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Research Paper

Evaluation of Iodine 131 Absorbed Dose in Graves's Disease Therapy: A Gate Geant 4 Monte Carlo Simulation Study in Niamey, Niger

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Abstract

In this study, a Monte Carlo simulation in Gate Geant4 was used to calculate the Iodine-131 absorbed fractions for beta particles with the mean energy of 167 keV and gammas with a mean energy of 397 keV. The radiation sources are uniformly distributed in ellipsoid phantoms made from PMMA material. The simulations for the electrons and gamma sources were done separately in order to shoe the contribution of each type of radiation. Each patient was administered with the same activity and the volume of the ellipsoidal phantom corresponding to the size of his thyroid. The absorbed dose fractions for beta and gamma were thus evaluated for all the 45 patients referred to the Nuclear Medicine departments of the Radioisotopes Institute in Niger and the University hospital of Bab el Oued, Algiers, for Radioiodine therapy of Graves' disease. The mean beta absorbed dose fractions was 5.11 E-05 and 4.99E-06 for gammas rays. The S factor is a factor that indicates the value of the energy absorbed in a target organ when a Radionuclide decays in a source organ. The mean S factor in this study was 1.04E-03 for the absorbed dose fractions β and γ. The mean absorbed dose evaluated using MIRD method was 205.01 Gy while the simulations gave an average absorbed dose of 256.35 Gy using for both methods a target dose of 200 Gy. This approach showed that the Gate code GEANT4 is a suitable tool for dose calculations in internal dosimetry in Nuclear Medicine applications, as well as in radiation protection.

Keywords: Absorbed dose fractions; Gate; GEANT4; Monte Carlo simulation; Graves' disease.

Introduction

Graves' disease is an autoimmune disease characterized by hyper secretion of thyroid hormones (T4 and T3) and the presence of antibodies that activate the Thyroid Stimulating Hormone (TSH) [1].

Radioiodine 131 is most widely used in radiotherapy for hyperthyroidism and for the treatment of differentiated thyroid cancers, due to its appropriate value of half-life and favorable values of its beta- and gamma-ray energies. Although it has been in clinical use for over 50 years, significant controversy persists regarding the types of diseases and the recommended quantities of doses of radioiodine to administer during Iodine 131 therapy [2].

To evaluate the risks and benefits of radiopharmaceuticals used for diagnostic or therapeutic purposes in Nuclear Medicine, precise values of radiation-absorbed dose are necessary. [3-4]

The most popular methodology for dosimetry of internally administered radionuclides is the Medical Internal Radiation Dose (MIRD) schema. This method of dose calculation provides a systematic approach towards combining biological data distribution, clearance and physical properties in order to estimate the internal doses. The standard MIRD schema assumes a uniform deposition and distribution of radiation energy within the target volume.[5] It makes use of S-factor, the mean absorbed dose rate per unit activity. Estimation of absorbed dose fractions for I-131 include both β- and γ- contributions, the total energy deposition per decay of I-131 for various thyroid masses, using ellipsoidal geometry comprising PMMA material. The S-factors are generally tabulated for adult thyroids having standard sizes of body and organs. But for thyroid Grave's disease, patients have a different range of values of thyroid sizes. Previous research [6] suggested a scaling law for penetrating and non-penetrating radiation to incorporate the adjustment in calculations for a size of an organ different from the standard. This scaling law, however, is an over-approximation for ellipsoidal organs [7].

Monte Carlo (MC) simulation is widely recognized as a suitable method to study the Physics of Nuclear Medicine, Radiology, and Radiation Therapy. The concepts of deposited energy and absorbed dose are of particular interest for Radiotherapy and Radiodiagnostic applications involving ionizing radiations [8]. Many MC simulation tools have been developed for imaging and dosimetry [8-10]. Figure 1 represents simulated energy deposition per disintegration of I-131 [9]. At the moment, GATE is the only open-source MC simulation platform supporting the user-friendly simulation of imaging, Radiotherapy and dosimetry in the same environment.[11] Gate is an application based on the Geant4 tool: GeantT4 manages the kernel that simulates the interactions between particles and matter, and Gate provides additional high-level features to facilitate the design of Geant4 based simulations.

Gate is developed by the Open Gate collaboration and is a community-driven initiative, where every user can access the source code and propose new features. Gate is potentially useful for a broad range of simulations, including those where the absorbed dose is the principal observable. As Gate is based on Geant4 applications related to dosimetry, it could be successfully used [11-12].

