Dose enhancements and cellular S-values of nanoparticle-enhanced Auger therapy

Wonmo Sung [a, b], Seongmoon Jung [a, b], Sung-Joon Ye [a, b, c*]
[a] *Program in Biomedical Radiation Sciences, Department of Transdisciplinary Studies, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, South Korea*
[b] *Biomedical Research Institute, Seoul National University Hospital, Seoul, South Korea*
[c] *Robotics Research Laboratory for Extreme Environment, Advanced Institutes of Convergence Technology, Seoul National University, Suwon, South Korea*
[*] *Corresponding author: sye@snu.ac.kr*

1. Introduction

Recently, another type of nanoparticle-enhanced radiation therapy, which is called a nanoparticle-enhanced Auger therapy, was introduced [1]. However, a continuous atomic structure of gold sheet and simple energy spectra measurement were not sufficient to assess its clinical applicability. We calculated the dosimetric properties and S-values to predict its physical and biological effectiveness in radiation therapy.

2. Methods and Results

The Geant4-DNA Monte Carlo (MC) simulations [2] were performed to assess electron energy spectra, dose enhancement distributions, and cellular S-values with nanoparticle. Three major inputs were considered: nanoparticle elements, its size, and auger-electron emitting radionuclides. Clinically applicable candidates were assumed: Two nano-structures (nanoshell and nanosphere) with five elements (Fe, Ag, Gd, Au, and Pt), various sizes (2-100 nm), and three isotopes (I-125, In-111, and Tc-99m). More detail description of methods is described in our previous work [3].

2.1 Electron energy spectra

The nanoshell can be fabricated with simple galvanic replacement reactions between solutions containing metal precursor salts and Ag nanostructures prepared by polyol reactions [4]. Electron energy spectra were acquired at the outer surface of nanoparticle or volume source with water (Fig. 1). The height of the Auger peak was clearly reduced with the Au nanoshell but the number of secondary electrons was decreased. This is because low-energy electrons failed to escape the Au nanoshell if they have penetration ranges less than shell thickness

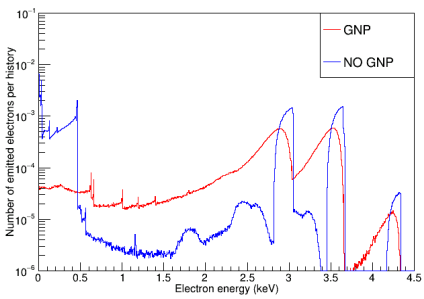

Fig. 1 Electron energy spectra for I-125 obtained at two outer interfaces; one between gold nanoshell (inner/outer diameter: 40/50 nm) and water, and the other between volume source (diameter: 50 nm) and water.

Iodine ions have high affinity for Au atoms and thus can be effectively conjugated to gold nanoparticle to from Au-I bonds on gold surfaces [5]. As described in nanoshell, the energy spectra around the nanosphere was also acquired and compared with volume source with only water (Fig. 2). The gold nanosphere of 50 nm diameter generated a larger number of low energy electrons than did the absence of nanosphere. This effect is due to the higher fraction of backscatter electrons escaping from the sizable nanoparticle.

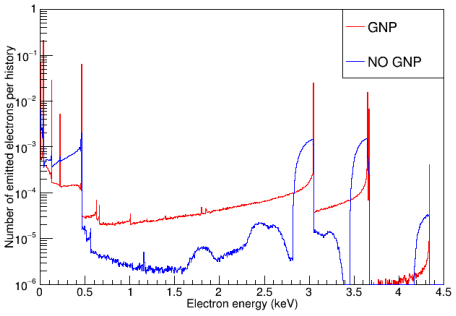

Fig. 2 Electron energy spectra for I-125 obtained at two outer interfaces; one between gold nanosphere (diameter: 50 nm) and water, and the other between volume source (diameter: 50 nm) and water.

2.2 Dose enhancements

Fig. 3 represents the dose ratio (DR) distributions along the radial distance from the surface of nanoshell for various simulations setups. Here DR is defined as dose with nanoparticle divided by without it. Overall trend of microscopic distributions shows up and down. Within 20 nm distance from nanoparticle, DR values were less than 1.0. After that, DR rapidly increased at certain distances from the nanoshell. It was decreased again within larger distances became one. The effective enhancement ranges, which is larger than DR values of one, vary depending on nanoparticle sizes, materials, and isotopes.

