^{90}Y Dosimetry with Monte Carlo Method: GATE Validation with STL Formatted Phantom

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In ^{90}Y treatment, it is important to implement patient-specific dosimetry. The study was aimed at creating an STL-based liver model phantom with multiple tumor mimics to test the GATE program and to perform ^{90}Y dosimetry with the Monte Carlo method. First, the liver model phantom with the outer dimensions of $22 \times 14 \times 8$ cm^3 was made of plexiglass and two cylindrical tumor mimics were placed in it. ^{99m}Tc activities with 62.9 MBq and 7 MBq were placed in both tumor mimics. Thermoluminescent dosimeters were used at 10 positions in the liver model phantom. Next, the same conditions were simulated in GATE and the absorbed doses were determined with DoseActors. After GATE validation, the absorbed doses were calculated for ^{90}Y source of 40.7 MBq. Based on this, the absorbed doses were estimated for the average amount of therapeutic ^{90}Y activity. The average instant absorbed doses in the liver model phantom for ^{99m}Tc activities were found to be between 0.337 ± 0.002 and 0.0059 ± 0.0008 μGy/s via thermoluminescent dosimeters and between 0.367 ± 0.002 and 0.0052 ± 0.0003 μGy/s via GATE. When the ^{99m}Tc results were compared, the mean overlap ratio and R-squared value were 10.68% and 0.9966, respectively. The mean absorbed doses in the first tumor mimic, the second tumor mimic and normal liver parenchymal tissue were 1350.0 ± 7.7, 450.0 ± 4.4 and 3.9 ± 0.2 Gy for 1480 MBq therapeutic ^{90}Y activity. The GATE simulation showed significantly similar dosimetric results with the thermoluminescent dosimeter measurement for a liver dose calculation. As the tumor and liver dose estimation is a key limiting factor in ^{90}Y dosimetry, the practical application of the GATE simulation is an advantage for dose calculations and can improve the dosimetry.

topics: radionuclide dosimetry, Monte Carlo method, GATE, ^{90}Y

1. Introduction

The ^{90}Y microsphere treatment is emerging as a promising treatment modality in the management of patients with liver cancer. In treatment, microspheres are selectively infused into an affected hepatic region by transarterial catheterization. Microspheres that reach the tumor microcirculation use beta emission to destroy the tumor. The half-life of ^{90}Y is 64.2 h and it decays to ^{90}Zr. It emits high energy beta particles (max. 2.27 MeV, average 0.9 MeV) that have an average tissue penetration of 2.5 mm and a maximum penetration of 11 mm [1]. Considering high energy of particles emitted from ^{90}Y, the patient-specific radiation dosimetry is very important to ensure radiation safety. All the dosimetric methods serve to address the same problems, such as determining the amount of activity to be administered to patients, checking the accuracy and reliability of treatment applications and determining the absorbed doses (AD) of irradiated tissues or organs after treatment.

The radiation dosimetry of radiopharmaceuticals used for treatment in nuclear medicine clinics has been described in different ways as the determination of the absorbed dose per injected activity [2] or the calculation of the energy absorbed in tissue as a result of the energetic emission of radioactive atoms [3].

Phantoms with characteristics similar to patients' anatomy are used as the basis for dosimetry studies. The most effective way to model these phantoms is to use simple geometric shapes such as spheres, cubes and cylinders to define patients' anatomy [4]. For simple geometric shapes, it is easy to calculate the absorbed dose analytically but when the geometry becomes more complex, it is more difficult. To solve this problem, the Monte Carlo method is

used which simulates the interaction of radiation with matter. Relevant simulations can be performed with the GATE package [5]. This code is the version of the geometry-tracking transport code GEANT4 [6], customized for application in nuclear medicine.

The aim of this study was to create a liver model phantom (LMP) with multiple tumor mimics (TM) and its virtual representation within GATE. Further, we aimed to test the accuracy of GATE and to perform the true ^{90}Y dosimetry.