The aim of this study is to compare the thyroid absorbed doses for iodine 131 using MIRD method with the corresponding predictions made by Gate-Geant4 simulations.

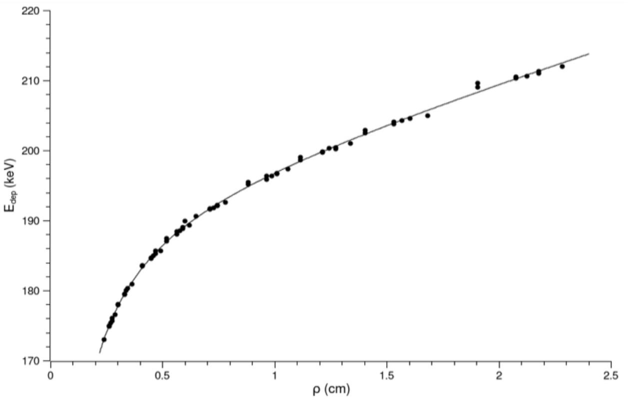

Figure 1. Energy deposition per disintegration for 131 I (Amato et al.)

Material and Methods

This prospective study employed 45 patients data suffering from Graves's disease (GD) clinically and biologically confirmed and reported at management for both the Nuclear Medicine departments of CHU de Bab El Oued, Algiers (35 patients) and Nuclear Medicine department of Radioisotopes Institute of Abdou Moumouni University (10 patients) for Graves' disease Iodine-131 therapy. S-factor values for ^{131}I were calculated in the thyroid of individuals of both genders, using Gate for Geant4 Monte Carlo simulation single lobe ellipsoidal model (Figure 2). A comparison was made of the different S-factors using various ellipsoidal thyroid geometries.

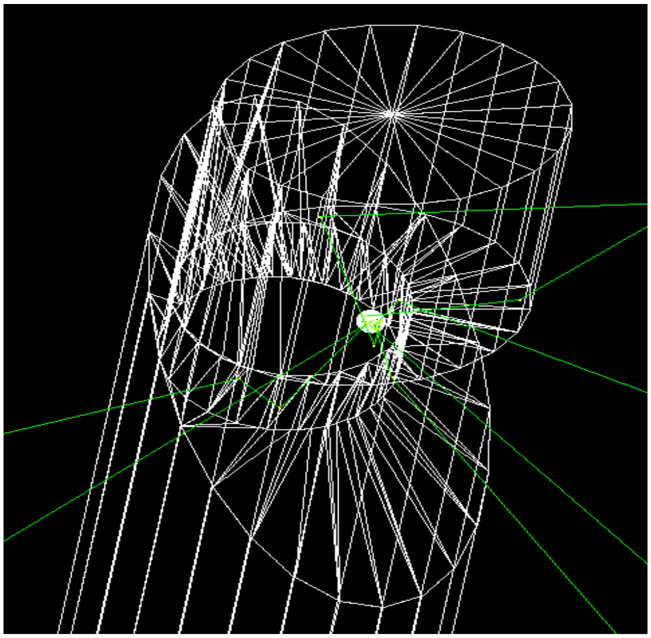

Figure 2. Single lobe ellipsoidal model (Amato et al.)

The correct estimation of S-factors requires an accurate knowledge of the biological distribution of radiopharmaceutical as well as the mass of the target organ. Therefore, the thyroid mass was determined with an ultrasound scanning using a three dimensional (3D) software from Midray DC-60 (Oriental Medical Equipment, China).

The S-factor is a characteristic of the type of radionuclide, target size and target source configuration and is defined as [13-14]:

$$S(r_T \leftarrow r_S) = \left(\frac{1}{M(rT)} \sum_i yiEi\phi(r\mathrm{T} \leftarrow rS),\ Ei\right) \qquad (1)$$

where $M(r_T)$ is the mass of the target (kg); y_i is number of radiations with energy E_i(MeV) emitted per nuclear transition; $\phi(r_T \leftarrow r_s, E_i)$is the fraction of energy emitted by the source and absorbed in the target region. This quantity is usually calculated using the Monte Carlo simulations [14]:

$$\phi(r_T \leftarrow r_s, E_i) = E_{dep} / E_{total}Eq \qquad (2)$$

where E_{dep} is the total energy deposited in the target region per disintegration and E_{total} is the total energy emitted from source region per disintegration. The absorbed fractions from γ-rays and β-particles can be calculated separately using the Monte Carlo simulations and then summed to compute S-factor (mGy $Bq^{-1}S^{-1}$) as follows:

$$S(r_T \leftarrow r_S) = (1.602 \times 10^{-10} / M(r_T)) \sum_i \{yi(\gamma)Ei(\gamma)\Phi\gamma(rT \leftarrow rS, Ei) + yi(\beta)Ei(\beta)\Phi\beta(rT \leftarrow rS, Ei)\} \qquad (3)$$

where the factor 1.602×10^{-10} converts MeV into joules. Using MIRD, it is still not practical to calculate the absorbed dose fractions (and consequently the S-factors) for a diverse range of sizes and shapes of the target volumes especially in the Case of thyroid treatment. However, the Monte Carlo simulations, being capable of handling complex geometries, are well suited to this task [15].

With the proposed formulation, the absorbed dose fractions for electrons and gammas were calculated for all patients with ellipsoidal shape.

The statistical analysis was performed using MicrosoftExcel sheet and analyzed using the software package Statistica 10 (Stat Soft, Tulsa, USA).

Results

MC simulation in Gate Geant4 was applied in order to evaluate the I-131 absorbed dose fractions for beta with mean energy of 167keV, the energy deposition spectrum of beta starting from o keV up to 500 keV for 4.01×10^8 entries. For gamma simulation, we found a mean energy of 397 keV, the energy deposition spectrum of gamma started from 280 keV up to 600 keV for 1.09×10^9 entries.

They were uniformly distributed in ellipsoids made of PMMA as material of thyroid phantom. For each volume, an ellipsoid shape was simulated.

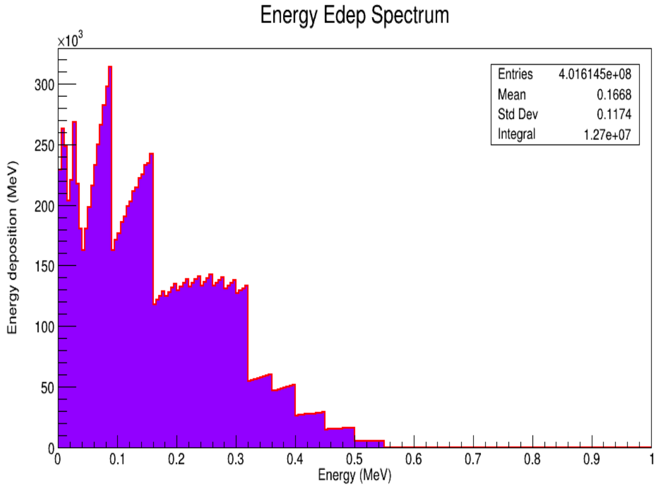

Figure 3. Electrons Energy Edep Spectrum

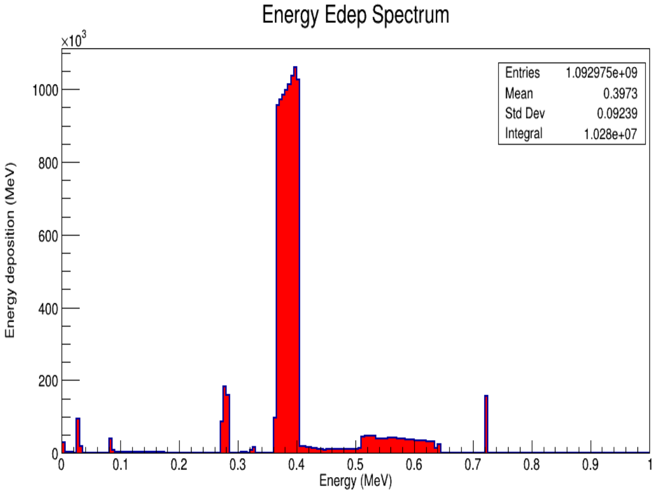

Figure 4. Gamma Energy Edep Spectrum

Electrons and gammas were simulated separately in order to see the contribution of each. The simulation of electrons took about 5 hours and gamma simulation took 7 hours. Each patient was simulated with the same radionuclide activity received and for the same volume of thyroid. For the simulation, single lobe ellipsoidal model with electrons (figure 5) and gammas (figure 6) were used. As a thyroid has two lobes, the absorbed dose fractions was automatically multiply by 2 in order to take into account the hall thyroid.

