

# A dose point kernel database using GATE Monte Carlo simulation toolkit for nuclear medicine applications: Comparison with other Monte Carlo codes

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**Purpose:** GATE is a Monte Carlo simulation toolkit based on the Geant4 package, widely used for many medical physics applications, including SPECT and PET image simulation and more recently CT image simulation and patient dosimetry. The purpose of the current study was to calculate dose point kernels (DPKs) using GATE, compare them against reference data, and finally produce a complete dataset of the total DPKs for the most commonly used radionuclides in nuclear medicine.

**Methods:** Patient-specific absorbed dose calculations can be carried out using Monte Carlo simulations. The latest version of GATE extends its applications to Radiotherapy and Dosimetry. Comparison of the proposed method for the generation of DPKs was performed for (a) monoenergetic electron sources, with energies ranging from 10 keV to 10 MeV, (b) beta emitting isotopes, e.g., <sup>177</sup>Lu, <sup>90</sup>Y, and <sup>32</sup>P, and (c) gamma emitting isotopes, e.g., <sup>111</sup>In, <sup>131</sup>I, <sup>125</sup>I, and <sup>99m</sup>Tc. Point isotropic sources were simulated at the center of a sphere phantom, and the absorbed dose was stored in concentric spherical shells around the source. Evaluation was performed with already published studies for different Monte Carlo codes namely MCNP, EGS, FLUKA, ETRAN, GEPTS, and PENELOPE. A complete dataset of total DPKs was generated for water (equivalent to soft tissue), bone, and lung. This dataset takes into account all the major components of radiation interactions for the selected isotopes, including the absorbed dose from emitted electrons, photons, and all secondary particles generated from the electromagnetic interactions.

**Results:** GATE comparison provided reliable results in all cases (monoenergetic electrons, beta emitting isotopes, and photon emitting isotopes). The observed differences between GATE and other codes are less than 10% and comparable to the discrepancies observed among other packages. The produced DPKs are in very good agreement with the already published data, which allowed us to produce a unique DPKs dataset using GATE. The dataset contains the total DPKs for <sup>67</sup>Ga, <sup>68</sup>Ga, <sup>90</sup>Y, <sup>99m</sup>Tc, <sup>111</sup>In, <sup>123</sup>I, <sup>124</sup>I, <sup>125</sup>I, <sup>131</sup>I, <sup>153</sup>Sm, <sup>177</sup>Lu, <sup>186</sup>Re, and <sup>188</sup>Re generated in water, bone, and lung.

**Conclusions:** In this study, the authors have checked GATE's reliability for absorbed dose calculation when transporting different kind of particles, which indicates its robustness for dosimetry applications. A novel dataset of DPKs is provided, which can be applied in patient-specific dosimetry using analytical point kernel convolution algorithms. © 2012 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4737096>]

Key words: dose point kernels, GATE, Monte Carlo simulations, dosimetry, radioimmunotherapy

## I. INTRODUCTION

Radionuclides are widely used for both therapeutic and diagnostic applications in nuclear medicine, though, accurate patient-specific dosimetry is still not routinely performed in clinical practice.<sup>1</sup>

Simulation of radiation transport across any medium is possible using several Monte Carlo codes and provides accurate dose estimation, in the form of voxelized dose maps (voxel-by-voxel). Although computational platforms are becoming more powerful, absorbed dose calculations based on

Monte Carlo simulations that use patient-specific characteristics are still time consuming, especially when attempting to assign absorbed dose at the voxel level for reporting of dose-volume histograms. Despite the continuous hardware and software improvements, the application of personalized Monte Carlo dosimetry in clinical practice will require time and analytical, fast approaches are still more attractive. One feasible approach is the use of dose point kernels (DPKs), which give the absorbed dose deposited at a certain distance from a point source, assuming a homogeneous transport medium. At the moment DPKs based algorithms assume

that human body is equivalent to water, without taking into account tissue variations. The combination of DPKs with patient CT data can provide a fast dose calculation, which takes into account patient specific anatomic information by using a proper, real time, algorithm as the authors have already proposed.<sup>2</sup> The calculation of DPKs for all isotopes and several tissues is required, in order to fully evaluate the proposed method against full Monte Carlo simulations, as well as optimize dose calculation algorithm. Finally, DPKs represent an interesting and quick way to benchmark the new versions of Monte Carlo codes.

For many years the calculation of the absorbed dose as a function of the distance from point or extended photon and/or electron emitting sources has been facilitated by the formula of Loevinger *et al.*<sup>3</sup> and the point kernels of Berger.<sup>4</sup> The point kernels described by Berger had the drawback of assuming homogeneous transport media. The concept of the scaled electron point kernel was firstly introduced by Berger in 1973.<sup>5</sup> The kernels as they were defined in Seltzer's work in 1991 have been widely used until now.<sup>6</sup> Many Monte Carlo codes have been used in order to produce accurate electron DPKs. To this end, MCNP, EGS, GEANT4, and ETRAN are considered as reference codes.<sup>7</sup> More recently, PENELOPE and FLUKA have given results that show great agreement with previously published data.<sup>8</sup> Older MC codes like SMOOPY,<sup>9</sup> SANDYL,<sup>10</sup> and GEPTS (Ref. 11) have been previously used to calculate the beta emitting DPKs.

As it was proposed by Furchang *et al.* Monte Carlo techniques have also been used for the calculation of the photon contribution for the most important radionuclides in nuclear medicine, as the electron component of the isotopes dominates self-organ absorbed dose.<sup>12</sup> Nevertheless, the absorbed dose to adjacent organs includes a significant photon contribution, which should be taken into account in patient specialized dosimetry. However, special attention should be paid for low energy emitting particles, where most of the codes show the largest discrepancies among them.<sup>13</sup> Beta and photon dose kernels have already been calculated, under the assumption that the human body is equivalent to water medium.<sup>5-7,9,10,12-16</sup> However, this assumption is insufficient for patient personalized dosimetry and DPKs should be also calculated for other materials existing in the human body. For those reasons, we propose to extend the existing DPKs dataset including a wide range of isotopes and tissue materials.