2. Material and methods

First, the LMP, designed for use in both the thermoluminescent dosimeter (TLD) and DoseActor-based measurement systems, has been developed primarily for the purposes of having similar characteristics to human liver anatomy and dimensions. It can be filled with water and obtained at an economical cost. A 30-cm diameter semi-anthropomorphic liver phantom (dimensions: 30 cm mediolateral $\times$20 cm anteroposterior $\times$10 cm craniocaudal length) (Quality Assurance in Radiology and Medicine [QRM], Möhrendorf, Germany) with interchangeable liver and spleen inserts was accepted as a sample. This sample was re-designed in AutoCAD. The re-designed phantom named LMP was made of plexiglass and its dimensions were $22 \times 14 \times 8$ cm^3. It included two tumor imitations of inner diameters of 30 mm (TM1) and 16 mm (TM2) and a range of 10 TLD slots, as shown in Fig. 1. TM1 and TM2 were inserted with ^{99m}Tc sources of 62.9 MBq and 7 MBq activities, respectively. A 2.5-fold difference in ^{99m}Tc concentration was generated between TM1 (1.906 MBq/ml) and TM2 (0.777 MBq/ml).

TLDs were used in the absorbed dose measurements in the LMP. Calibration of TLDs and post-irradiation evaluation were performed in

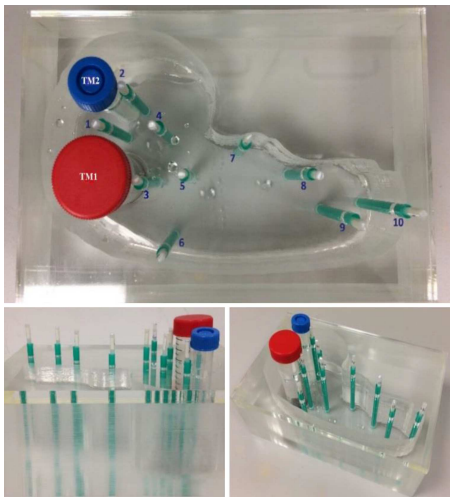

Fig. 1. The liver model phantom with two different tumor mimics and 10 TLD sticks.

Fig. 2. From left to right, (a) PVC, (b) heat shrink tube and (c) polyurethane material of one TLD stick.

the Secondary Standard Dosimetry Laboratory (SSDL). A Harshaw 4500 model reader was used. It was connected to the computer and signals were read out by the WinREMS software. The TLD reader heating process was carried out by hot nitrogen gas. The TLD chips made of lithum fluoride (LiF: Mg, Ti) crystals with dedicated doping were used and their dose range was from 0.01 mGy to 10 Gy. The reader calibration factor (RCF) for the TLD reader and the element correction coefficients (ECCs) of the TLD chips were determined using the standard Cs-137 gamma source in the SSDL according to the WinREMS software manual [7, 8]. TLDs are passive dosimeters with energy dependence. This dependence is very strong, especially in low energies. To eliminate energy dependence, the TLD calibration chips were irradiated with N300 kV reference source conforming to the ISO 4037-3 standard [9]. The calibration chips were read out in the TLD reading system, the calibration correction coefficient was obtained and the TLD system calibration was updated.

Ten TLDs sticks were placed in the areas where dose measurement would be performed in the LMP so as not to shield each other. These sticks have been developed to prevent the TLD chips from contacting with water and to fix the measuring positions. An exemplary TLD stick made of three layers was shown in detail in Fig. 2. The sticks were made of: polyurethane material to prevent contact with liquid, heat shrink tube material for fixing TLD chips and PVC material. The latter, intended for carrying the TLD chips, was of 4 mm radius and 90 mm height. It had three squarish slots of $4 \times 4 \times 2$ mm^3 size each. The total number of 30 TLD chips was placed at 10 positions of the measurement system (see Fig. 1), three per each stick. TLD chips were placed at the height of 30 mm from the base of the PVC material rod and at 2 mm gap between the slots.

Finally, the phantom was filled with water to create a soft tissue environment. With this system, measurements were collected for 11 half-life periods (66 h) since when the activity [MBq] of ^{99m}Tc was considered to be practically zero. To be able to compare the data to the simulation results, the TLD dose values [Gy] were converted to the instant doses [Gy/s] using:

$$\text{Inst. dose} = \frac{\text{TLD dose} \times \text{Activity for 1 s}}{\text{Total activity for 11 half-life}}. \quad (1)$$

In addition, four TLDs were placed in the room to make the background radiation correction. All the TLD measurements were performed at the Çekmece Nuclear Research and Training Center.