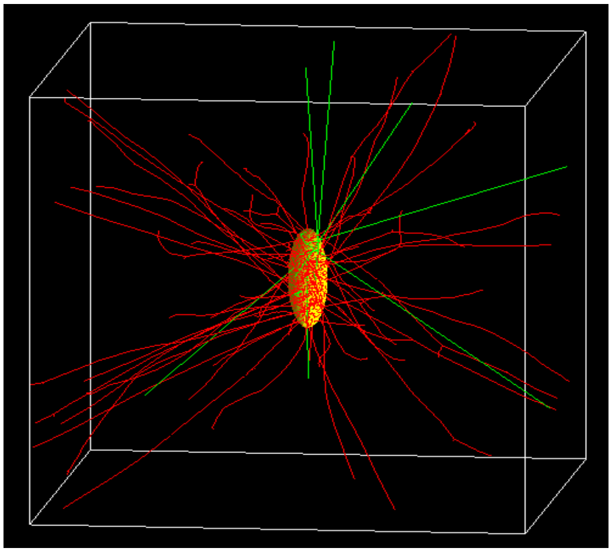

Figure 5. Electrons Geant 4 Gate simulation.

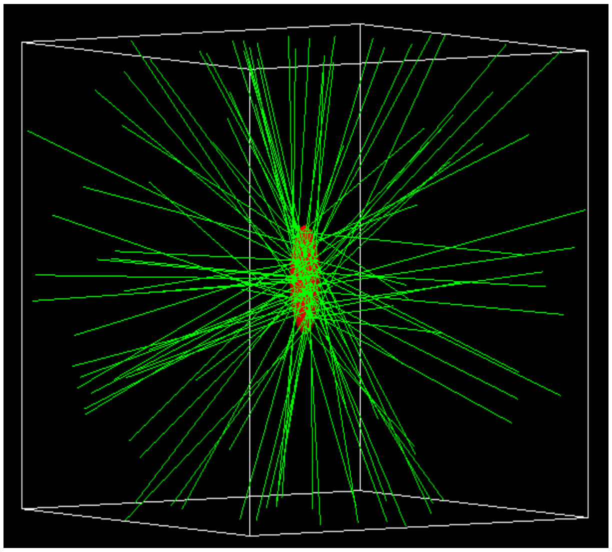

Figure 6. Gammas Geant 4 Gate simulation

Figure 5 showed the simulation box with beta and also a secondary radiation of gamma while figure 6 showed the simulation box with gamma radiation. As we saw, radiation protection measures are essential because 75% of radiation (beta and gamma) does not remain in the thyroid. Table 1 shows the distribution of patients according to the thyroid masses measured by ultrasound scanning. It was found that 66% of patients have a thyroid less than or equal to 25 g.

Table 2 shows the distribution of patients according to the absorbed dose fractions β and γ. It can be seen that γ radiation contributes up to 10% to the absorbed dose.

Table 3 shows the distribution of patients according to the thyroid uptake. The average activity received the thyroid mass after therapy and the reduced percentage of the thyroid parenchyma.

Table 1. Distribution of patients according to the thyroid masses measured by ultrasound scanning.

Thyroid masse (kg)	Number of patients	Percentage (%)
15x10^{-3}	**11**	**24.44**
16x10^{-3}	2	4.76
18x10^{-3}	**8**	**17.77**
19x10^{-3}	3	6.66
21x10^{-3}	1	2.22
23x10^{-3}	2	4.76
24x10^{-3}	2	4.76
25x10^{-3}	1	2.22
29x10^{-3}	3	6.66
31x10^{-3}	1	2.22
32x10^{-3}	1	2.22
33x10^{-3}	2	4.76
36x10^{-3}	1	2.22
37x10^{-3}	3	6.66
40x10^{-3}	1	2.22
41x10^{-3}	1	2.22
44x10^{-3}	1	2.22
53x10^{-3}	1	2.22
Total	45	100.00

Table 2. Distribution of patients according to the absorbed dose fractions β and γ.

