Dose point kernels in liquid water: An intra-comparison between GEANT4-DNA and a variety of Monte Carlo codes.

Christophe Champion, Sébastien Incerti, Yann Perrot, Rachel Delorme, Marie-Claude Bordage, Manuel Bardiès, Barbara Mascialino, Ngoc-Hoang Tran, Vladimir Ivanchenko, Mario Bernal, et al.

Dose Point Kernels in liquid water: an intra-comparison between GEANT4-DNA and a variety of Monte Carlo codes

C. Champion[a], S. Incerti[a], Y. Perrot[b], R. Delorme[c], M.C. Bordage[d], M. Bardiès[e], B. Mascialino[f], H.N. Tran[a], V. Ivanchenko[g], M. Bernal[h], Z. Francis[i], J.-E. Groetz[j], M. Fromm[j], L. Campos[k]

[a]Université Bordeaux 1, CNRS/IN2P3, CENBG, Gradignan, France.

[b]Laboratoire de Physique Corpusculaire, Université Blaise Pascal, CNRS/IN2P3, Aubière, France.

[c]CEA, LIST, Laboratoire Modélisation, Simulation et Systèmes, Gif-sur-Yvette, France.

[d]Laboratoire Plasmas et Conversion d'énergie, Université Paul Sabatier, Toulouse, France.

[e]CRCT, UMR 1037 INSERM, Université Paul Sabatier, Toulouse, France.

[f]Department of medical radiation physics, Stockholm University, Stockholm, Sweden.

[g]Ecoanalytica, 119899 Moscow, Russia.

[h]Instituto de Física Gleb Wataghin, Universidade Estadual de Campinas, SP, Brazil.

[i]Université Saint Joseph, Science Faculty, Department of Physics, Beirut, Lebanon.

[j]Université de Franche-Comté, Laboratoire Chrono-Environnement, UMR CNRS 6249, Besançon, France.

[k]Departamento de Física, Universidade Federal de Sergipe, São Cristóvão, Brazil

Abstract

Modelling the radio-induced effects in biological medium requires accurate physics models to describe in detail the main physical interactions induced by all the charged particles present in the irradiated medium (secondary as well as primary ones). These interactions include inelastic events like ionization and excitation processes as well as elastic scattering, the latter being the most important process in the low-energy regime. To check the accuracy of the

theoretical models recently implemented into the Geant4 toolkit for modelling the electron slowing-down in liquid water, the simulation of electron Dose Point Kernels remains the preferential test. In this work, normalized radial profiles of deposited energy at a distance from emissions point sources are then computed in liquid water by using the very low energy "Geant4-DNA" physics processes available in the Geant4 toolkit. We here report an extensive comparison with profiles obtained by a large selection of existing and well-documented Monte-Carlo codes, namely, EGSnrc, PENELOPE, CPA100, FLUKA and MCNPX.

Keywords: Dose Point Kernel; Geant4-DNA; Monte Carlo codes; liquid water.

PACS: 87.53.Bn; 02.70.Ss; 87.50.-a; 87.53.-j

Corresponding author

Christophe Champion

Université Bordeaux 1, CNRS/IN2P3, Centre d'Etudes Nucléaires de Bordeaux Gradignan, CENBG, Chemin du Solarium, BP120, 33175 Gradignan, France

Tel: +33-5-57-12-08-89; fax: +33-5-57-12-08-01

E-mail address: champion@cenbg.in2p3.fr

1. Introduction

Energy deposition functions from point isotropic sources - commonly denoted dose point kernel (DPK) functions - are of prime interest in many fields like dosimetry in particular for medical applications. To better understand the radiobiological effects resulting from the use of electron-emitting radiopharmaceuticals, it is necessary to have an appropriate knowledge of the cellular distribution of the radiopharmaceutical and then to model the microscopic distribution of energy deposited in irradiated matter [1]. Absorbed doses to targeted cancer cells play an important role in evaluating the relative merits of different radionuclides and pharmaceuticals. In this context, information on the bio-distribution at the tissue, cellular and sub-cellular levels can be obtained by autoradiography [2], micro-autoradiography [3], or alternative techniques such as secondary ion mass spectrometry [4]. Converting these data to absorbed dose distribution requires the use of analytic methods based on point-dose kernels or methods based on radiation transport calculations [5-7]. Indeed, Monte Carlo code event-by-event simulations can be particularly suitable [7-11]. The latter consist in describing, step-by-step, interaction after interaction, the history of each ionizing particle created during the irradiation of the biological matter. In this kind of numerical code, each projectile-target interaction is described either thanks to theoretical (differential as well as total) cross sections or by semi-empirical ones giving access to a more or less complete description of the kinematics before and after the collision.

