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Dose Distribution and Dose Enhancement by Using Gadolinium Nanoparticles Implant in Brain Tumor in Stereotactic Brachytherapy

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HIGHLIGHTS

- High atomic number elements have high photoelectric cross section.
- Radiation dose is enhanced in tumor injected with gadolinium nanoparticles.
- Dose enhancement factor increases with increasing gadolinium concentration.
- Dose enhancement factor increases with decreasing irradiation energy.
- Dose enhancement factor increases with increasing tumor depth.

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ABSTRACT

Background: The photoelectric and pair production processes increase when high-energy photons interact with materials with high atomic number Z. The energy loss results in a dose enhancement at the target implanted with these materials. This will lead to a higher active dose to be delivered to tumor, while sparing healthy tissues around the target volume.
Objective and method: The objective of this work was to compute the radial dose enhancement, using GEANT4 based Monte Carlo simulations, at and near a $1 \times 1 \times 1$ cm^3 brain tumor implanted with different concentrations of gadolinium nanoparticles when using ^{192}Ir, ^{137}Cs and ^{60}Co, brachytherapy sources with parallel beam geometry.
Results: Our outcomes show a dose enhancement factor of 1.45 for a concentration of 70 mg of gadolinium in the tumor when irradiated with 0.38 MeV γ-photon from ^{192}Ir source. It was also observed that this dose enhancement increased with increasing gadolinium concentration in the target and with photon energy.
Conclusion: Gadolinium nanoparticles are groundbreaking agents with strong advantageous potential in cancer radiotherapy due to the fact that they enhance the radiation dose within the tumor.

1. Introduction

In stereotactic radiotherapy cancerous the tumor is focally irradiated with high accuracy with the aim of maximizing the dose to the tumor while sparing surrounding healthy tissue. Nonetheless, radiation dose delivery should be optimized to keep the dose to the patient as low as reasonably achievable according to the ALARA principle (ICRP, 2007). Elements with high atomic numbers Z have their photoelectric cross section proportional to Z^n/E^3, where E is the energy of the absorbed photon and $4 < n < 5$ (Podgorsak, 2010). Within this scope, recent studies showed that gold, platinum, silver, ferrous oxide Fe_2O_3 nanoparticles implants in cancerous prostate tumor (Sinha et al., 2015; Ghorbani et al., 2013) during brachytherapy could significantly enhance radiation dose to the tumor and moderate damage to surrounding non-malignant tissue when irradiated with low energy photons. The radiosensitivity induced by high atomic number nanoparticles can be explained by the fact that when incident radiation interacts with these nanoparticles at the early stage process that takes place in the cells, electrons and highly reactive radical clusters are emitted and then react with biomolecules. This cell killing enhancement occurs even though the nanoparticles do not enter cell nuclei (Chang et al., 2008; Usami et al., 2008). Gadolinium is known to have a high probability of the interaction with photons by photoelectric effect (Robar et al., 2002). The high LET and short

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Abbreviations: ALARA, As Low As Reasonably Achievable; ASTM, American Society for Testing and Materials; DEF, Dose Enhancement Factor; GdNp, Gadolinium Nanoparticles; GAMOS, Geant4-based Architecture for Medicine-Oriented Simulations; STD, Source-Tumor Distance

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range of photo-electrons and Auger electrons produce localized dose enhancement at the vicinity of the point of the interaction (Rahman et al., 2009).

According to the “American Society for Testing and Materials” ASTM, nanoparticles are particles with lengths that range from 1 to 100 nm. The role of nanoparticles as radiosensitizers has been studied in numerous works (Rahman et al., 2009; Babaei and Ganjalikhani, 2014; Ni et al., 2008; Jain et al., 2011). Gadolinium ($Z=64$) is a rare-earth metal in the F block and Period 6 of the periodic table. Its salts exist in the trivalent form. As free ion the gadolinium is highly toxic, however when chelating with organic ligands, its toxicity is greatly reduced (Bartolini et al., 2003). The concentration range taken in this work, 10–70 mg, shows no indication of toxicity for the brain tissue (Rima et al., 2013) and is swiftly eliminated by the kidneys (Roux et al., 2010; Bianchi et al., 2014).

Measurements of the absorbed radiation doses in very small sample volume similar to the tumor volume is very difficult and will upset the condition medium and the radiation beam. In this work, we used GAMOS toolkit to quantify the dose enhancement effects near and at the tissue implanted with gadolinium nanoparticles and investigated the effect of the implant concentration and the beam energy on the dose enhancement.