GATE is a well validated Monte Carlo simulation toolkit for SPECT, PET, CT and recently Radiotherapy (RT) applications, based on the Geant4 core,<sup>17</sup> whose applications include high energy, nuclear and accelerator physics, as well as studies in medical and space science.<sup>18,19</sup> An older version of GATE based on Geant4 4.8.1 was validated by Ferrer *et al.*<sup>20</sup> by comparison of ETRAN and MCNPX codes. GATE v6.0, which makes use of the Geant4.9.2 Electromagnetic Physics Package, has already been validated for electron transport, generating electron DPKs and pencil beam kernels for an energy range between 15 keV and 20 MeV by Maigne *et al.*<sup>13</sup> This release of GATE introduces a large number of modifications to the electron transport algorithms.<sup>21-23</sup> The more recent release of Geant4 (4.9.4) has introduced a number of

modifications to the electron transport algorithms, which may lead to differentiations in the production of DPKs. In particular, the electron multiple scattering algorithms were improved in the latest release of Geant4, and are expected to provide more accurate results.<sup>19</sup>

The latest version of GATE v6.1 which is used in this study and is based on the Geant4 4.9.4.p02 implements these modifications in the electron transport algorithms in comparison with the older versions.<sup>20,24</sup> Also the default multiple scattering model has changed in Geant4 4.9.4, to the G4UrbanMscModel93. New updated versions of the data sets (G4RadioactiveDecay.3.3 and G4PhotonEvaporation.2.1) are also used in this version of Geant4.<sup>25</sup> Thus, a complete comparison of the DPKs has done (including photon and beta emitting sources), before producing the new total DPKs taking into account the whole spectrum of each isotope. Due to the changes of the physics algorithms of Geant4 4.9.2-4.9.4 we include also a comparison of the monoenergetic electron DPKs with Maigne *et al.* study.<sup>13</sup> By this we standardize the method we used for the production of the DPKs as also we include a further comparison with the most recently published electron DPKs of FLUKA code.<sup>8</sup>

In the current study an extensive validation of GATE was carried out for DPKs calculation for different particles and in different media. Specifically, monoenergetic electron DPKs were generated for energies ranging from 15 keV up to 10 MeV in water and were compared to already published literature.<sup>7,8,10,11,13,14</sup> In addition, electron DPKs were generated for bone using 10 keV and 1 MeV monoenergetic electron sources. Beta DPKs were calculated for <sup>177</sup>Lu and <sup>90</sup>Y beta spectra, both in water and bone, as well as for <sup>32</sup>P beta spectrum only in water medium, which were also compared against reference data.<sup>8,9,14</sup> Finally, photon DPKs were calculated into water medium taking into account the gamma emitting contribution of <sup>99m</sup>Tc, <sup>111</sup>In, <sup>131</sup>I, and <sup>125</sup>I isotopes and were also compared with published results.<sup>12</sup> The end goal of this study was to provide a complete dataset for the most common radionuclides used in nuclear medicine. This dataset includes the total DPKs for <sup>67</sup>Ga, <sup>68</sup>Ga, <sup>90</sup>Y, <sup>99m</sup>Tc, <sup>111</sup>In, <sup>123</sup>I, <sup>124</sup>I, <sup>125</sup>I, <sup>131</sup>I, <sup>153</sup>Sm, <sup>177</sup>Lu, <sup>186</sup>Re, and <sup>188</sup>Re generated in water, bone and lung. With the term total DPKs we mean that the whole isotope spectrum is simulated, considering all possible interaction mechanisms. The presented database enlarges all previously published DPK datasets. Finally, a comparison of both total DPKs in water and soft tissue, available in GATE, was performed. The entire dataset of GATE total DPKs is given as supplementary material,<sup>37</sup> in order to be reproducible and easily comparable to future Monte Carlo dosimetric studies, as well as be used in kernel based convolution algorithms.

## II. MATERIALS AND METHODS

### II.A. GATE Monte Carlo toolkit

This study is based on the latest version of GATE (version v6.1), which has been extended for radiotherapy and dosimetry applications and includes new tools called "actors".<sup>26</sup> This version makes use of the Geant4.9.4.p02.<sup>18,27</sup> GATE provides

a wide range of sources that the user can easily handle, even by simulating all the emitting particles of each isotope using the Geant4 “ion” source, or by generating a monoenergetic electron or gamma source and beta or gamma spectrum sources. The model used for simulating physical processes is the “Standard” model of Geant4.9.4,<sup>27</sup> GATE’s default model, which describes electron and photon interactions at energies ranging from 1 keV to 100 TeV. The physical processes that were included in the performed simulations are: Photoelectric effect, Rayleigh and Compton scattering, Bremsstrahlung, GammaConversion, PositronAnnihilation, ElectronIonisation, and eMultipleScattering. The Rayleigh process was simulated using the Penelope model, which is the only choice in the current release of Geant4. In all performed simulations the following parameters were set: EMin = 0.1 keV, EMax = 10 GeV, DEDXBinning = 220, and LambdaBinning = 220 as it is proposed by the GATE collaboration. EMin and EMax, set the kinetic energy range for the physical processes of Geant4, while the DEDXBinning sets the number of the bins for the mean energy loss on a given step in Geant4 physics and the LambdaBinning sets the number of the bins for the Lambda tables.

## II.B. Dose point kernel calculation

Electron, photon, and ion (for the isotopes) DPKs were calculated in different media (water, bone, lung, and soft tissue). In all simulations a homogenous spherical phantom was used, with a point source located at the center of the sphere, emitting isotropically. The size of the simulated sphere differs according to the kind of the simulated particles (details are given in each section), as the photons deposit their energy at distances further away from the point source compared to the electrons. To calculate the DPKs a “tissue” sphere was used in an “air” environment and a dose actor was attached to it. The “dose actor” tool provided in GATE was used to tally the absorbed dose in a 3D matrix, where the dose was directly deposited in Gy units per particle.<sup>28</sup> The 3D matrix corresponds to the dose map, and it is divided by scoring voxels. Adding the voxels that are in same distance away from the source, concentric scoring shells around the isotropic point source are defined (voxelized shells). The thicknesses of these shells are equal to the voxel size of the 3D dose matrix in each distance as it is shown in Fig. 1. The “dosel” has been defined<sup>28</sup> as the scoring voxel of the volume.

