Dependence of Dose Enhancement on Gold Nanoparticle Shape in Photon Radiotherapy

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I. Indroduction

Gold nanoparticles (AuNPs) have emerged as a promising radiosensitizer in photon radiotherapy due to:

- their high atomic number,
- ease of production in various shapes and sizes,
- and biocompatibility.

Targeted delivery of AuNPs can further improve the precision of dose deposition.

This study investigates how AuNP shape affects energy deposition efficiency

- independently of other tested influencing factors (photon energy, nanoparticle size, and concentration), but still in relation to these factors.

Optimized Monte Carlo simulations of radiation transport are employed to model energy deposition patterns in nanoparticle-laden regions with nanoscale accuracy.

Three shapes of AuNPs are tested for the ability to deliver a higher dose to the tumor:

- nanospheres,
- nanorods,
- and square nanoplates.

The obtained results offer guidelines into:

- designing nanoparticles,
- optimizing future dosimetric Monte Carlo studies in metal nanoparticle enhanced photon radiotherapy.

Nanoscopic precision of dose calculation is achieved.

- Geant4 Monte Carlo toolkit (version 10.7) was used for performing simulations.
- Dose distributions were obtained by utilizing the advanced condensed history algorithm for electron transport, so that simulations came closest to true event-by-event tracking.

List of GEANT4 processes with connected physics models used to simulate photon and electron interactions.

Interaction	GEANT4 process	GEANT4 model
	Photon	
Rayleigh scattering	G4RayleighScattering	G4LivermoreRayleighModel
Photoelectric effect	G4PhotoElectricEffect	G4LivermorePhotoElectricModel
Compton scattering	G4ComptonScattering	G4LivermoreComptonModel
	Electron	
Elastic scattering	G4eMultipleScattering	G4GoudsmitSaundersonMscModel
Ionisation and excitation	G4eIonisation	G4LivermoreIonisationModel
Bremsstrahlung	G4eBremsstrahlung	G4LivermoreBremsstrahlungModel

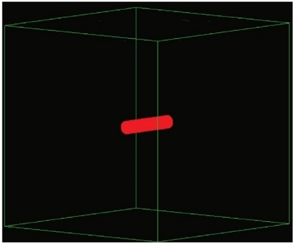
- Relaxation processes (including fuorescent photon and Auger electron emissions) was carried out using the algorithm implemented in the G4UAtomicDeexcitation class and data provided in Livermore's library EADL.
- Adjustable simulation parameters were optimized to make the physical models of radiation transport pertinent to the discrete representation of MNPs:
  - *the production cut* $= 10\ \mathrm{eV}$ (the energy limit for a secondary electron at the instance of creation below which it is not propagated, but rather has its energy deposited locally)
  - *the step-size limit for electrons* $= \mathrm{DBL\_MAX}$ (the upper bound to the distance along which an electron is propagated with the CSDA energy loss)
  - *the lowest electron energy* $= 1\ \mathrm{eV}$ (below which the propagation of an electron is terminated and its energy deposited locally)

Geometric model

- Smaller *representative volume* (a water-flled cube containing a single gold nanoparticle) was introduced, instead of modeling a macro-scale target volume.
  - For each specifed size of the nanoparticle (V_{np}) and each specifed nanoparticle concentration (k), the volume of the cube was determined as:

$$V_{cube} = V_{np} + V_w = V_{np}\left(1 + \frac{\rho_{Au}}{k\rho_w}\right), \tag{1}$$

where ρ_{Au} and ρ_w are the mass densities of gold and water.



A single gold nanorod at the center of the water-flled cubic representative volume. In simulations probing the infuence of nanoparticle shape, the representative volume contained only a single nanoparticle–either a nanosphere, a nanorod, or a nanoplate–in each simulation run. The edge of the cube, obtained from equation (1), ranged between 79.70 nm and 2.163 µm.

- Three diferent nanoparticle sizes were used.
  - The diameter of the nanosphere was set at $d = 10, 50, \text{or } 100\ \mathrm{nm}$.
  - Dimensions of cylindrical nanorods and square nanoplates were calculated so that all three shapes had the same volume.
  - The ratio of dimensions was set arbitrarily at diameter:height = 1:5 for nanorods, and at a:b:c = 1:100:100 for nanoplates.
  - A uniform distribution of nanoparticles inside the region with regard to both position and orientation was assumed.
- The energy of monoenergetic photon field ranged from 20 keV to 4 MeV.
  - Rather than simulating a unidirectional beam and changing the orientation of the nanoparticle for each incoming photon, the nanoparticle was positioned at the center of the cubic repres. volume and fixed in an arbitrarily chosen orientation. The cube with the nanoparticle was then exposed to an isotropic feld of photons, incident on the cube from all possible directions.