In the next step, the GATE 8.1 version was used for simulation. All simulation applications were executed on a computer with macOS Sierra Version 10.12.6, Core i5, 2.7 GHz, 8 GB, 1867 MHz, DDR3 memory and Intel Iris 6100 graphics processor. The preparation of simulation was started for the performed TLD experiment with ^{99m}Tc source. While creating the simulation geometry, the lower left corner of the LMP was accepted as the coordinate center. The TM1 and TM2 coordinates were defined (45, 60, 40) and (45, 100, 40) in mm units. The geometric information (see Fig. 3) including the material densities was encoded and all the electromagnetic processes (such as Rayleigh scattering, photoelectric effect, Compton scattering, radioactive decay) were included. The source was set to the same

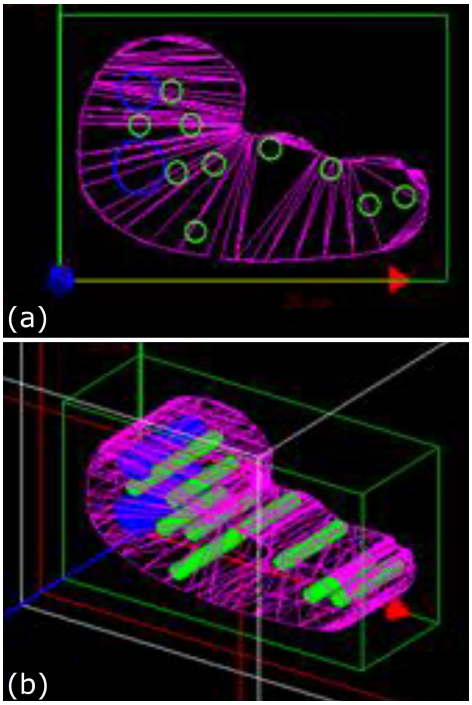

Fig. 3. Geometric information for ^{99m}Tc simulation with the GATE program. Blue, green and magenta indicate tumor mimics, 10 TLD slots and liver model phantom, respectively. (a) xy plane image, (b) $\varphi = 45^\circ$ oblique image.

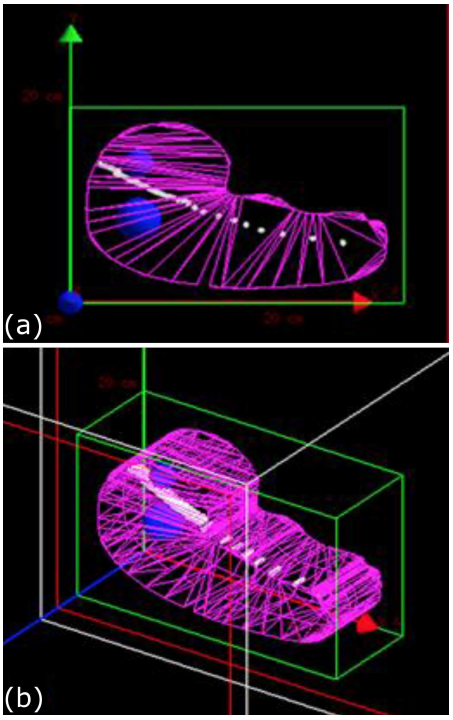

Fig. 4. Geometric design for simulation of ^{90}Y radiation and detection within the GATE code. Blue, white and magenta indicate tumor mimics, 40 TLD slots and liver model phantom, respectively. (a) DoseActors numbered 1–40 from left to right on xy plane image, (b) $\varphi = 45^\circ$ oblique image.

radioactivity as in the experiment. For pulling the random numbers, the Mersenne Twister algorithm was used. In addition, $3 \times 3 \times 3$ mm^3 voxel-sized DoseActors were identified at the locations where TLDs were placed. In this way, the absorbed dose and the stored energy, with their uncertainties, as well as the energy information were taken as an output file in the TXT format with DoseActors command. The simulation performed to calculate the instant doses left by particles during 11 half-life periods was run for a total of 180 h through the Tier-3g system [10] of Istanbul Aydın University. Using ^{99m}Tc radionuclide, the accuracy between the experimental system and the simulation results was tested and the correlation between them was examined.

Finally, to perform the ^{90}Y dosimetry, two sources of ^{90}Y radiation were inserted into TM1 and TM2 areas, with the activities of 37 and 3.7 MBq (total amount of 40.7 MBq), respectively. The physical processes as decay kinetics of ^{90}Y radioactive source affecting the system were defined in GATE. The ion source option was also selected. In addition, DoseActors were placed in 40 different positions by increasing the number of samples in order to obtain more detailed dose distribution, as shown in Fig. 4a and b. The measurement time was chosen as 1 s and the instant dose distribution was found. The simulation was run for 6 h.