## II.C. Monoenergetic electron ( $e^-$ ) DPKs

Water DPKs were produced for 15 keV, 50 keV, 100 keV, 500 keV, 1 MeV, 2 MeV, and 10 MeV electron sources. For comparing GATE toolkit with other MC codes, DPKs of 10 MeV electron source were also calculated, even though this energy goes far beyond the energy range seen in Nuclear medicine applications. For bone, DPKs were produced for 10 keV and 1 MeV electron sources. The size of the sphere for each simulation was calculated based on the method proposed by Maigne *et al.*<sup>13</sup> The radius of the sphere where the dose is deposited is equal to  $24 \times 0.05 \times R_{\text{CSDA}}$  (Ref. 13)

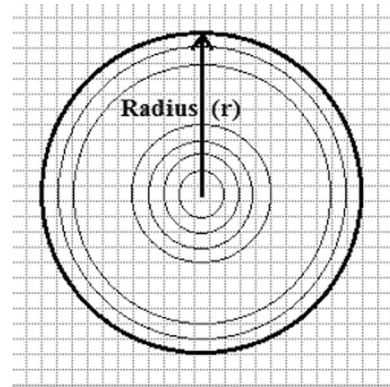


FIG. 1. Schematic of the concentric scoring spherical shells (2D view).

where  $R_{\text{CSDA}}$  is the continuous slowing down approximation range of electrons. Following this approach, we designed the spheres for each energy electron source and tested them with the visualization tools that GATE provides, to have spheres that would include all generated particles. This resulted in spheres which are slightly bigger than those of the reference study, which ensure that they include the entire absorbed dose. To determine the “electronStepLimiter” parameter, we run preliminary simulations from which we concluded that the electronStepLimiter should be equal to 100–120 times smaller than the size of the sphere. In this study the electronStepLimiter was chosen so as to provide good agreement with the results of other MC codes. For low energy electrons we set the electronStepLimiter almost  $\sim 5$  times smaller than the CSDA for 15 keV electrons and  $\sim 7$  times smaller than the CSDA for the 50 keV electrons. For higher energies we did not observe differences when the electronStepLimiter is  $\sim 9$  times smaller than the CSDA. The number of the shells follows from the sphere size by defining the size of the dosels equal to the electronStepLimiter in the dose actor, in order to have at least one interaction in each dosel.<sup>7</sup> Thus, the radius of the sphere that was used for each simulation can be calculated by multiplying the number of shells with the size of the dosel. The number of the shells was not the same in each simulation, since the magnitude of the radius varies from  $\mu\text{m}$  to mm. Defining a dosel size of a few micrometers can result in differentiations in the number of the voxels in the calculated dose map. In this case, we suppose that for 15 keV 60–70 shells with the used radius will not alter the results, for 50 keV 80–90 shells are required and for the higher electron energies 100–120 will also give robust results. The parameters that were set for the monoenergetic electron DPKs are shown in Table I for water and in Table II for bone.

This is an empirical method and further investigation of the electronstepLimiter needs to be done, but goes beyond the aim of the current study. On one hand, the electron step limit should be small enough, so as to simulate more accurately the nonlinear electron track. On the other hand, small electron step significantly increases the computational cost of the simulation.

GATE provides the option to choose, in which level of the electron step, the energy will be deposited, by setting the

TABLE I. Parameters for monoenergetic e<sup>-</sup> DPKs in water.

e <sup>-</sup> energy (MeV)	CSDA (g/cm <sup>2</sup> )	Number of shells	Dosel size—electronStepLimiter (mm)
0.015	$5.147 \times 10^{-4}$	62	$1.123 \times 10^{-4}$
0.05	$4.320 \times 10^{-3}$	86	$6.227 \times 10^{-4}$
0.1	$1.432 \times 10^{-2}$	110	$1.576 \times 10^{-3}$
0.5	$1.766 \times 10^{-1}$	116	$1.909 \times 10^{-2}$
1.0	$4.360 \times 10^{-1}$	114	$4.722 \times 10^{-2}$
2.0	$9.875 \times 10^{-1}$	112	$1.058 \times 10^{-1}$
10.0	4.975	114	$5.377 \times 10^{-1}$

“stepHitType” parameter. By default the “PostStep” parameter is chosen, which means that the energy is deposited at the end of an electron step. In this study, the “random” parameter was set for the stepHitType.<sup>13</sup> With the random value, the stored information will be randomly distributed from the beginning of the electron step to its end.<sup>29</sup> The DPKs are presented using dimensionless axes, as it was suggested by Cross *et al.*<sup>10</sup> The y axis represents the scaled absorbed dose, defined as

$$J(r/R_{\text{CSDA}}) = 4\pi r^2 D(r, E) R_{\text{CSDA}}/E, \quad (1)$$

where  $r$  is the radial distance from the center of the sphere,  $R_{\text{CSDA}}$  is the continuous slowing down approximation range of electrons with initial energy  $E$ , and the  $D(r, E)$  is the absorbed dose per source particle at a certain distance  $r$ .  $R_{\text{CSDA}}$  values were taken by the National Institute of Standards and Technology database.<sup>30,31</sup> The x axis of the calculated DPKs represents the dimensionless scaled distance defined as

$$\text{Scaled distance} = r/R_{\text{CSDA}}. \quad (2)$$

The number of the particles simulated for the electron DPKs is equal to  $2 \times 10^7$ , while the associated statistical uncertainty is lower than 2.5%, 4.3%, 11.1%, and 39.7% for distances  $r/R_{\text{CSDA}} < 0.2, 0.4, 0.8,$  and 1.0, respectively, whereas in the border of the sphere the uncertainty reaches the 100%.

The results were compared to published kernels calculated by different Monte Carlo codes.<sup>7,8,10,11,14</sup> The monoenergetic electron DPKs were also compared to kernels recently produced by Botta *et al.*<sup>8</sup> using the FLUKA code for bone (bone-ICRU) medium, as this was defined in the NIST database.<sup>32</sup>

#### II.D. Beta isotope (b<sup>-</sup>) DPKs

For the beta DPKs the simulated sources were “nonmonoenergetic” electron point sources, emitting isotropically.

TABLE III. Parameters for beta emitting isotopes DPKs.

Isotope	$X_{90}$ (mm)		Average energy (keV)	Number of shells	Dosel size—electronStepLimiter (mm)	
	Water	Bone			Water	Bone
<sup>90</sup> Y	5.40	2.96	935.3	113	$1.106 \times 10^{-1}$	$6.195 \times 10^{-2}$
<sup>177</sup> Lu	0.62	0.34	133.5	113	$1.504 \times 10^{-2}$	$8.850 \times 10^{-3}$
<sup>32</sup> P	3.66	...	696.3	113	$0.690 \times 10^{-1}$	...