The simulations assumed that electronic equilibrium existed in the representative volume.

- This assumption was based on the idea that in the macro-scale target volume, each representative volume would be surrounded by other similar volumes exposed to the same photon field.

Simulation outputs

- The energy deposited in the nanoparticle E_{np}.
- The energy deposited in the surrounding water E_w.
- Fraction of deposited energy which went into water was then found as:

$$\delta_w^i = \frac{E_w^i}{E_w^i + E_{np}^i}, \qquad i = sphere, rod, plate$$

III. Results and Discussion

Table 1: Properties of gold nanoparticles used in simulations probing the influence of nanoparticle shape. [1]

Nanoparticle shape	Linear dimensions (nm)	Volume (nm^3)	V/S (nm)	Mean straight-line path (nm)
Sphere	d: 10.00		1.667	3.749
Nanorod	D, H: 5.109, 25.54	523.6	1.161	2.952
Nanoplate	a, b, c: 0.3741, 37.41, 37.41		0.1834	0.9355
Sphere	d: 50.00		8.333	18.75
Nanorod	D, H: 25.54, 127.7	65450	5.805	14.76
Nanoplate	a, b, c: 1.871, 187.1, 187.1		0.9170	4.678
Sphere	d: 100.0		16.67	37.49
Nanorod	D, H: 51.09, 255.4	523600	11.61	29.52
Nanoplate	a, b, c: 3.741, 374.1, 374.1		1.834	9.354

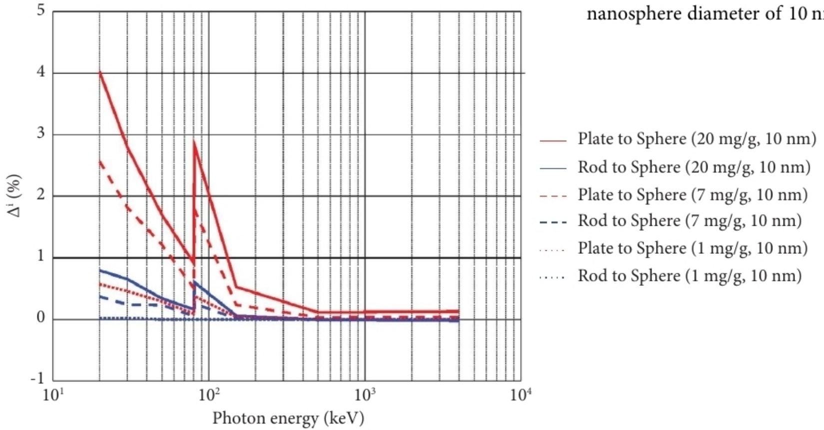
Mean straight-line path is the mean distance between the position at which an electron is produced within a nanoparticle by an incident photon and the point at which that electron would exit the nanoparticle, if it were moving along a straight line.

[1] S. Milutinović, M. Pandurović, and M. Vujisić, "Influence of Gold Nanoparticle Shape and Single-Cell Localization on Energy Deposition Efficiency and Irradiation Specificity in Photon Radiotherapy," *Nanomaterials and Nanotechnology*, vol. 2023, pp. 1–18, Aug. 2023.

The influence of nanoparticle shape was quantitatively expressed by the relative usable fraction of deposited energy with respect to spherical AuNPs:

$$\Delta^i = \frac{\delta_w^i - \delta_w^{sphere}}{\delta_w^{sphere}}, \qquad i = rod, plate$$

