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Technical notes

Does the setup of Monte Carlo simulations influence the calculated properties and effect of gold nanoparticles in radiation therapy?

Spiridon V. Spirou*, Dimitris Makris, George Loudos

Department of Biomedical Engineering, Technological Educational Institute of Athens, Greece

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ABSTRACT

Purpose: To investigate whether the dose-scoring process of Monte Carlo (MC) simulations of Gold nanoparticles (GNPs) in radiation therapy affects the results.
Methods: The GATE MC toolkit was used to simulate the irradiation of a water phantom containing a single solid or hollow GNP with 250 kVp and 6 MV photons. The dose was scored in 20 nm × 20 nm × 50 μm, 100 nm × 100 nm × 50 μm and 200 nm × 200 nm × 50 μm volumes using dose-scoring voxels of size 1 nm × 1 nm × 50 μm, 10 nm × 10 nm × 50 μm, 50 nm × 50 nm × 50 μm and 100 nm × 100 nm × 50 μm Excess dose depth-dose (EDDD) curves and lateral beam profiles were used to compare the dose-scoring voxels.
Results: In a given volume, neither the EDDD curves nor the lateral beam profiles are affected by the size of the dose-scoring voxels, subject to noise and uncertainty. Certain features of the EDDD curves are clearly seen in larger volumes, but hidden within the uncertainty and noise levels in smaller volumes. For the lateral beam profiles, it is the larger volumes that result in misleading results and the smaller ones that give the expected results. However, the limited statistics result in asymmetries and skewness in the profiles.
Conclusion: For a given volume, the dose curves are not affected by the size of the dose-scoring voxels. However, the voxel size may hide or reveal the finer structure of the dose curves and/or may result in misleading curves.

Introduction

External beam radiation therapy has witnessed a significant increase in dose to the tumor and sparing of normal tissues in recent years, primarily due to the development of advanced delivery techniques, such as Intensity-Modulated Radiation Therapy, Volumetric Modulated Arc Therapy, Tomotherapy, Image-Guided Radiation Therapy etc, that have the potential to more accurately conform the high-dose region to the tumor. An alternative pathway towards increasing the dose differential between the tumor and normal tissues is to increase the deposition of dose in the tumor volume using high-Z materials [1,2].

Gold nanoparticles (GNPs) have a number of characteristics that make them promising candidates in achieving this goal [3]: they are relatively non-toxic and biocompatible, they can penetrate the tumor through its vasculature, they can be manufactured in different sizes, they can be labeled with peptide, antibodies or ligands for improved specificity and targeting, the dose-enhancement effect can extend over several cells, and they can be imaged [4–6].

MC simulations are a valuable tool in: (a) determining the properties of individual GNPs, such as the excess dose arising from a single GNP in a water phantom, the spectra, range, angle and energy of the electrons produced by the GNP for photon and electron beams, as well as various radionuclides [7–10], (b) modeling the interaction of GNPs with tissue [8,11–14], (c) assessing which NP designs, e.g. size, solid vs hollow, will have the optimal properties and highest Dose Enhancement Ratio and cell-killing etc.

The results, however, produced by the various MC software packages at the nanoscale level suffer from the difficulty of experimental validation. In the absence of such experimental validation, the best approach in determining the properties of GNPs is to compare different MC codes. In principle, for a given setup, these

* Corresponding author. Department of Biomedical Engineering, Technological Educational Institute of Athens, Ag. Spyridonos 28, Egaleo, 12210 Athens, Greece. Tel.: +30 2105385376; fax: +30 2105385302.
E-mail address: spiridonspirou@yahoo.com (S.V. Spirou).

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side-by-side comparisons should be done for a wide range of simulation parameters for each code.

An alternative approach is to compare each code with itself with respect to the simulation parameters, and then compare different MC codes for only some values of those parameters. If the results of MC code X can be shown to be insensitive to the value of some parameter p, then it is not necessary to compare X with MC code Y for each value of p. It suffices to compare codes X and Y for only some representative values of p.

It should be pointed out that comparing X with itself against p, and getting an unexpected result may reveal underlying and deeply hidden flaws in the code. However, the converse is not true: the fact that nothing unexpected results does not imply that the code is correct. The case may still turn out to be that a comparison between X and Y results in disagreements.

In this work we investigate whether the GATE MC software tool is robust against the Dose Actor that is used to score dose and how simulation parameters may affect the results. The question we ask is: "Is the calculated energy (and dose) that is deposited in a given volume the same, regardless of whether the volume is considered as an aggregate of larger or smaller voxels?" In Section Methods the method and procedures are described. Results are presented in Section Results, and in Section Discussion they are discussed.