TABLE II. Parameters for monoenergetic e-DPKs in bone.

e <sup>-</sup> energy (MeV)	CSDA (g/cm <sup>2</sup> )	Number of shells	Dosel size—electronStepLimiter (mm)
0.010	$2.761 \times 10^{-4}$	101	$1.891 \times 10^{-5}$
1.0	$4.711 \times 10^{-1}$	111	$2.521 \times 10^{-2}$

For each of the beta emitting isotopes, the beta spectrum was considered, by using the “histogram” type of Geant4 for the emission source. The beta spectrum data that were inserted in GATE were taken from the LBNL database.<sup>33</sup>

GATE v6.1 validation was performed for <sup>90</sup>Y and <sup>177</sup>Lu both in water and bone, while the <sup>32</sup>P DPK was produced only in water to be compared with already published results.<sup>8,9,14</sup> The absorbed dose distribution is presented in scaled DPKs similar to monoenergetic electron DPKs. The scaled absorbed dose in this case is defined as

$$J(r/X_{90}) = 4\pi r^2 D(r, E) X_{90}/E. \quad (3)$$

$X_{90}$  corresponds to the radial distance, where the 90% of the dose is absorbed. In this case  $E$  is the average energy over the beta spectrum that was inserted in GATE. The results are reported showing the  $J(r/X_{90})$  as a function of  $r/X_{90}$ .  $X_{90}$  values were derived from the study of Botta *et al.*<sup>8</sup> for isotopes <sup>177</sup>Lu and <sup>90</sup>Y and from Mainegra *et al.*<sup>14</sup> study for <sup>32</sup>P.

These simulations were carried out with the same procedure as the monoenergetic electron DPKs. The average energy of each isotope spectrum is given in Table III, which is in the range of 0.1–1.0 MeV. As described in Sec. II.C, 100–120 spherical shells should be defined (as the  $R_{\text{CSDA}}$  was calculated according the average energy of each spectrum). The entire sphere (which size is calculated by the number of shells multiplied by the dosel size given in Table III) was divided into 113 concentric scoring shells. The dosel size was set equal to the electronStepLimiter, in order to have at least one interaction within each bin. For each one simulation of the beta spectrum  $2 \times 10^7$  particles were generated, as in the monoenergetic electrons, while the resulted statistical uncertainty was lower than 1.7%, 2.8%, 7.7%, 11.8% and 48% for distances  $r/X_{90} < 0.2, 0.4, 0.8, 1.0,$  and 1.5, respectively, as it was calculated from the <sup>32</sup>P beta source. The parameters that were set to run the simulation are shown in Table III.



## II.E. Photon ( $\gamma$ ) DPKs

Photon DPKs were generated for  $^{99m}\text{Tc}$ ,  $^{111}\text{In}$ ,  $^{125}\text{I}$ , and  $^{131}\text{I}$  and the results were compared to those published by Furhang *et al.*<sup>12</sup> A water sphere phantom was used, with a radius equal to 400 mm. The DPK absorbed dose in this case is defined as

$$K(r) = D(r) * r^2, \quad (4)$$

where  $K(r)$  is the produced DPK,  $D(r)$  is the absorbed dose per source particle at a certain distance  $r$ , and  $r$  is the radial distance from the center of the sphere.

We have used two types of sources for the photon DPKs. For  $^{111}\text{In}$ ,  $^{125}\text{I}$ , and  $^{131}\text{I}$  the “ion” source of Geant4 was used, taking into account the entire gamma spectrum of these isotopes. All photons of the gamma spectrum of each isotope contributed to the absorbed dose, with the additional contribution of secondary particles from each electromagnetic interaction. The “dose actor” was combined with a “kill actor”, in order to kill all the primary electrons of each isotope, and keep only the generated photons spectrum. The photon DPKs were generated using four different dosel sizes for each simulation. The selected dosel sizes were  $0.5 \times 0.5 \times 0.5 \text{ mm}^3$  for radial distances 0–50 mm,  $1.5 \times 1.5 \times 1.5 \text{ mm}^3$  for 50–150 mm,  $2.5 \times 2.5 \times 2.5 \text{ mm}^3$  for 150–250 mm and  $3.0 \times 3.0 \times 3.0 \text{ mm}^3$  for 250–400 mm away from the point source. For each distance a separate dose actor was attached. The reduction of dosel size near the source gives a more accurate absorbed dose calculation for distances close to the center of the sphere, whereas bigger dosel sizes were used at larger distances from the source to reduce the statistical uncertainty.<sup>34</sup>  $2 \times 10^7$  particles were generated in order to produce the DPKs, while the statistical uncertainty was variable due to the dosel size variability and lower than 13.4%, 25.7%, 15.7%, 26.2%, and 38.2% for distances  $R < 5.0$ , 10.0, 15.0, 20.0, and 30.0 cm, respectively, as it was calculated from the  $^{111}\text{In}$  gamma source. The 400 mm sphere was divided in 258 concentric scoring shells. The first 101 shells were equal to 0.5 mm, the next 68 shells were equal to 1.5 mm, the next 40 shells were equal to 2.5 mm and the final 49 shells were equal to the 3.0 mm dosel size ( $101 \times 0.5 \text{ mm} + 68 \times 1.5 \text{ mm} + 40 \times 2.5 \text{ mm} + 49 \times 3.0 \text{ mm} = 399.5 \text{ mm}$  of the sphere).

In the case of  $^{99m}\text{Tc}$ , the source was defined as monoenergetic gamma particles of 140.5 keV. This means that there was no gamma emission spectrum with low x-ray energies that would consequently require high accuracy in regions close to the source, thus the dosel size was set  $3.0 \times 3.0 \times 3.0 \text{ mm}^3$ , which resulted in 133 concentric scoring shells ( $133 \times 3.0 \text{ mm} = 399 \text{ mm}$ ).