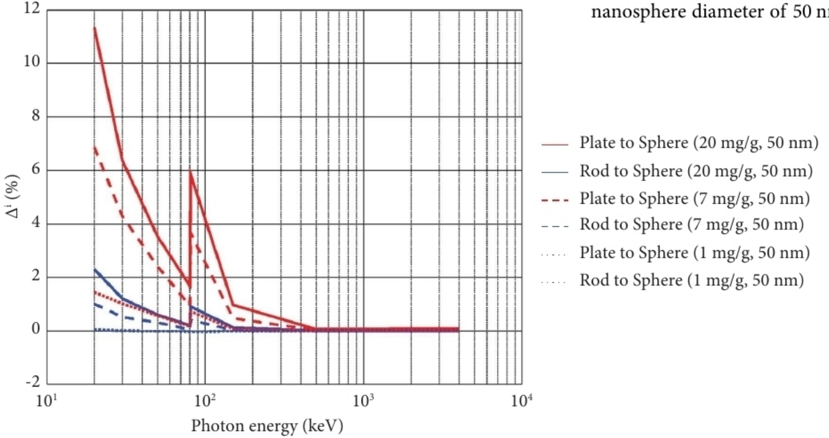
nanosphere diameter of 10 nm



Graph 1 shows the dependence of the relative usable fraction of deposited energy with respect to spherical AuNPs Δ^i ($i = rod, plate$) on the photon beam energy for the nanosphere diameter of 10 nm. Nanorods and nanoplates were of the same volume as the nanospheres. [1]

[1] S. Milutinović, M. Pandurović, and M. Vujisić, "Influence of Gold Nanoparticle Shape and Single-Cell Localization on Energy Deposition Efficiency and Irradiation Specificity in Photon Radiotherapy," *Nanomaterials and Nanotechnology*, vol. 2023, pp. 1–18, Aug. 2023.

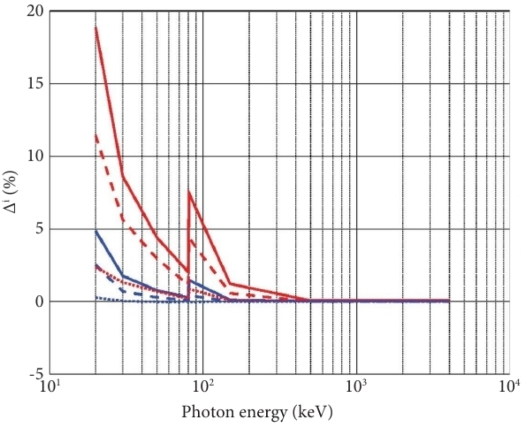
nanosphere diameter of 50 nm



Graph 2 shows the dependence of the relative usable fraction of deposited energy with respect to spherical AuNPs Δ^i ($i = rod, plate$) on the photon beam energy for the nanosphere diameter of 50 nm. Nanorods and nanoplates were of the same volume as the nanospheres. [1]

[1] S. Milutinović, M. Pandurović, and M. Vujisić, "Influence of Gold Nanoparticle Shape and Single-Cell Localization on Energy Deposition Efficiency and Irradiation Specificity in Photon Radiotherapy," *Nanomaterials and Nanotechnology*, vol. 2023, pp. 1–18, Aug. 2023.

nanosphere diameter of 100 nm



Graph 3 shows the dependence of the relative usable fraction of deposited energy with respect to spherical AuNPs Δ^i ($i = rod, plate$) on the photon beam energy for the nanosphere diameter of 100 nm. Nanorods and nanoplates were of the same volume as the nanospheres. [1]

[1] S. Milutinović, M. Pandurović, and M. Vujisić, "Influence of Gold Nanoparticle Shape and Single-Cell Localization on Energy Deposition Efficiency and Irradiation Specificity in Photon Radiotherapy," *Nanomaterials and Nanotechnology*, vol. 2023, pp. 1–18, Aug. 2023.

The following has been concluded from simulation results:

- Shapes with a larger mean straight-line path lead to less radiation energy being deposited in the surrounding medium (water or tissue), at all photon energies and for all AuNP sizes and concentrations.
  - Out of the three investigated shapes, nanoplates would be the most favorable with regard to this usable deposited energy, while nanospheres would be the least benefcial.
- The infuence of nanoparticle shape varies with the photon beam energy, being most distinct at low energies, subsiding as the energy rises, and becoming absent at higher energies.
  - The usable deposited energy difering up to 19%.
- As the concentration or size of AuNPs rise, the importance of their shape becomes more prominent with regard to the usable deposited energy.

IV. Conclusion

- Results and conclusions provided by the present study can serve as guidelines in the designing phases of gold nanoparticles intended for use in photon radiotherapy.

- It has been shown that future MC studies can be limited to photon beams of low energies, which are less demanding of computational resources.

Thank you for the attention!

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