Thyroid masse (kg)	ß absorbed fractions (mGy/MBq.s)	ɣ absorbed fractions (mGy/MBq.s)	ɣ contribution (%)
15x10^{-3}	3.74E-05	1.20E-06	5.39
16x10^{-3}	3.47E-05	1.25E-06	18.70
18x10^{-3}	3.80E-05	3.07E-06	9.99
19x10^{-3}	4.20E-05	2.88E-06	6.60
21x10^{-3}	4.97E-05	4.28E-06	8.61
23x10^{-3}	3.97E-05	2.14E-06	5.42
24x10^{-3}	4.55E-05	6.02E-06	14.80
25x10^{-3}	4.56E-05	6.02E-06	13.20
29x10^{-3}	4.67E-05	6.32E-06	13.60
31x10^{-3}	4.96E-05	7.03E-06	14.20
32x10^{-3}	5.10E-05	6.87E-06	13.50
33x10^{-3}	4.78E-05	7.27E-06	15.30
36x10^{-3}	5.97E-05	6.23E-06	10.40
37x10^{-3}	5.93E-05	5.58E-06	9.42
40x10^{-3}	6.57E-05	6.65E-06	10.10
41x10^{-3}	5.96E-05	6.69E-06	11.20
44x10^{-3}	6.84E-05	5.40E-06	7.90
53x10^{-3}	7.96E-05	4.86E-06	6.10
Median 30×10^{-3}	**5.11E-05**	**4.99E-06**	**10.80**

Table shows the distribution of patients according to S-factors, MIRD and Simulated absorbed doses.

Table 5 presents the comparison of the S factors. It is noted that the S factors obtained in this study are 30% lower than those of Ziaur et al. and the ICRP.

Table 3. Distribution of patients according to the thyroid uptake.

Thyroid masse before therapy(kg)	Thyroid uptake (%)	Mean activity Received (MBq)	Thyroid masse after therapy(Kg)	Thyroid volume reduction (%)
15×10^{-3}	37	605	6×10^{-3}	60.00
16×10^{-3}	52	480	5×10^{-3}	68.75
18×10^{-3}	49	578	13×10^{-3}	27.78
19×10^{-3}	54	468	12×10^{-3}	36.81
21×10^{-3}	57	370	13×10^{-3}	38.10
23×10^{-3}	35	592	13×10^{-3}	43.48
24×10^{-3}	48	480	15×10^{-3}	37.50
25×10^{-3}	46	555	13×10^{-3}	48.00
29×10^{-3}	57	629	12×10^{-3}	58.62
31×10^{-3}	63	592	14×10^{-3}	54.84
32×10^{-3}	22	592	17×10^{-3}	46.87
33×10^{-3}	72	629	15×10^{-3}	54.55
36×10^{-3}	48	592	16×10^{-3}	55.56
37×10^{-3}	67	570	19×10^{-3}	48.65
40×10^{-3}	25	666	17×10^{-3}	57.50
41×10^{-3}	49	666	19×10^{-3}	53.66
44×10^{-3}	66	592	19×10^{-3}	56.87
53×10^{-3}	73	592	21×10^{-3}	60.38
30×10^{-3}	51.1	570	14.47×10^{-3}	50.44

Table 4. Distribution of patients according to S-factors, MIRD and Simulated absorbed doses.

Thyroid masse	S factor, absorbed doses for MIRD and simulations		
	Single lobe model (MGy/MBq.s)	MIRD dose (Gy)	Simulation dose (Gy)
15×10^{-3}	1.50E-03	301.46	271.93
16×10^{-3}	1.09E-03	301.46	215.75
18×10^{-3}	1.21E-03	312.66	259.79
19×10^{-3}	9.71E-04	229.9	210.35
21×10^{-3}	8.81E-04	200.74	166.30
23×10^{-3}	9.99E-04	180.06	266.09
24×10^{-3}	9.27E-04	174.41	223.84
25×10^{-3}	1.08E-03	204.12	249.46
29×10^{-3}	1.09E-03	243.96	282.72
31×10^{-3}	1.02E-03	240.47	266.09
32×10^{-3}	1.01E-03	81.35	266.09
33×10^{-3}	9.96E-04	273.18	282.72
36×10^{-3}	1.02E-03	157.77	266.09
37×10^{-3}	9.39E-04	206	256.20
40×10^{-3}	1.14E-03	83.2	299.35
41×10^{-3}	1.03E-03	159.09	299.35
44×10^{-3}	9.34E-04	177.49	266.09
53×10^{-3}	8.91E-04	162.98	266.09
30×10^{-3}	**1.04E-03**	**205.01**	**256.35**

Table 5. Comparison of the S factors.