For comparison, all the produced photon DPKs were normalized to the absorbed dose value at 15 cm distance from the center of the sphere. This distance was selected as providing low statistical uncertainty and avoiding the high discrepancies due to the presence of low energy photons near the source.<sup>34</sup>

## II.F. Total DPKs for isotopes in different media

A total DPK dataset for the most important radionuclides in nuclear medicine was generated for four different materi-

als. More specifically DPKs were generated for  $^{67}\text{Ga}$ ,  $^{68}\text{Ga}$ ,  $^{90}\text{Y}$ ,  $^{99m}\text{Tc}$ ,  $^{111}\text{In}$ ,  $^{123}\text{I}$ ,  $^{124}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{153}\text{Sm}$ ,  $^{177}\text{Lu}$ ,  $^{186}\text{Re}$ , and  $^{188}\text{Re}$  for water, bone, and lung medium, whereas simulations in soft tissue medium were only done for  $^{90}\text{Y}$ ,  $^{111}\text{In}$ , and  $^{177}\text{Lu}$ . Water is the basis of the theory for the generation of DPKs.<sup>5,6</sup> Lung, bone, and soft tissue are the basic materials of a human body, and their densities greatly differ. These materials were simulated following the ICRU and ICRP reports;<sup>35,36</sup> the compact bone ICRU (density  $d = 1.85 \text{ g/cm}^3$ ), the lung ICRU (density  $d = 0.26 \text{ g/cm}^3$ ) and the soft tissue ICRP (density  $d = 1.0 \text{ g/cm}^3$ ). The total DPKs were generated by taking into account all emitting particles of each point source. All DPKs were generated by simulating  $4 \times 10^7$  particles in order to provide an absorbed dose distribution. Calculated absorbed dose incorporates contributions from beta, Auger and gamma emissions. All secondary particles from internal conversion have also contributed to the absorbed dose.

The deposited energy from the electrons is about  $\sim 1000$  times higher than the photon contribution. In addition, electrons deposit their energy at very small distances from the point source, whereas photons deposit their energy at much larger distances away from the source. For these reasons the generated kernels are presented in logarithmic scale in accordance to Eq. (4). The y logarithmic axis represents the absorbed dose multiplied by the square of the radial distance  $r$  (in mm), while the x axis represents the radial distance from the point source in mm. The total DPKs that were generated in this study can be easily reproduced using the supplementary material data.<sup>37</sup>

## III. RESULTS

### III.A. Monoenergetic electron ( $e^-$ ) DPKs validation

The 15 keV, 1 MeV, and 10 MeV DPKs in water as well as the DPKs that already exist in the current literature, are shown in Figs. 2(a)–2(c). The DPKs for all other electron energies are given in Figs. S1(a)–S1(d) as supplementary material.<sup>37</sup>

In Figs. 3(a) and 3(b) the DPKs produced in bone by GATE are compared to those produced by FLUKA (Ref. 8) for electron energies of 10 keV and 1 MeV, respectively.

The results of the electron DPKs produced by GATE v6.1 are in very good agreement to kernels already existing in the literature. The mean differences of the values in the same distance from the source were calculated for each profile, in order to compare GATE v6.1 against each cited code. The comparison results are presented in Fig. 7. The differences of the points were calculated as

$$\frac{|D_a(r) - D_b(r)|}{\max(D_a, D_b)} \times 100\%, \quad (5)$$

for distances lower than 0.8 ( $r/R_{\text{CSDA}} < 0.8$ ) for water medium and distances lower than 0.5 ( $r/R_{\text{CSDA}} < 0.5$ ) for bone medium.  $D_a(r)$  is the absorbed dose at distance  $r$  as calculated by code A and  $D_b(r)$  is the absorbed dose at the same distance calculated by code B.

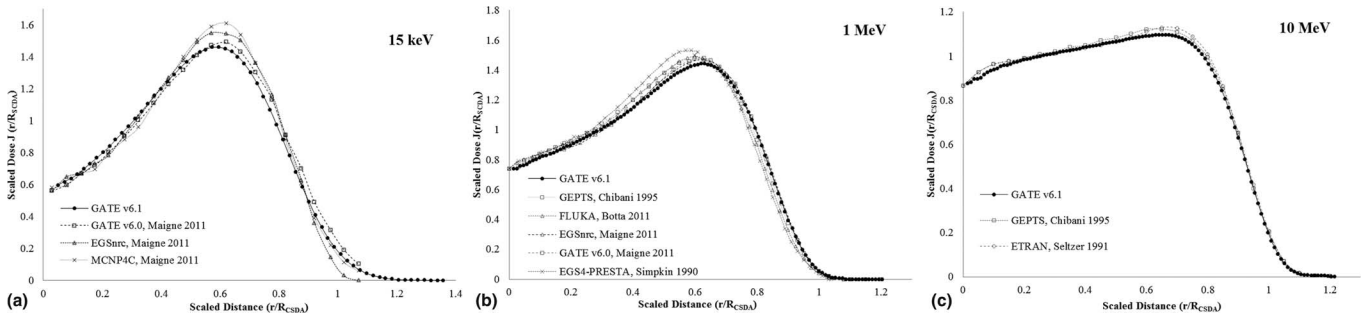


FIG. 2. Comparison of scaled DPKs for monoenergetic electron sources for energies (a) 15 keV, (b) 1 MeV, and (c) 10 MeV between GATEv6.1 and other Monte Carlo codes.

Also some differences of the maximum values are reported for additional information on the codes' comparison.

Larger discrepancies are observed for electrons with energies less than 100 keV. For the 15 keV DPK in water, the difference between the highest values in GATE and EGSnrc is 5.8%, whereas the difference between EGSnrc and MCNP4C is 9.3%. For the 50 keV electrons, similar differences are observed and are comparable to the variations between other Monte Carlo codes. More specifically, a 2.2% mean difference with a 4.4% difference of the maximum value between GATE and EGSnrc are observed, a 2.0% mean difference between GATE and EGS4-PRESTA and a 4.8% mean difference with a 6.7% difference of the maximum value between GATE and FLUKA are also observed. In Maigne *et al.*<sup>13</sup> a mean difference of almost  $\sim 3.5\%$  is reported between EGSnrc and MCNP4C, while in Botta *et al.*<sup>8</sup> differences lower than 6% are reported between FLUKA and PENELOPE for 500 keV electrons and energies higher than 1 MeV. The comparison between the results of our study and FLUKA as far as the bone medium is concerned provides also very good agreement, with differences smaller than 6.5%. In fact, 1.5% discrepancies are observed in the maximum values for 10 keV electrons (in bone) and 3.1% in the maximum values for 1 MeV electrons (in bone) between GATE and FLUKA codes.