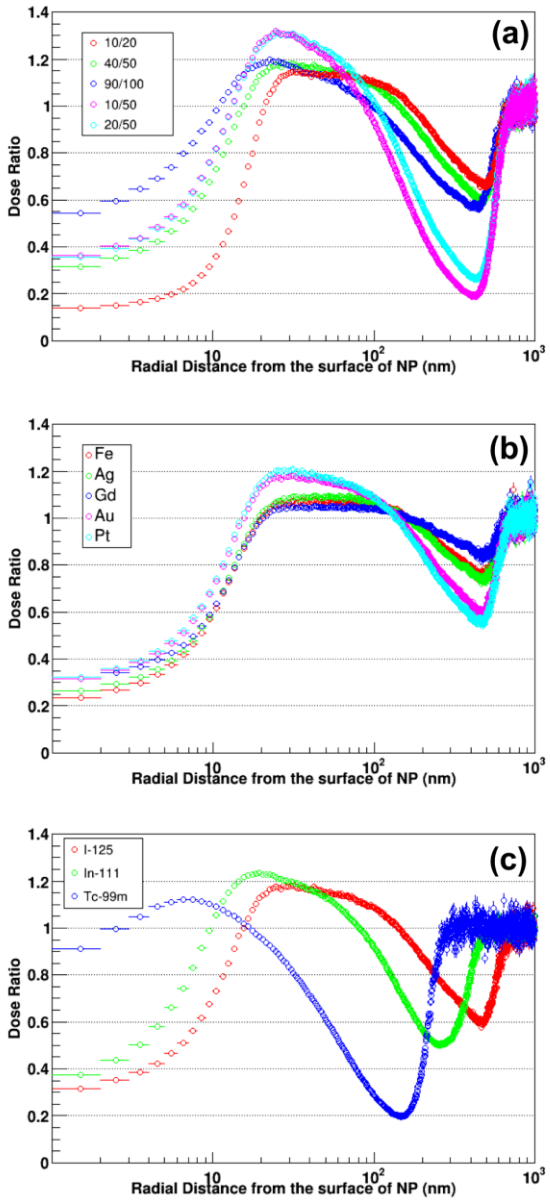

Fig. 3 DRs for nanoparticle shell with respect to the absence of nanoparticle for (a) various sizes (inner/outer diameter) with gold-I-125, (b) different elements with 40/50 nm diameter with I-125, and (c) different isotopes with 40/50 nm diameter gold nanoshell

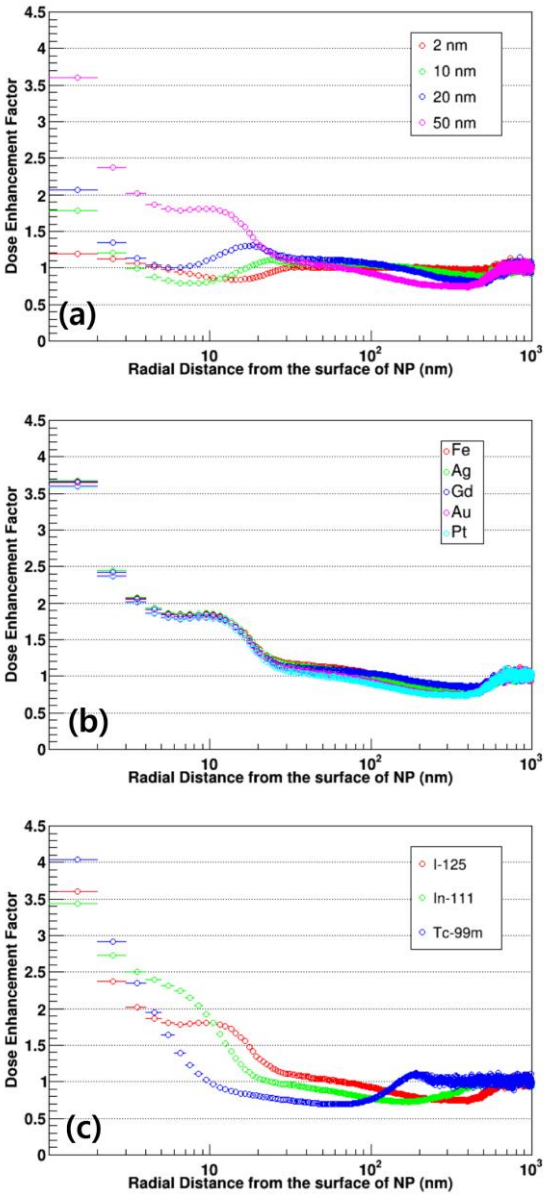

Fig. 4 DRs for nanosphere with respect to the absence of nanosphere for (a) various sizes (diameter: m) with gold-I-125, (b) different elements of 50 nm diameter nanosphere with I-125, and (c) different isotopes with an gold nanosphere of 50 nm diameter

Fig. 4 shows that the DR distributions versus radial distances for four different diameters of nanosphere. Within 4 nm, increase dose (DR > 1.0) were observed for all setups but it has fluctuations up to 1 μm. The maximum DR near the surface was around 3.6 for 50 nm diameter nanosphere.

2.3 Cellular S-values

According to the MIRD (Medical Internal Radiation Dose) scheme [6], the cellular S-value is defined as the dose to the target per unit cumulated activity in the source region. The spherical cell geometry was assumed: cell of 5 μm diameter and nucleus of diameter 4 μm. Various cellular compartments (nucleus, cytoplasm, surface) were considered as source or target volumes. The S-values were calculated using the absorbed dose in the target compartment due to the energy released from the source compartment. The previously acquired radial doses from randomly distributed nanoparticles were summed to calculate the

absorbed dose to target. The increase of cellular S-values with nanoparticle was observed (~ up to 300%) but highly dependent on geometry of cell and source to target regions.

3. Conclusions

This new type of treatment modality can deliver an enhanced microscopic dose to the target if the GNPs is effectively internalized into the cytoplasm and close proximity to the biological target (e.g., DNA). Meanwhile, Auger therapy combined with nanoparticles could have the potential to provide a better therapeutic effect than conventional Auger therapy alone.

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