In fact, there are in the literature a large number of Monte Carlo electron track-structure codes in water, which have been developed independently to investigate the microscopic features of ionizing radiation, the ensuing chemical pathways and the molecular nature of the damages in bio-molecular targets (see [11] and references therein). The aim of the present study is to compare dose point kernels - for particular electron energies - calculated by using different Monte Carlo codes, namely, EGSnrc [12], PENELOPE [13], CPA100 [14], FLUKA

[15], MCNPX [16] and GEANT4-DNA [17]. To do that, the energy deposited by the emitted electrons as well as all the secondary particles produced along the primary trajectories are scored in spherical shells placed around an isotropic source for distances ranging from 0 to 1.2 times the continuous slowing-down approximation range hereafter denoted R_{CSDA} and provided by the different codes here studied.

2. Methods

The Monte Carlo numerical simulations used in the present study are well-documented and nowadays extensively used by many groups. Only a brief description is then hereafter reported and for more details we refer the interested reader to the corresponding literature whose examples are cited as references.

2.1 The GEANT4-DNA code

The Geant4-DNA code is fully included in the general purpose Geant4 Monte Carlo simulation toolkit. It simulates track structures of electrons, hydrogen and helium atoms of different charge states (H^0, H^+) and (He^0, He^+, He^{2+}) respectively, as well as C^{6+}, N^{7+}, O^{8+} and Fe^{26+} ions, in liquid water. The physical processes include ionization (for all particles), electronic excitation (for electrons, protons, hydrogen atoms and α-particles including their different charge states), charge exchange (for hydrogen and helium atoms with the above-mentioned charge states), and, for electrons, elastic scattering, vibrational excitation and dissociative attachment. Electron interactions cover the 7.4eV - 1MeV energy range, whereas proton and hydrogen interactions are simulated from 100eV to 100MeV while helium ions of different charged states are followed from 1keV up to 400MeV. These processes are further described in [17].

2.2 The EGSnrc code

EGSnrc is a general-purpose package for the Monte Carlo simulation of the photons and the electrons transport from a few keV up to 100GeV. EGSnrc uses a condensed history approach based on the formalism developed by Kawrakow and Bielajew to sample angular distributions from the any-angle form of the screened Rutherford cross section [18]. The Möller inelastic cross-sections are used for the generation of secondary electrons. For this study, the simulations were based on the user-code EDKnrc developed by Mainegra *et al.* [19]. We applied the PRESTA II electron-step algorithm and the EXACT boundary crossing algorithm to switch to single scattering when a particle comes closer to a boundary. The "skin depth" parameter was set to 3: it represents the number of elastic mean free paths to the next boundary at which the simulation switches into single scattering mode. We set the cut-off parameter ECUT to 1 keV in order to track primaries and secondaries until they leave the geometry or their energy falls below 1 keV. We produced a PEGS4 data set describing cross sections and stopping powers adapted for this low cut-off value.

2.3 The PENELOPE code

PENELOPE (2006 version) is a general-purpose Monte Carlo code for the coupled simulation of electron and photon transport. The cross sections database used in PENELOPE covers a wide range of elements (Z = 1-99) and various materials useful for medical applications in the energy range of 50 eV - 1 GeV. This code has the flexibility to generate electron and positron histories on the basis of a mixed procedure, which combines detailed simulation of hard events with the continuous slowing down approximation for soft interactions. The level of detail of electron transport processes is controlled in PENELOPE by specifying values for several parameters, C_1, C_2, W_{CC} and W_{CR}. The C_1 and C_2 parameters are associated to the condensation of electron and positron elastic scattering processes. W_{CC} and W_{CR}, respectively, represent the cut-off energy losses for hard inelastic collisions and for hard Bremsstrahlung emission. A detailed description of the algorithms used in PENELOPE can be found in its

manual [20]. These simulations were done with detailed event-by-event transport setting $C_1 = C_2 = 0$, $W_{CC} = W_{CR} = 50$ eV and using 50 eV as the lower absorption energy allowed in this code.