### III.B. Beta DPKs validation

The  $^{177}\text{Lu}$  beta DPKs are presented in Figs. 4(a) and 4(b) for water and bone media, respectively. The  $^{90}\text{Y}$  (water and bone media) and  $^{32}\text{P}$  beta DPKs, are given as supplementary material in Figs. S2(a), S2(b), and S3.<sup>37</sup> Beta DPKs differences were compared according to Eq. (5). The comparison between GATE and the other MC codes are represented in Fig. 8. The differences were calculated for scaled distances lower than 1.4 ( $r/X_{90} < 1.4$ ).

More specifically, GATE simulated beta DPKs were compared to those of the EGS4 and FLUKA codes for  $^{90}\text{Y}$ , FLUKA code for  $^{177}\text{Lu}$  and EGSnrc and SMOOPY codes for the  $^{32}\text{P}$  isotope.

The results show very good agreement and the differences between GATE and the other Monte Carlo codes range between 2.5% and 5.0%, with the exception of the SMOOPY code, where the discrepancies are about 8.4%. The higher discrepancies are observed for bone and the mean difference is equal to 4.2% for  $^{177}\text{Lu}$  and 4.7% for  $^{90}\text{Y}$  between GATE and FLUKA. PENELOPE and FLUKA code in Botta *et al.*<sup>8</sup> study, have discrepancies in case of water  $< 1\%$  and  $< 2\%$  in case of bone. Data comparison of literature reports for  $^{90}\text{Y}$  (in water) for codes EGS4 (Ref. 13) and FLUKA (Ref. 8) show differences of about 1.7%.

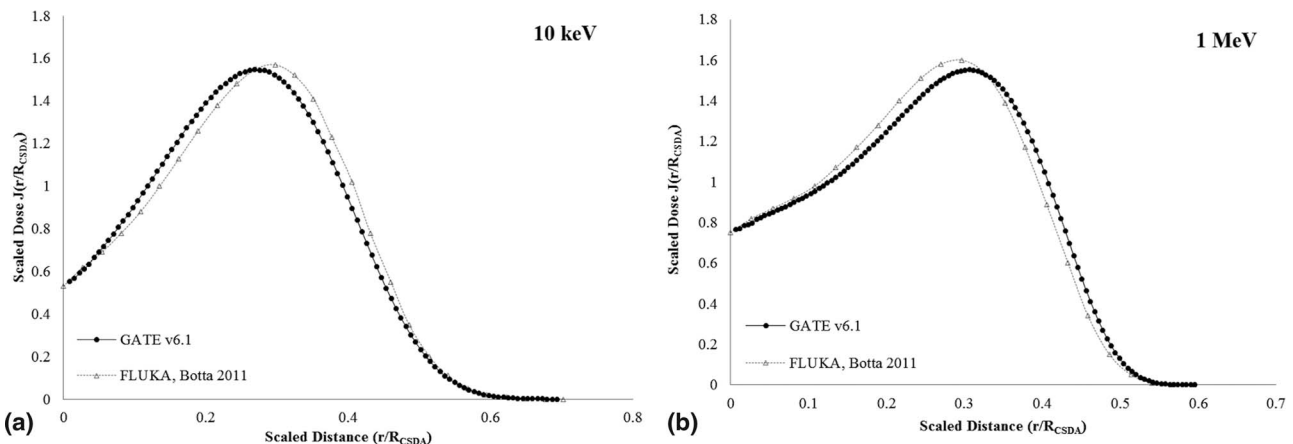


FIG. 3. Comparison among GATE v6.1 and FLUKA for monoenergetic electron DPKs (a) 10 keV and (b) 1 MeV for bone medium.

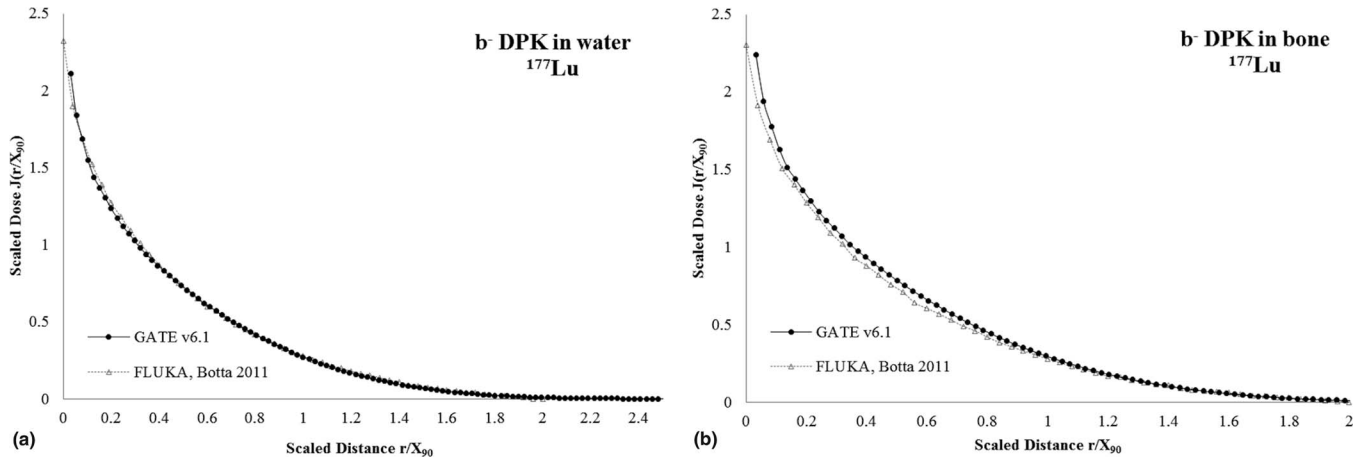


FIG. 4. Comparison of  $b^-$  DPKs for  $^{177}\text{Lu}$  in (a) water and (b) bone medium between GATE v6.1 and FLUKA.

**III.C. Photon ( $\gamma$ ) DPKs validation**

In Fig. 5 the photon DPK of  $^{111}\text{In}$  is shown. The DPKs for  $^{131}\text{I}$ ,  $^{125}\text{I}$ , and  $^{99\text{m}}\text{Tc}$  are given as supplementary material in Ref. 37. The results are compared to those produced by EGS4 Monte Carlo code in Furhang *et al.* study<sup>12</sup> and both show very good agreement.

