Grassi E, Chendi A, Bertolini M, Piccagli V, et al. Iori eye lens dose estimation in peptide receptor radionuclide therapy: monte carlo simulations versus experimental measurements OP-735. Eur J Nucl Med Mol Imaging 2019;46 (Suppl 1):S1–952. https://doi.org/10.1007/s00259-019-04486-2.
[46] Behrens R, Engelhardt J, Figel M, Hupe O, Jordan M, Seifert R. H p (0.07) photon dosemeters for eye lens dosimetry: Calibration on a rod vs. a slab phantom. Radiat Protect Dosimetry 2012;148(2):139–42. https://doi.org/10.1093/rpd/ncr028.
[47] Principi S, Farah J, Ferrari P, Carinou E, Clairand I, Ginjaume M. The influence of operator position, height and body orientation on eye lens dose in interventional radiology and cardiology: Monte Carlo simulations versus realistic clinical measurements. Phys Med 2016;32:1111–7.
[48] Phillipe J, Calais J. Harvey Turner Radiation safety of outpatient 177Lu-octreotate radiopeptide therapy of neuroendocrine tumors. Ann Nucl Med 2014;28:531–9. https://doi.org/10.1007/s12149-014-0843-8.
[49] Riveira-Martin M, Struelens L, Muñoz Iglesias J, Schoonjans W, Tabuenca O, Manuel Nogueiras J, Salvador Gómez FJ, López Medina A. Radiation exposure assessment of nuclear medicine staff administering [177Lu] Lu-DOTA-TATE with active and passive dosimetry. 70 EJNMMI Phys 2023;10. https://doi.org/10.1186/s40658-023-00592-1.
[50] Abuqbeitah M, Demir M, Uslu-Besli L, Yeyin N, Sonmezoglu K. Blood clearance and occupational exposure for 177Lu-DOTATATE compared to 177Lu-PSMA radionuclide therapy. Radiat Environ Biophys 2018;57:55–61. https://doi.org/10.1007/s00411-017-0721-6.
[51] Sulieman A, et al. Occupational and ambient radiation exposures from Lu-177 DOTATATE during targeted therapy. Appl Radiat Isotopes 2020;164. https://doi.org/10.1016/j.apradiso.2020.109240. ISSN 0969-8043.
[52] Kollaard R, et al. Review of extremity dosimetry in nuclear medicine. J Radiol Prot. 2021;41(4). https://doi.org/10.1088/1361-6498/ac31a2. PMID: 34670207.