2.4 The CPA100 code

CPA100 is an event by event Monte Carlo track structure code, developed in Toulouse (France), for understanding fundamental aspects of radiation track interaction [14]. It simulates complete electron/photon transport in liquid water for energy range from 10 to 200 keV. It generates all the electronic and photonic cascades occurring after a particle passage in the volume of interest (Auger electron, X-Rays, atomic reorganization). It is also able to describe the various stages of the particle transport not only the early physical stage, but also the physico-chemical and the chemical ones, during the very early passage of particles in matter say up to one microsecond. Primary physical and chemical damages not only in liquid water but also in complex DNA targets and its higher order structures can be calculated to estimate the radio-induced damage to the DNA molecular scale (DSB, SSB, base lesion).

2.5 The FLUKA code

FLUKA is a multi-purpose Monte Carlo particle transport code that considers all particle interactions including electromagnetic interactions, nuclear interactions of the primary or incident particles and the generated secondary particles, energy loss fluctuations and Coulomb scattering [15]. The version 2011.2.15 with the default configuration ‘PRECISION’ was used, with an energy cut-off lowered at 1 keV for electrons and 0.1 keV for photons. To reach a good accuracy, the single scattering model through the ‘MULSOPT’ option was activated, because the Moliere multiple scattering model could be unreliable with thin shells, disturbing the propagation of electrons between the boundaries [21].

2.6. The MCNPX code

MCNPX is a general-purpose Monte Carlo code for modelling the interaction of radiation with matter [16]. MCNPX stands for MCNP eXtended and transports electrons, photons, neutrons and several particle types, like nearly all energies. It utilizes the latest nuclear cross section libraries and covers various materials useful for medical applications. The tallies have extensive statistical analysis and the convergence is enabled by a wide variety of variance reduction methods. For this work, the version 2.7.0 was used with the F8* energy deposition tally in coupled electron-photon mode. The photon and electron cut-off energies were set above 1 keV. A specific consideration was focused on electron transport conditions, through the ITS option and the ESTEP parameter, due to the very narrow shells. The ITS energy indexing algorithm was used to have a better definition of the energy group and their boundaries [22] and the ESTEP parameter was increased in order to divide the major electron energy step into smaller sub-steps [23]: ESTEP = 10 for 100 keV and ESTEP = 100 for 10, 30 and 50 keV.

3. Results and discussion

To obtain the dose point kernel (DPK) around an isotropic point source, the geometry here used consists in a spherical water phantom divided into 120 spherical shells of thickness $R_{CSDA}/100$, where R_{CSDA} stands for the continuous-slowing-down-approximation range whose values calculated by the different codes here studied are reported in Table 1. Note that for the EGSnrc, the CPA100, the FLUKA and the MCNPX codes, the corresponding values are taken from the NIST web database ESTAR [24], what generates stopping powers and ranges for electrons which are the same as those tabulated in ICRU Report 37 [25]. Besides, let us remind that the present GEANT4-DNA version transports electrons down to an energy threshold of 7.4 eV contrary to the other codes studied which use higher energy cut-off, what undoubtedly affects the R_{CSDA} values.

Finally, the GEANT4-DNA DPK distributions have been compared to those obtained with the other Monte Carlo codes by using Kolmogorov-Smirnov statistical tests. Thus, we found that the GEANT4-DNA simulations are statistically compatible with EGSnrc and PENELOPE simulations (p-value > 0.05) with a maximum distance (D) between distribution functions less than 0.2. On the contrary, much smaller p-values (< 0.05) and larger D distances were obtained when comparing GEANT4-DNA simulations with the MCNPX and CPA100 simulations.

The DPK distributions also obtained by the different numerical codes are reported in Figure 1 for four particular electron energies, namely, 10 keV, 30 keV, 50 keV and 100 keV. These quantities are defined as the fraction of the emitted energy absorbed (per unit mass) at a certain distance from the point source and are usually reported by means of scaled distributions defined as $F(r/R_{CSDA}) = \frac{\delta E(r)/E_0}{\delta r/R_{CSDA}}$ where r is the distance from the point source, $\delta E(r)$ stands for the energy absorbed in the spherical shell sited at a distance r from the point r/R_{CSDA} source, E_0 being the initial kinetic energy of the electron and δr the shell thickness (here $R_{CSDA}/100$). The obtained distributions will be hereafter reported as a function of r/R_{CSDA} and refer to scoring of the deposited energy at the mid-radius of the shell.