More specifically, in  $^{111}\text{In}$  DPK maximum values, a difference of 1.4% is observed between GATE and EGS4 codes where, in  $^{99\text{m}}\text{Tc}$  the difference of the maximum values is equal to 1.8%.

In the case of  $^{125}\text{I}$  the difference of the maximum values reaches 10.2%. The differences in this region very close to the source could exist because of the used source spectrum taking, into account the whole photon spectrum (including the x-rays) of the isotope, instead of having only the monoenergetic gamma rays as it was done with the EGS4 code. The mean differences between GATE and EGS4, for points at the same distances from the source are lower than 2% for all the isotopes.

**III.D. Total DPKs**

In Fig. 6 the generated total DPK for  $^{90}\text{Y}$  is presented. In the figure the DPKs are presented for one isotope and for

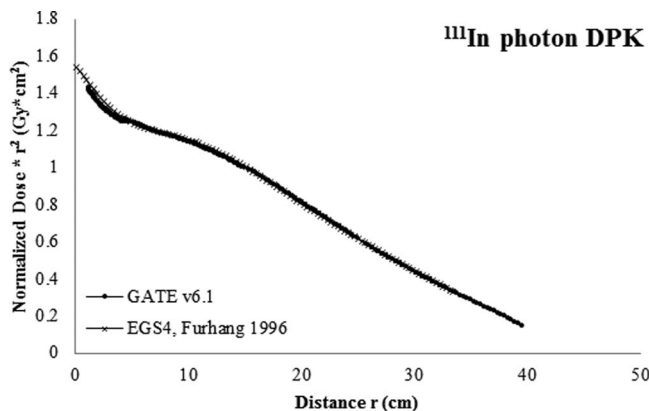


FIG. 5. Comparison of  $^{111}\text{In}$  photon DPK between GATE and EGS4.

the four different transport media. Differences between the absorbed doses in each medium can be clearly observed between soft tissue, lung, and bone. Water and soft tissue have almost the same absorbed dose distribution, due to the density of those materials, which is equal to  $1.0 \text{ g/cm}^3$ . The observed discrepancies between water and soft tissue are lower than 1%. Total DPKs for soft tissue medium were also calculated for the  $^{177}\text{Lu}$  and  $^{111}\text{In}$  in Figs. S7 and S8, respectively. Thus, the soft tissue at this level can be represented by water, Figs. 6, S7, and S8. The DPKs for the remaining isotopes are given as supplementary material in Ref. 37.

**IV. DISCUSSION**

GATE has been initially designed for the simulation and optimization of nuclear medicine imaging systems, as well as the optimization of reconstruction and correction algorithms. However, the latest versions extend its applications to the fields of radiotherapy and dosimetry, thus making validation against other existing Monte Carlo codes an absolutely necessary process. GATE's tools allow importing medical images for making patient specific 3D absorbed dose calculations. However, even though realistic dosimetric simulations based

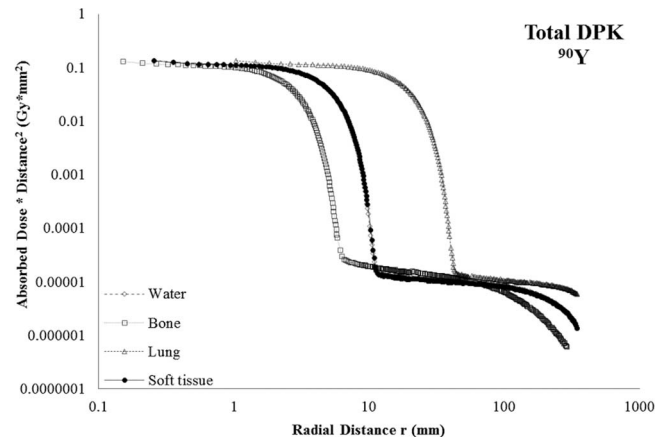


FIG. 6. Total DPKs for  $^{90}\text{Y}$  in water, bone, lung, and soft tissue, by GATE v6.1.

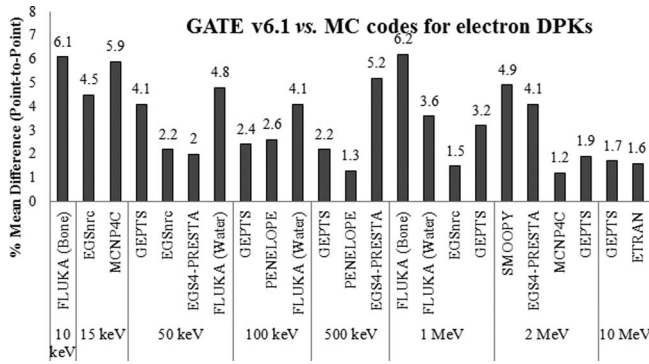


FIG. 7. Differences between GATE v6.1 and the other MC codes for all the calculated electron DPKs for energies ranging between 10 keV and 10 MeV.

on CT/MRI and SPECT/PET data are possible, they are computationally demanding and, at the moment, cannot be used in clinical routine. For this reason a hybrid approach that would use both patient anatomic data and material based kernel convolution would be of interest. To this end a first step is the validation of GATE for DPKs calculation, as well as the construction of a total DPKs database.

In this study, we have performed an extensive literature search of published DPKs and compared GATE accuracy in simulating DPKs for monoenergetic sources, electrons, photons, as well as their combinations. In all cases GATE results were comparable to previously published data to demonstrate the appropriateness of GATE Monte Carlo code as an adequate tool for dose calculations in the field of nuclear medicine. For monoenergetic electron sources, the larger discrepancies were observed for low energy emitting sources, especially 10 keV and 15 keV. More specifically, differences of almost  $\sim 6\%$  were observed when comparing GATE with FLUKA and MCNP4C. At energies higher than 50 keV the discrepancies were lower than 5.0%, with the exception for the EGS4-PRESTA (for 500 keV) and FLUKA (for 1 MeV in bone).

For beta radionuclides the results showed discrepancies close to 4.0% when comparing with FLUKA and EGS. In the study of Botta *et al.*<sup>8</sup> the discrepancies for the beta isotopes between PENELOPE and FLUKA were no higher than 2%.

