Dose Enhancement by Radiolabeled Gold Nanoparticle: *in silico* Study

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1. Introduction

Today, radiation therapy (RT) is the most widely used treatment method for tumors [1]. A golden rule of RT is to minimize the radiation dose to normal organs while maximizing the radiation dose to the tumor. However, conventional external beam radiotherapy (EBRT) limits the delivered dose to a tumor by the adjacent critical organ. It means that all tumor cells cannot receive a lethal dose. So, in order to maximize the therapeutic effect, it is necessary to increase the dose delivered to the tumor.

The use of high-Z nanoparticles to increase the dose delivered to the tumor is one of the most promising developments in RT. When external radiation interacts with high-Z nanoparticles, it releases tremendous numbers of secondary particles; mostly low-energy electrons called auger electrons, that increase the dose delivered to the tumor. A previous *in vivo* study with living mice compares the therapeutic effects of RT using gold nanoparticles (GNP) and RT only [2]. When GNP was used, the tumor volume was significantly smaller, which means that the delivered dose was significantly increased with GNP. This phenomenon is called the dose enhancement of the nanoparticles.

Targeted radionuclide therapy (TRT) is an alternative treatment approach to achieve more localized dose delivery than EBRT [3]. TRT injects radionuclide through blood vessels, and radionuclide accumulated in the tumor region delivers dose locally only to the tumor, so the therapeutic effect is maximized and side effects are reduced. At this time, radionuclide labeled with nanoparticles can be used in TRT for dose enhancement. Prior to the use of radiolabeled nanoparticles, a study on dose enhancement is essential. *In silico* study allows evaluation of dose enhancement for radiolabeled nanoparticles [4].

In this study, we investigated the dose enhancement of radiolabeled GNP using Monte Carlo (MC) simulations. In particular, we focused on microscopic scale dose enhancement in the region around the GNP. To confirm this, microscopic dose distributions were obtained around the GNP.

2. Materials and Methods

2.1 MC simulation geometry

Fig. 1 shows the MC simulation geometry. First, we tried to confirm the feasibility of Cs-131 labeled GNP dose enhancement through slab geometry. The slab geometry was simulated using MCNP version 6.2 and Geant4 version 10.5, and the results were cross-verified. The dose enhancement factor (DEF) of the Au + Cs mixture was calculated using a 100 nm to 5 um thick water slab under a 10 nm thick slab. Au + Cs mixture was made by mixing a 0.1 atomic percent of Cs-131 with pure Au.

Nanoshell geometry was simulated only in MCNP 6.2. Fe was placed in the core in order to mimic the nanoparticles for magnetic hyperthermia. Radial DEF of Au + Cs mixture was calculated around 50 nm diameter Cs-131 labeled GNP. The radial DEF was calculated in spherical shells having a thickness of 1 nm to 500 nm up to a distance of 50 µm from the surface of the nanoshell geometry. The photon and electron spectra of Cs-131 were taken from LiveChart of Nuclides.

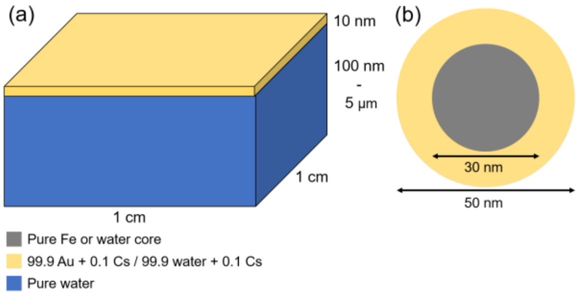

Fig. 1. Illustration of simulation geometry (a) Slab geometry in MCNP6.2 and Geant4. (b) Nanoshell geometry in MCNP6.2.

3. Results and Discussion

3.1 Simulation results: slab geometry

The DEFs of slab geometry are given in Table I. Similar DEFs were obtained in MCNP 6.2 and Geant4, except for the 100 and 200 nm thickness of the water slab. This discrepancy is because the inelastic scattering cross-section data of MCNP 6.2 for the low-energy electron is larger than that of Geant4. The photon-induced DEF was greater than 1 for all water slab thicknesses, but the electron-induced DEF was less than 1. DEF by both photon and electron was very similar to DEF by electron only. This is because the energy that electron deposits on the water slab is very dominant compared to the photon.

Table I: Slab geometry DEFs by photon and electron

Water slab thickness	MCNP 6.2		Geant4	
	Photon	Electron	Photon	Electron
100 nm	9.44	0.84	8.51	0.79
200 nm	6.05	0.86	5.68	0.82
500 nm	3.65	0.86	3.53	0.83
1 μm	2.81	0.87	2.75	0.85
2 μm	2.29	0.89	2.26	0.87
4 μm	1.91	0.91	1.90	0.90
5 μm	1.80	0.92	1.78	0.91

3.2 Simulation results: nanoshell geometry

Fig. 2 shows the radial DEF profile of nanoshell geometry. Similar to the case of slab geometry, the photon-induced DEF was much greater than the electron-induced DEF. However, since the energy deposited by the electron is much more dominant than that of the photon, the DEF by both the photon and the electron overlapped with the electron only DEF.

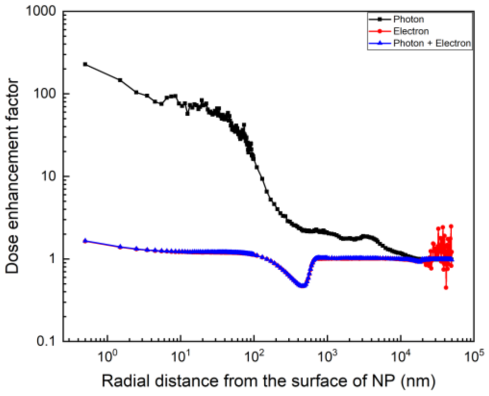

Fig. 2. Radial DEF profile of nanoshell geometry.

4. Conclusions

In this study, we investigated the dose enhancement of radiolabeled GNP using MCNP 6.2 and Geant4. Both simulation codes obtained similar DEF results in slab geometry and completed code-to-code verification. However, in nanoshell geometry, an additional code-to-code comparison is required. Since electrons contribute much more to energy deposits than photons, it is necessary to focus on electron spectra when considering various radionuclide candidates. We plan to investigate additional *in silico* studies with more realistic scenarios such as nanoparticles clusters in the future.

Acknowledgement

This research was supported by a fund (PQ20201B010) by the Research of Animal and Plant Quarantine Agency, South Korea.

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