3. Results

The background radiation of the room where the LMP was located was determined by four TLD chips. The doses of four TLD chips were found to be between the maximum 43.50 and the minimum 30.60 μGy. The mean background radiation dose was thus obtained to be 39.32 ± 5.09 μGy.

For the 66-h long measurement of irradiation of the LMP by ^{99m}Tc, the values of total dose were obtained and corrected for the background radiation, as shown in Table I. The information on upper, central and lower TLD chips were shown in row 1, 2 and 3, respectively. The mean doses and instant doses, together with uncertainty, were also listed.

The range of instant doses was found to be between 0.337 ± 0.002 μGy/s and 0.006 ± 0.001 μGy/s, respectively. While the high instant dose values were seen at the positions (numbered 1, 2, and 3) close to the tumor imitations, especially near TM1, the doses decreased when moving away from the source. Statistical uncertainty was found to be negligible in the TLD measurements.

For the GATE simulation of the 66-h long irradiation of the LMP with ^{99m}Tc decay products, three DoseActors were placed in each of 10 predetermined points. The mean doses and instant doses, together with uncertainty, were also listed in Table II. The information on upper, central and lower data was shown in row 1, 2 and 3, respectively.

TABLE I

Determination of mean instant dose values (in μGy/s) with standard deviations caused by ^{99m}Tc from the total dose values measured in 10 different positions via TLDs.

Positions	Total dose [μGy]	Total dose adjusted for background radiation [μGy]	Mean dose [μGy]	Mean instant dose [μGy/s]	Std. deviation of mean instant dose [$\pm$ μGy/s]
1	9640	9600.68	9317.34	0.299	0.032
	10200	10160.68			
	8230	8190.68			
2	7420	7380.68	6227.34	0.199	0.041
	6510	6470.68			
	4870	4830.68			
3	10500	10460.68	10494.01	0.337	0.002
	10500	10460.68			
	10600	10560.68			
4	4600	4560.68	4480.68	0.144	0.005
	4620	4580.68			
	4340	4300.68			
5	3320	3280.68	3104.01	0.099	0.007
	3220	3180.68			
	2890	2850.68			
6	2680	2640.68	2627.34	0.084	0.002
	2720	2680.68			
	2600	2560.68			
7	1140	1100.68	1070.68	0.034	0.001
	1110	1070.68			
	1080	1040.68			
8	507	467.68	476.68	0.0153	0.0003
	528	488.68			
	513	473.68			
9	335	295.68	289.34	0.0092	0.0002
	321	281.68			
	330	290.68			
10	209	169.68	186.01	0.006	0.001
	256	216.68			
	211	171.68			

TABLE II

Determination of mean instant dose values (μGy/s) with standard deviations caused by ^{99m}Tc from the total dose values measured in 10 different positions via DoseActors.

Positions	Instant dose [μGy/s]	Mean instant dose [μGy/s]	Std. deviation of mean instant dose [$\pm$ μGy/s]
1	0.326 0.331 0.335	0.331	0.004
2	0.205 0.205 0.198	0.203	0.003
3	0.366 0.365 0.369	0.367	0.002
4	0.172 0.177 0.169	0.173	0.003
5	0.104 0.114 0.104	0.107	0.005
6	0.012 0.133 0.134	0.093	0.069
7	0.048 0.041 0.040	0.042	0.001
8	0.015 0.017 0.015	0.016	0.001
9	0.007 0.009 0.007	0.008	0.001
10	0.0052 0.0048 0.0057	0.0052	0.0003

Mean instant doses at the determined points in the LMP by the simulation system were found to be between 0.367 ± 0.002 and 0.0052 ± 0.0003 μGy/s. The same dose-position relation at the TLD experiment showed in Table I was observed. The high instant dose values were seen at the positions (numbered 1, 2 and 3) close to the tumor imitations and doses decreased at the distant positions from the source.

Statistical uncertainty was found to be negligible in DoseActors mesurements. The mean instant dose values (μGy/s) measured by both the TLD experiment and GATE simulation from the same coordinates in the LMP were shown in Table III, together with the percentage of relative difference (%) for comparison.

When the results of the GATE simulation and TLD experiment were compared, the mean overlap ratio was found to be 10.63% (maximum 19.10% and minimum 1.39%). There was a strong correlation between $r^2 = 0.9966$, between two dose measurement systems.

TABLE III

Comparison of TLD experiment and GATE simulation results with percentage of relative difference.