In Figure 1, we observe that the shape of the dose point kernels generated by the different codes is very similar. However, we note that the CPA100 code exhibits a peak closer to the source in comparison to the other codes ($r/R_{CSDA} \cong 0.53$ vs 0.58), the amplitudes being all of the same order of magnitude - from 1.45 to 1.55 - except for the MCNPX which largely overestimates the other results. When the incident electron energy increases, these observations are confirmed with in particular an improvement of the agreement between the CPA100 and the other simulations. Thus, from Fig.1b) to Fig.1d) all the curves tend to converge except again the MCNPX simulation which provides higher DPKs (of about 20%).

Besides, for the four energetic cases here reported, the GEANT4-DNA DPK distributions have been compared to those obtained with the other Monte Carlo codes by using Kolmogorov-Smirnov statistical tests. Thus, we found that the GEANT4-DNA simulations are statistically compatible with EGSnrc, PENELOPE and FLUKA simulations (p-value > 0.05) with a maximum distance (D) between distribution functions less than 0.3. On the contrary, much smaller p-values (< 0.05) and larger D distances were obtained when comparing GEANT4-DNA simulations with the MCNPX (for the four incident energy values) and CPA100 (for 30 keV and 50 keV) simulations.

4. Conclusions

Normalized radial profiles of deposited energy - commonly referred to as dose point kernels - have been here reported by using the very low energy “Geant4-DNA” physics processes available in the Geant4 toolkit. In comparison with profiles obtained by a large selection of existing and well-documented Monte-Carlo codes, namely, EGSnrc, PENELOPE, CPA100, FLUKA and MCNPX, we have here emphasized evident discrepancies undoubtedly relied to the physics models implemented into the different codes. In this context, the Geant4-DNA code has been shown to provide accurate dose point kernels for incident electron energies ranging from 10 keV to 100 keV.

Acknowledgements

The Geant4-DNA project received funding partly from the French Agence Nationale de la Recherche under contract number ANR-09-BLAN-0135-01 and from the European Space Agency under contract number AO6041- 22712/09/NL/AT**.** This work has been developed as part of the activities planned in the project PICS 5921 (THEOS) of the Centre National de la Recherche Scientifique.

Figure 1:

(Color online) Comparison between the scaled dose point kernel distributions obtained by the different numerical track-structure codes studied in the present work: GEANT4-DNA (red), EGSnrc (green), PENELOPE (blue), CPA100 (cyan), MCNPX (magenta) and FLUKA (orange). Panel a) E_0 = 10 keV. Panel b) E_0 = 30 keV. Panel c) E_0 = 50 keV. Panel d) E_0 = 100 keV.