Methods

The GATE Monte Carlo toolkit (v6.2) was used to simulate the irradiation of a water phantom containing a single gold nanoparticle. GATE is based on the Geant4 code, which is highly acclaimed for its basic physics modeling, and it is dedicated to numerical simulations in the fields of medical imaging and radiation therapy. The toolkit has already been used in PET, SPECT, CT and radiotherapy applications for the design of new medical imaging devices, the optimization of acquisition protocols, the development and assessment of image reconstruction algorithms and correction techniques, the calculation of dose etc [15]. For clinical photon and electron fields GATE/Geant4 has been validated using both measurements and comparison with other MC codes [16]. All of our simulations were run in the Virtual Imaging Platform[1], which uses distributed computing for increased efficiency [17]. Each simulation required up to a few days of computation time, depending on the platform load.

The "Penelope" model was used to describe the physical processes [18,19]. This model incorporates all the electromagnetic processes that are effective between 250 eV and 1 GeV, including the photoelectric effect, Compton and Rayleigh scattering, pair production, electron and ion ionization, Bremsstrahlung, positron and electron annihilation, and electron and positron single and multiple scattering. The production threshold, below which secondary particles are not generated, was left at the default of 100 eV.

The water phantom was cubic, $20 \times 20 \times 20$ mm^3, and it contained a single GNP at 5 mm depth along the beam central axis [10]. The GNPs were both solid and hollow, 10, 50 and 100 nm in diameter.

A realistic 250 kVp and 6 MV photon source (Fig. 1) was placed 2 mm outside the phantom [20,21]. The source was rectangular and covered the GNP. The number of particles generated was 5×10^9 for the 1x1 and 10×10 nm^2 Dose Actors, and 10^9 for the 50×50 and 100×100 nm^2 Dose Actors. The direction of the photons was perpendicular to the phantom. Also simulated was the irradiation of the phantom without the GNP for each source size.

[1] http://www.creatis.insa-lyon.fr/vip/.

For dose calculation, GATE uses the Dose Actor (DA). The DA is a 3D structure (matrix) that scores the energy deposited, the dose and the uncertainty. Due to computer memory issues, the DA is practically limited to approximately $400 \times 400 \times 400$ voxels, although the voxels are not required to be cubic. Therefore, smaller voxel sizes provide fine detail in a limited volume, whereas larger voxel sizes cover a larger volume at the expense of lower resolution.

For all the DAs, the dimension of the voxels along the central axis of the beam (CAX) was 50 μm in order to cover the entire phantom. Perpendicular to the CAX the dimensions of the voxels was 1×1, 10×10, 50×50, and 100×100 nm^2. To simplify the notation, the dimension along the CAX will be dropped, and only the dimensions perpendicular to the CAX will be used. For example, a volume of "100×100 nm^2" means a volume of "100 nm $\times$ 100 nm $\times$ 50 μm".

To compare the various DAs, we considered the dose recorded from using different DAs in the same volume. For example, in a volume of 100×100 nm^2, we compared the dose arising from using 100x100 voxels each of size 1×1 nm^2, 10x10 voxels each of size 10×10 nm^2, and 2x2 voxels each of size 50×50 nm^2. The setups used are shown in Table 1. After subtracting the dose in water alone from the dose in the GNP simulation, excess dose depth-dose curves and excess dose lateral beam profiles were calculated. To account for statistical fluctuations, the excess doses in Gy were divided by the entrance dose in water alone, also in Gy, and then normalized to the maximum.

Results

Volumes larger than 200×200 nm^2 did not show any differences and are omitted for the sake of brevity. Results are presented for 6 MV since this is the more clinically relevant beam. The 250 kVp simulations yielded similar results with respect to the agreement between the various Dose Actors.

Figure 2 shows the relative excess dose along the CAX for the 100 nm solid GNP, for two volumes: 20x20 and 100×100 nm^2. In the 20x20 volume the 1x1 and 10×10 nm^2 DAs are compared at a finer level, whereas in the 100x100 volume the 1x1, 10x10 and 50×50 nm^2 DAs are compared at a more coarse level. Figure 3 shows the corresponding results for the 100 nm hollow GNP.

For both GNPs, the EDDD curves obtained using the 20×20 nm^2 volume exhibit more noise compared with those resulting from using the 100×100 nm^2 volume. This is a consequence of the lower statistics in the smaller volume.

The EDDD curves of both GNPs in the 100×100 nm^2 volume exhibit a drop immediately prior to the location of the GNP. In the 20×20 nm^2 volume, this feature is within the uncertainty of the curves and is hard to discern.

Figures 4 and 5 show the relative lateral beam profiles at 1 mm below the GNP. The beam profiles obtained with the 20×20 nm^2 volume contain a significant amount of noise due to the statistics achieved in such small volumes. There is also an asymmetry in the profiles for the 10×10 nm^2 Dose Actor. This is probably a statistical artifact as evidenced by the fact that it was significantly reduced when the number of photons was increased 5-fold, from 10^9 to 5×10^9. In addition, in this particular case, the asymmetry is further enhanced by the fact that the asymmetries in the profiles with and without the GNP are in the opposite direction.

Discussion

Nanoparticles, acting as drug carriers and/or radiosensitizers, are expected to be a major new weapon in the arsenal against cancer. Monte Carlo simulations can be a valuable tool for investigating the basic properties of NPs at the nanoscale level, and for

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