Positions	Mean instant dose by GATE simulation [μGy/s]	Mean instant dose by TLDs [μGy/s]	Relative difference [%]
1	0.331	0.299	9.53
2	0.203	0.199	1.39
3	0.367	0.337	8.40
4	0.173	0.144	16.80
5	0.107	0.099	7.21
6	0.093	0.084	9.41
7	0.042	0.034	17.80
8	0.016	0.0153	3.77
9	0.008	0.0092	19.10
10	0.0052	0.006	12.90
		Mean overlap ratio [%]:	10.63

Following this comparison step, the simulation was run to obtain doses of irradiation of 1.1 mCi ^{90}Y source. Table IV shows the total doses taken by TM1, TM2 and at subsequent places in the LMP.

The mean total doses caused by ^{90}Y source with the activity of 40.7 MBq in TM1 and TM2 were found to be 37.10 ± 0.21 and 12.40 ± 0.12 Gy. The mean dose value in the volume representing the normal parenchymal tissue in the LMP was 0.1 ± 0.0 Gy (maximum 0.836 ± 0.033 Gy, minimum 0 Gy).

The dose values caused by 40.7 MBq activity of ^{90}Y source were considered as reference. When the simulation was implemented for the mean therapeutic ^{90}Y source with the activity of 40 mCi (1480 MBq), the absorbed doses were found to be 1350.0 ± 7.7 Gy in TM1, 450.0 ± 4.4 Gy in TM2 and 3.97 ± 0.24 Gy in normal liver parenchymal tissue on average (maximum 30.4 ± 1.2 Gy, minimum 0 Gy).

4. Discussion

There are a lot of paid (MIRDOSE, OLINDA/EXM, etc.) and free simulation programs (SIMIND, Geant4, etc.) that do dosimetry using or not using the MC method. When selecting the appropriate simulation program, the nature of the study, the energy range of the radiation to be used in the study and the knowledge of the physicist who will actively use the program are taken into consideration. Recently, the GATE simulation code has gained popularity. It offers a wide range of features to the user, requiring the basic knowledge of C++ language. It is an open source package program published in 2004 in cooperation with the international OpenGATE collaboration for use in nuclear medicine imaging and radionuclide dosimetry [6]. In GATE, phantoms prepared in different formats (filename extension .stl, etc.) or images containing the anatomical information of patients can be used as geometry. The required material can be selected from the items

TABLE IV

Total dose values in TM1, TM2 and normal liver parenchyma in the LMP with uncertainty with GATE simulation.

DoseActor No.	Total Doses [Gy]	Uncertainty	DoseActor No.	Total Doses [Gy]	Uncertainty
1[a]	37.10	0.21	21	0.020	0.004
2[b]	12.40	0.12	22	0.015	0.003
3	0.0003	0.0002	23	0.015	0.004
4	0.0004	0.0001	24	0.003	0.009
5	0.0011	0.0003	25	0.005	0.001
6	0.002	0.001	26	0.002	0.001
7	0.055	0.008	27	0.003	0.001
8	0.276	0.019	28	0.002	0.001
9	0.016	0.004	29	0.0013	0.0005
10	0.104	0.011	30	0.0019	0.0005
11	0.296	0.019	31	0.0009	0.0003
12	0.554	0.026	32	0.0012	0.0005
13	0.798	0.032	33	0.0008	0.0003
14	0.836	0.033	34	0.0006	0.0003
15	0.607	0.028	35	0.0012	0.0009
16	0.32	0.02	36	0.0004	0.0002
17	0.15	0.01	37	0	0
18	0.033	0.006	38	0.0001	0.000
19	0.012	0.003	39	0	0
20	0.015	0.004	40	0	0

[a]shows total dose in TM1, [b]shows total dose in TM2.

defined in the library or added to the library by the user. Given these advantages, GATE has become a widely used modeling platform in nuclear medicine clinics [11] and was preferred to be used in this study.

The LPM used in our study was created by utilizing the semi-anthromorphic phantom. The use of a semi-anthromorphic phantom has been reported in the literature, with imaging studies [12–14]. In our study, it was made smaller at a scale of 1:2.5 to shorten the simulation time and reduce the production cost. It was re-designed and produced in AutoCAD with the size of $22 \times 14 \times 8$ cm^3. Additionally, it contained two tumor imitations with different diameters. In this way, the LMP was easily used in both the TLD and GATE measurement systems.