Adult thyroid	**S factors(mGy/MBq.s)**			**Difference (%)**	
	Our Study	**Ziaur et al.**	**ICRP**	**Our study and Ziaur et al.**	**Our study and ICRP**
	0.00104	0.00156	0.00165	**33**	**37**

Discussion

The treatment of hyperthyroidism and mainly Graves' disease with radioactive I-131 is very effective, safe and simple to implement. The treatment of hyperthyroidism is the most common nuclear medicine therapy procedure in the world. It is performed most of the time on an outpatient basis and however requires the full collaboration of the patient with strict application of radiation protection rules [18-19].The aim of measuring thyroid uptake in iodine-131 therapy for hyperthyroidism and in particular Graves' disease is to optimize the procedure, by better defining the activity to be administered in order to better control the doses of radiation administered to the patient [21].

Many methods have been proposed for determining the activity to be administered to the patient. The most common is the Marinelli method which first requires the knowledge of the thyroid mass and therefore allows a rapid calculation of the effective half-life using the curve passing through at least two points [20].

In order to determine the activity of iodine-131 to be administered, the volume of the thyroid, the thyroid uptake and the effective half-life (T_e) are the main variables required. These parameters also depend on the target dose of radiation to be delivered to the thyroid gland, taking into account the irradiation of other organs [22-23]. The median of thyroid volume was 30 g, which was similar to the study by Nwatsock et al. (2012) [24].

The therapeutic activities determined by personalized dosimetry and administered in this study are comparable to those of Rezgani et al. (2017) [25] who reported an average activity administered from 539 to 740 MBq and of Aschawa et al. (2017) [26] who found moderate activity, from 437 to 540 MBq.

The absorbed dose fractions obtained during the simulations were 5.11E-05 and 4.99E-06 respectively for β and γ radiation with a contribution of 10.80% of γ radiation to the total dose received by the patients. These results are similar to those obtained by Micheal G. Stabin et al. (2005) [27] and Ziaur R. et al. (2014) [5] who obtained respectively 2.24E-05 and 3.2E-05 for the β, 8.39E- 06 and 3.05E-06 for γ.

The second thyroid ultrasound performed on the patients showed that the thyroid parenchyma is reduced by 56% when an average activity of 570 MBq is administered over an average thyroid volume of 30 ml.

In our study, we found an average absorbed dose of 205 Gy by the MIRD method and 256 Gy by Gate Geant4 simulation method, a difference of 20%. We found the S-factors of 1.04 E-05 which differ by 30% on average from those found by Ziaur et al. (2014) [5] and the ICRP (2008) [16] which are respectively 1.56 E-05 and 1.65 E-05 respectively.

This difference may be due to the fact that we used real data from treated patients, unlike the two authors who used anthropomorphic phantoms.

Conclusions

In this work we applied Gate Geant4 for the evaluation of absorbed dose fractions with a single lobe ellipsoid geometry, closer to the thyroid echo structure. The absorbed fractions β and γ from the different simulations allowed us to calculate the S factors and finally, to estimate the dose received by the patients. The dose was then compared with that obtained by the MIRD method.

This study proved the importance of determining the dose for each specific patient when treating Graves' disease. All the methods detailed in this work (measurement of uptake, MIRD or simulation by Gate Geant4) can be used to determine the dose absorbed by the thyroid. Nevertheless, Gate Geant4 remains the best estimation method because it can more accurately consider all particle energies, density, thyroid volume, and dose deposition heterogeneity in volume.

This study concludes that Gate Geant4 is a tool suitable for internal dosimetry, in particular for the treatment of hyperthyroidism in general and Graves' disease specifically.

Abbreviations

IAEA: International Atomic Energy Agency; ICRP: International Commission of Radiological Protection and measurement; CT: Computed Tomography; FOV: Field of View; GEANT4: GEometry and Tracking 4eme generation; GATE: Geant4 Application for Tomography Emission; Gy : Gray; RAI : Radioactive Iodine; IRI: Institut des Radio-Isotopes ; MRI : Magnetic Resonance Imaging; J : joules; KeV : Kilo electronvolts; MBq : Mega Bequerel; MCi : millicurie; MIRD: Medical Internal Radiation Dose; MOBY : Mouse whole Body Phantom; PENELOPE: PENetration and Energy LOss of Positrons and Electrons; PMMA: Polymethylmethacrylate; Sv : Sievert; T3 : Triiodothyronine; T4 : Tetraiodothyronine; FT3 : Free T3; FT4: Free T4; LET: Energy linear Transfer; PET: positrons Emission Tomography; TSH : Thyroid Stimulating Hormone; TSHus: TSH ultrasensitive.

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Author Contributions

All authors contributed to this study. All authors gave their final approval.

Competing Interests

We declare no competing interests.

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