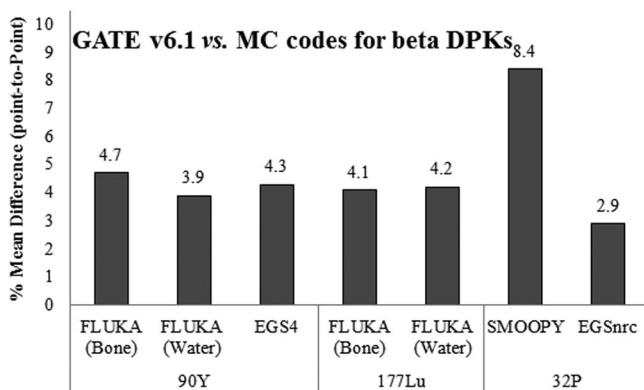


FIG. 8. Differences between GATE v6.1 and the other MC codes for all the calculated beta DPKs ( $^{90}\text{Y}$ ,  $^{177}\text{Lu}$ , and  $^{32}\text{P}$ ).

In that case the same beta spectra were used, as in the present study, where the beta spectra were derived from the LBNL database.<sup>33</sup> These slightly higher discrepancies observed, are acceptable as different algorithms are applied in each code and the final result depends on the used simulation parameters. Finally, the photon DPKs showed discrepancies with a mean value lower than 2% when compared to the kernels produced by EGS4. In case of patient dosimetry these differences would have a minor impact as they are lower than the uncertainty normally affecting internal dose estimation.

A larger difference was observed in the maximum value of  $^{125}\text{I}$  photon DPK which was equal to 10.2%. This resulted from the fact that we chose to simulate the whole gamma spectrum of the isotope instead of using only the gamma monoenergetic emission, as it was done with the EGS4 code. The difference of the deposited dose due to the low energy photons is observable as  $^{125}\text{I}$  emits very low energy photons compared to  $^{131}\text{I}$  and  $^{111}\text{In}$ . For these two isotopes, the “ion” source was also used, taking into account the whole photon spectrum, but the contribution of low energy emissions is very low. The complete comparison of GATE v6.1 against various codes is given in Figs. 7 and 8 where the mean values of the discrepancies between GATE and the other codes are presented.

Discrepancies among the codes can be expected as different Monte Carlo packages use different simulation algorithms. In GATE many parameters still need to be tested in detail for accurate dosimetric simulations as it is mentioned in the study of Maigne *et al.*<sup>13</sup> More specifically, electron step limiter plays a crucial role, which should be further investigated. Preliminary simulations have been implemented in order to choose an appropriate value of the “electronStepLimiter” for the purpose of this study. As it was discussed briefly in Sec. II.C, the electronStepLimiter parameter can alter the results. We have observed the following behavior; as smaller was the specific parameter the generated profile of the DPK was shifted in left, closer to the point source. In this study the values that were set for the electronStepLimiter, were determined so as to have comparable DPKs to the DPKs produced by other MC codes. An extended investigation of the influence of the parameter should be done (which is not in the scope of this study), so as to standardize this parameter for each energy, as we also observed that for low energy electrons, this parameter should be bigger than higher energies.

Following GATE validation, a novel dataset of total DPKs was generated for three different media namely water, bone, and lung and for the most widely used isotopes in nuclear medicine. Reported variations according to the material variation show that the assumption of using water based kernels for absorbed dose calculation using kernel convolution is not a sufficient approach. Convolution algorithms should be modified to take into account patient anatomic information, which can be easily extracted from a CT scan. Although the absorbed dose in soft tissue and water is almost the same, the calculation of DPKs for other materials could be further explored; GATE materials database accurately describes various organs and tissues and provides options to insert new ones. However, in this study DPKs in soft tissue were



generated only for  $^{111}\text{In}$ ,  $^{90}\text{Y}$ , and  $^{177}\text{Lu}$ . Since no significant differences were observed (for those isotopes), the rest of the dataset includes the DPKs generated only for bone, lung, and water.

The various material-specific DPKs could be used in appropriate convolution based absorbed dose calculation algorithms towards patient specialized dosimetry. The contribution of the photon emitters to the total deposited absorbed dose is almost  $10^2$ – $10^4$  times lower compared to the electrons energy deposition. However, the photon DPKs were mainly calculated in order to have a complete comparison of the different particles energy deposition in GATE. Accurate dosimetric schemes using personalized anatomy information represent a cutting edge research topic. Constructing a database, which gives the dose estimation in every organ/tissue (not only in the target organs) for various isotopes could be useful in clinical practice for imaging applications, especially when multiple imaging sessions are required. Another field where dosimetry issues raise is small animal imaging, where relatively high doses are repeatedly injected. Some initial work towards this direction has been conducted<sup>2</sup> where the DPKs are used to calculate dose decrease from the source voxel to a target voxel. This algorithm takes into account the materials and corresponding DPKs of all voxels along the path that connects source voxel and target voxel. By using this dataset we plan to continue these studies and quantify the effect of using several DPKs on the total absorbed dose for different organs and isotopes, as well as introducing a more accurate dose calculation approach. Preliminary assessment could be in parts of the body that show strong tissue variations, e.g., head and thorax. A full Monte Carlo simulation will be the gold standard and will be compared to the standard convolution of water based kernels, as well as tissue based kernels.

## V. CONCLUSION

Total DPKs have been calculated using the GATE Monte Carlo toolkit for a variety of isotopes that are commonly used in nuclear medicine, both for imaging and radioimmunotherapy applications. The DPKs were compared against published data for different Monte Carlo codes and very good agreement was observed for electrons, beta particles, photons, as well as full isotope spectra. Discrepancies of the maximum values were  $\sim 6\%$ , which is a typical difference among other Monte Carlo packages. A novel and complete dataset was produced, which extends the published DPKs to other tissues that exist in the human body, e.g., bone and lung. In addition, this dataset includes several radioisotopes used in nuclear medicine, for which total DPKs did not exist and is hereby publicly available. This dataset can be very important in patient-specific dosimetry for the implementation of a hybrid absorbed dose calculation method that will combine analytical convolution methods and patient specific anatomical information. It supports the appropriateness of GATE Monte Carlo code as an adequate tool for absorbed dose calculations in the field of nuclear medicine.

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