In order to test the accuracy of the GATE program and the MC method in the study, ^{99m}Tc recommended by [14] was selected for comparison between the TLD experiment and GATE simulation because it is a short half-life radiopharmaceutical. In the TLD experiment, doses in the LMP were found between maximum 0.337 ± 0.002 μGy/s and 0.006 ± 0.001 μGy/s. In the GATE simulation, doses in the LMP were found between maximum 0.367 ± 0.002 μGy/s and minimum 0.0052 ± 0.0003 μGy/s. The dose results of the TLD experiment and the GATE simulation were highly correlated ($r^2 = 0.9966$). When the dose values of the TLD experiment and the GATE simulation were compared, the relative differences at positions 4, 7, 9 and 10 were found to be high, equalling 16.80%, 17.80%, 19.10% and 12.90%, respectively. This is thought to be due to the fact that DoseActors are not placed in correct TLD coordinates in the GATE simulation. In the study, the average relative difference for a total of 10 different locations was found to be 10.63%. In a similar study which was recommended by [15], the rate was found to be 9.70% and the rate reported by [16] was observed to be 19.00%. Therefore, our ratio was found to be in line with uncertainties found in these analyses. In both measurement systems, it was observed that the dose values absorbed in the LMP decreased as we moved away from radioactive sources.

GATE performs the simulation in accordance with all the information defined. The activity of ^{99m}Tc used in the TLD experiment was measured with a dose calibrator and 15 min passed before being placed in the LMP. It is known that the amount of activity decreases depending on this time. Therefore, the GATE results are thought to be higher than the TLD experiment results.

After testing the accuracy of the two measurement system results, the ^{90}Y dosimetry was performed in GATE for the activity of 1.1 mCi (40.7 MBq) ^{90}Y. The mean total doses obtained by simulation in TM1, TM2 and the volume

representing the normal parenchymal tissue in the LMP were 37.10 ± 0.21, 12.40 ± 0.12 Gy and 0.1 ± 0.0 Gy (maximum 0.836 ± 0.033 Gy, minimum 0 Gy), respectively. Our results were found to be consistent with the study of [18] where it was reported that a normal liver parenchymal tissue dose should be between 0.07–9.95 Gy and tumor dose should be between 4–49.48 Gy for the same amount of ^{90}Y activity. Additionally, tumor doses were found to be higher and a mean dose of normal liver parenchymal tissue lower according to the study of [19] where it was reported that a dose for normal liver parenchymal tissue should be 1.42 Gy and for tumor should be between 4 and 6.11 Gy.

The above-mentioned results for 1.1 mCi activity of ^{90}Y case were considered as reference. When the simulation was implemented for the mean therapeutic ^{90}Y activity of 40 mCi (1480 MBq), the absorbed doses obtained from GATE were compared with studies which were reported by [20–22]. In [20], it was reported that the absorbed dose for normal liver tissue should be below 40 Gy and tumor dose should be in the local band range of 100–600 Gy. Further, in [21], it was reported that the absorbed dose for normal liver tissue should be in the range of 36–54 Gy. In [22], in turn, it was reported that a tumor dose should be within the 100–3000 Gy local band range. According to our results, the dose values in TM1 and TM2 were found to be just higher than in [20]. These data were found to be consistent with other studies.

5. Conclusion

In the GATE simulation, a phantom can be made using known geometric shapes. Phantoms prepared in different formats (stl extension, etc.) can be implemented in the simulation and all the necessary tissue and radiopharmaceutical information is available in the library of the program. Thanks to these advantages, GATE is very suitable for use in internal radionuclide dosimetry and gives consistent results. Additionally, instead of standard anatomical phantoms with a license fee, such as XCAT and NCAT, phantoms can be easily created via AutoCAD and transported to GATE.

In the study, it was primarily tested whether the GATE program was working correctly for dosimetry calculations. When the TLD and DoseActor results were compared, it was observed that in the GATE simulation realistic results were obtained. We provided the data of the radiation dose into the LMP for ^{90}Y source. The absorbed doses in TM1 and TM2 caused by total activity of 1.1 mCi were found to be low and the unwanted radiation to the other region in the LMP was very low. According to these results, a safe radiation dosimetry was provided. The results of 1.1 mCi ^{90}Y dosimetry calculated in the study can be adapted to different amounts of therapeutic activity in the clinic.

As tumor and liver dose estimation is a key limiting factor in ^{90}Y dosimetry, the practical application of the GATE simulation is an advantage for dose calculations and can improve the dosimetry.

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