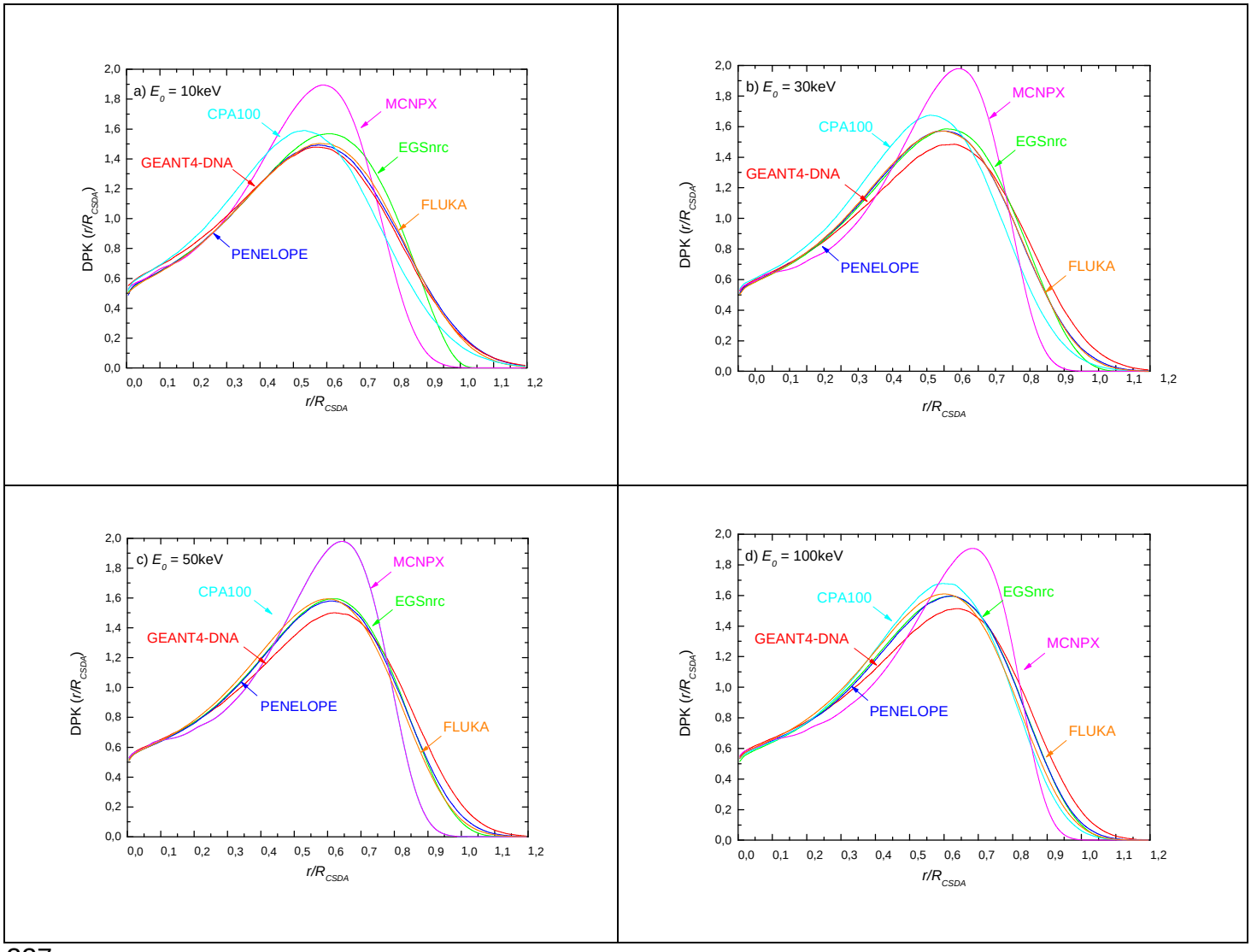

Table 1:

Comparison between the continuous-slowing-down-approximation range R_{CSDA} (µm) obtained by the different numerical track-structure codes studied in the present work.

E_0	R_{CSDA} **(GEANT4-DNA)**	R_{CSDA} **(PENELOPE)**	R_{CSDA}^{*} **(EGSnrc, CPA100, KLUKA, MCNPX)**
10 keV	2.76	2.52	2.52
30 keV	18.16	17.57	17.56
50 keV	44.07	43.21	43.20
100 keV	144.12	143.06	143.10

**Note that the EGSnrc, CPA100, FLUKA and MCNPX values have been taken from the NIST web database ESTAR [24] contrary to the other data here reported.*

References

[1] A.I. Kassis, Radiobiologic principles in radionuclide therapy, J. Nucl. Med. **46** (2005) 4S12S.

[2] E.D. Yorke, L.E. Williams, A.J. Demidecki, D.B. Heidorn, P.L. Roberson, B.W. Wessels, Multicellular dosimetry for beta-emitting radionuclides: autoradiography, thermoluminescent dosimetry and three-dimensional dose calculations, Med. Phys. **20** (1993) 543-550.

[3] M.R. Puncher, P.J. Blower, Radionuclide targeting and dosimetry at the microscopic level: the role of microautoradiography, Eur. J. Nucl. Med. **21** (1994) 1347-1365.

[4] F. Chehade, C. de Labriolle-Vaylet, N. Moins, M.F. Moreau, J. Papon, P. Labarre, P. Galle, A. Veyre, E. Hindié, Secondary ion mass spectrometry as a tool for investigating radiopharmaceutical distribution at the cellular level: the example of I-BZA and 14C-I-BZA, J. Nucl. Med. **46** (2005) 1701-1706.

[5] W.E. Bolch, L.G. Bouchet, J.S. Robertson, B.W. Wessels, J. A. Siegel, R.W. Howell, A.K. Erdi, B. Aydogan, S. Costes, E.E. Watson, A.B. Brill, N.D. Charkes, D.R. Fisher, M.T. Hays, S.R. Thomas, MIRD Pamphlet No. 17: the dosimetry of nonuniform activity distributions-radionuclide S values at the voxel level. Medical Internal Radiation Dose Committee, J. Nucl. Med. **40** (1999) 11S-36S.

[6] L. Strigari, E. Menghi, M. d'Andrea, M. Benassi, Monte Carlo dose voxel kernel calculations of beta-emitting and Auger-emitting radionuclides for internal dosimetry: a comparison between EGSnrcMP and EGS4, Med. Phys. **33** (2006) 3383-3389.