2. Materials and methods

The use of Monte Carlo computer codes in nuclear medicine and radiotherapy is of great help especially in the dose determination (Bolch, 2010; Fog and Collins, 2008). In this study, we used the GAMOS toolkit Monte Carlo computer code to assess the effect of “Gadolinium Nanoparticles” GdNps on dose enhancement for treatment of brain malignant tumor (Arce et al., 2008, 2014). This code uses a three-dimensional heterogeneous geometry and the transport of high energy photons in the energy range from few eV to 10 TeV. The computed value in MeV per incident photon for each section of the tumor was then converted to absorbed dose. In order to attain a relative statistical error of less than 1%, 10^8 photon history have been followed in the dose simulation.

The effects of the gadolinium nanoparticles were computed by simulating a cubic volume of soft tissue and the tumor was modeled by $1 \times 1 \times 1\ \text{cm}^3$ volume and voxilized to cells of $1\ \text{mm}^3$ volume loaded with various concentration of GdNp and located at different distances from the source supposed to be a point source (Fig. 1). Table 1 gives the elemental composition of the human brain soft tissue (ICRU Report 46, 1992) of density $1.00\ \text{g/cm}^3$ and mean excitation energy of 72.30 eV.

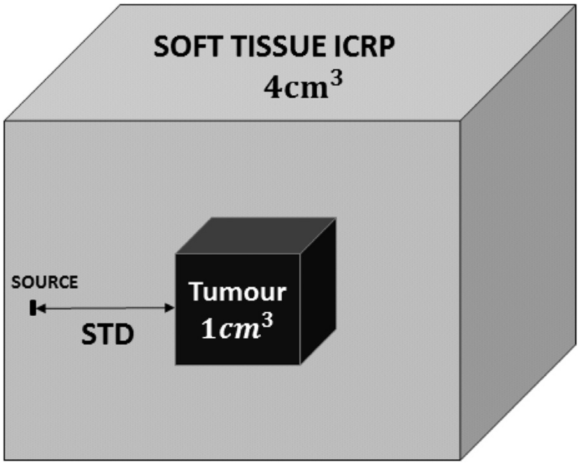

Fig. 1. Tumor – irradiation source system in 4 cm^3 soft tissue phantom.

Table 1
Elemental composition of the human brain soft tissue.

Element	Fraction by weight
1	0.104472
6	0.232190
7	0.024880
8	0.630238
11	0.001130
12	0.000130
15	0.001330
16	0.001990
17	0.001340
19	0.001990
20	0.000230
26	0.000050
30	0.000030

The GAMOS simulation toolkit has been developed for many application of radiation transport. The Radiotherapy is one of these applications, where they has developed a special toolkit for radiation oncology and dosimetry. The data from NIST “the National Institute of Standards and Technology” for photon transport and material cross section are already implanted within the Geant4 (Berger, 2005). The standard Electromagnetic physics was used in this study with a photon cutoff energy of 1.09 keV for soft tissue. In addition, the voxilized of the soft tissue were then set as a scoring detector for the primary beam of gamma ray coming from the source to calculate the deposited dose inside the 1 cm^3 tumor. The data were then written in a text file for each segment as a dose deposition in Gy, calculated using the deposited energy divided by the voxel mass (Arce et al., 2008; Bhatnagar, Sirisha). Finally, the data were processed and plotted using MATLAB.

3. Results and discussion

The average computed radial DEF for uniformly distributed GdNp in different concentrations was computed as follows.

$$\text{DEF} = \frac{\text{Dose at a given point in the tumour with GdNp}}{\text{Dose at the same point in the tumour without GdNp}}.$$

Our calculations show that, the radial DEF increased with increased GdNp concentration and was as high as 1.45 within the tumor when implanted with 70 mg gadolinium for the lowest energy photon from the ^{192}Ir source (Fig. 2). This increase is a consequence of the increase in the photoelectric absorption of the photons at high GdNp. The dose was not enhanced outside the tumor. This is very advantageous in term of sparing the

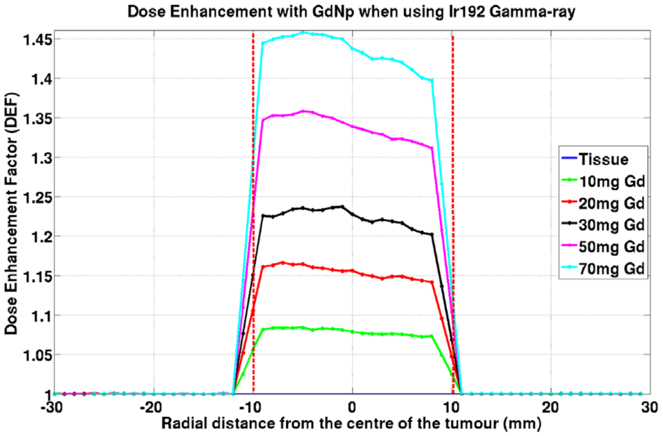

Fig. 2. Computed dose enhancement factor for ^{192}Ir source.