[7] W.B. Li, W. Friedland, E. Pomplun, P. Jacob, H. Paretzke, M. Lassmann, C.H.R. Reiners, Track structures and dose distributions from decays of 131I and 125I in and around water spheres simulating micrometastases of differentiated thyroid cancer, Radiat. Res. **156** (2001) 419-429.

[8] C. Champion, Theoretical cross sections for electron collisions in water: structure of electron tracks, Phys. Med. Biol. **48** (2003) 2147-2168.

[9] C. Champion, A. L'hoir, M.F. Politis, P.D. Fainstein, R.D. Rivarola, A. Chetioui, A Monte Carlo code for the simulation of heavy-ion tracks in water, Radiat. Res. **163** (2005) 222-231.

[10] C. Champion, C. Le Loirec, Positron follow-up in liquid water. I. A new Monte Carlo track-structure code, Phys. Med. Biol. **5** (2006) 1707-1723.

[11] S. Uehara, H. Nikjoo, D.T. Goodhead, Comparison and assessment of electron cross sections for Monte Carlo track structure codes, Radiat. Res. **152** (1999) 202-13.

[12] I. Kawrakow, Accurate condensed history Monte Carlo simulation of electron transport : I. EGSnrc, the new EGS4 version, Med. Phys. **27** 485-98 (2000).

[13] S. Salvat, J.M. Fernandez-Varea, J. Sempau, PENELOPE-2006, A Code System for Monte Carlo Simulation of Electron and Photon Transport, OECD ISBN 92-64-02301-1 (2006).

[14] M. Terrissol and A. Baudre, A simulation of space and time evolution of radiolytic species induced by electrons in water, Radiat. Prot. Dosim. **31** (1990) 175-177.

[15] FLUKA: A Multi-Particle Transport Code. Geneva: CERN European organization for nuclear research; 2005.

[16] MCNPX User's Manual, Version 2.5.0, Laurie Waters, ed., LA-CP-05-0369 (2005).

http://mcnpx.lanl.gov/documents.html.

[17] S. Incerti, A. Ivanchenko, M. Karamitros, A. Mantero, P. Moretto, H.N. Tran, B. Mascialino, C. Champion, V.N. Ivanchenko, M.A. Bernal, Z. Francis, C. Villagrasa, G. Baldacchino, P. Guèye, R. Capra, P. Nieminen, C. Zacharatou, Comparison of GEANT4 very low energy cross section models with experimental data in water, Med. Phys. **37** (2010) 4692-4708.

[18] I. Kawrakow and A.F. Bielajew, On the representation of electron multiple elastic-scattering distributions for Monte Carlo calculations, Nucl. Instrum. Methods Phys. Res. B **134** (1998) 325-35.

[19] E. Mainegra-Hing, D.W.O. Rogers, I. Kawrakow, Calculation of photon energy deposition kernels and electron dose point kernels in water, Med. Phys. **32** (2005) 685-699.

[20] F. Salvat, J. Sempau, and J.M. Fernandez-Varea, Tech. Rep., Universitat de Barcelona, 2006.

[21] F. Botta, A. Mairani, G. Battistoni, M. Cremonesi, A. Di Dia, A. Fassò, A. Ferrari, M. Ferrari, G. Paganelli, G. Pedroli, M. Valente, Calculation of electron and isotopes dose point kernels with FLUKA Monte Carlo code for dosimetry in nuclear medicine therapy, Med. Phys. **38** (2011) 3944-3954.

[22] D.R. Schaart, J.T.M Jansen, J. Zoetelief, P. De Leege, A comparison of MCNP4C electron transport with ITS 3.0 and experiment at energies between 100 keV and 20 MeV: Influence of voxel size, substeps and energy indexing algorithm, Phys. Med. Biol. **47** (2002), 1459-1484.

[23] H. Koivunoro, T. Siiskonen, P. Kotiluoto, I. Auterinen, E. Hippeläinen, S. Savolainen, Accuracy of the electron transport in MCNP5 and its suitability for ionization chamber response simulations: A comparison with the EGSNRC and PENELOPE codes, Med. Phys. **39** (2012) 1335-1343.

[24] ESTAR, National Institute of Standards and Technology, « Stoping powers and Range table for electrons », http://physics.nist.gov/PhysRefData/Star/Text/ESTAR.html.

[25] ICRU, « Stopping powers for electrons and positrons », ICRU Report 37, ICRU, Washington, DC, 1984.