CALCULATION OF THE DOSE ENHANCEMENT RATIO WHEN USING GOLD NANOPARTICLES IN PHOTON ACTIVATION THERAPY OF ONCOLOGICAL DISEASES

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Monte Carlo simulation of irradiation of the gold nanoparticles with diameters from 2 to 100 nm in aqueous medium by 20-100 keV photons is performed. Radial distributions of the absorbed dose and dose enhancement ratios are obtained. It is shown that at distances from the nanoparticle center up to 150-200 nm, the absorbed dose increases hundreds of times as compared with the case of the irradiation of pure water. The main transmitters of energy from NPs to the environment are Auger electrons emitted by ionized gold atoms during the cascade decays of inner-shell vacancies.

Keywords: vacancy cascade; metal nanoparticles; photon activation therapy; radiosensitizers; dose enhancement ratios; Monte Carlo simulation; Auger electrons.

Introduction

Currently, nanoparticles (NPs) based on metals with a high atomic number are used in photon therapy of oncological diseases as radiosensitizers [1, 2]. Delivery of nanoparticles to tumor tissue followed by irradiation with hard X-rays or gamma radiation allows localizing the absorbed dose directly inside the tumor and reducing the radiation damage to healthy tissues. This direction of radiation therapy is called photon activation or photon capture therapy.

The effect of local enhancement of the absorbed dose when using metal nanoparticles with a high atomic number is due to three physical reasons. First, the heavy atoms in NPs have much larger photoabsorption cross-section in the X-ray range compared to that of the light atoms of biological tissues. Second, ionized atoms of NPs re-emit most of the energy of the absorbed photons by secondary photons and Auger electrons during the cascade decays of vacancies in their inner electron shells [3-5]. Third, Auger electrons emitted during cascade decays of the vacancies have small mean free paths in biological tissues (1-100 nm), due to which they deposit their energy inside one cancer cell.

In [6], the Monte Carlo method was used to simulate the processes of energy re-emission by isolated gold NPs of different diameters after photoionization by photons with energies near the L_1, L_2, and L_3 ionization thresholds.

In [7], Monte Carlo simulation of secondary ionization processes and energy absorption in water around gold NPs with diameters from 2 to 100 nm after photoionization of nanoparticles by photons with energies in the 20-80 keV range was performed.

In this work, the Monte Carlo method is used to calculate the dose enhancement ratios when using gold nanoparticles as radiosensitizers in photon activation therapy.

Method of calculation

A detailed description of the Monte Carlo algorithm and the approximations used is given in [7]. Here we give a brief description with an emphasis on the geometry of the numerical Monte Carlo model used to determine the dose enhancement ratio.

A homogeneous round source of collimated monochromatic X-ray radiation with a diameter d_S 10 nm larger than the diameter of the NP d_{NP} is located at a distance of $L = 100$ μm from the center of the NP (Fig. 1). The space around the NP is filled with water and divided into concentric spherical layers with a thickness of $\Delta r = 10$ nm.

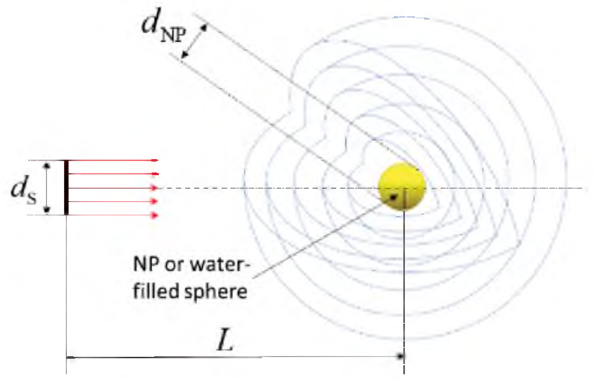

Fig. 1. Scheme illustrating the geometry of the numerical Monte Carlo experiment for determining the dose enhancement ratio

For a given energy of incident photons $h\nu_0$ and NP diameter, two simulations are carried out: in the presence of a gold NP and in its absence (the central sphere in the latter case is filled with water).

Each Monte Carlo test begins with a photoionization process, which results in the knocking out of a photoelectron from an atom (in water molecule or inside NP), and the formation of a vacancy in the ionized atom.

The routine for the simulation of the cascade relaxation is then started, and the secondary photons and electrons emitted during the cascade progression are added to the list of secondary particles for further tracking.

When simulating the tracks of secondary photons and electrons, the most probable processes in the energy region under consideration are taken into account. For photons: photoionization of atoms, for electrons: ionization of atoms by electron impact and elastic scattering.

If, as a result of secondary photoionization or electron impact ionization of any atom, a vacancy is formed in the inner shell, then the procedure for simulating the cascade decay of vacancy is launched.

The Monte Carlo test is considered complete if all secondary photons or electrons have left the interaction zone, or if their energies have become insufficient for further ionization of the medium atoms. After running a large number of tests, $N_{MC} = 10^8$, the results are processed statistically.

During the simulation, the absorbed dose in each spherical layer is determined with

$$D(r) = \frac{\Delta E_{abs}(r)}{\rho \Delta V(r)}, \qquad (1)$$

where $\Delta E_{abs}(r)$ is the energy absorbed in the acts of secondary photoionization and electron impact ionization of the atoms of water molecules located inside a spherical layer limited by radii $r - \Delta r/2$ and $r + \Delta r/2$, ρ is the density of water, and $\Delta V(r)$ is the volume of the spherical layer.

The energy absorbed by an individual atom as a result of the act of secondary ionization is calculated as the difference between the total energy of the final ion formed after ionization and subsequent cascade decay of the vacancy, and the energy of the neutral atom in the ground state.

The dose enhancement ratio (DER) at a given distance r from the NP center is calculated as the ratio of the absorbed dose in presence of the NP, and the absorbed dose in absence of the NP

$$DER(r) = \frac{D_{\text{with NP}}(r)}{D_{\text{without NP}}(r)}. \qquad (2)$$

Results and discussion

Fig. 2 shows calculated radial distributions of the absorbed dose in water near the surface of gold NPs with diameters of 2, 20 and 50 nm after absorption by the NPs of one photon with an energy of 40 keV. The highest value of the local absorbed dose is observed in the immediate vicinity of the NP surface. With increasing distance from the NP center, the absorbed dose decreases rather quickly, remaining, however, up to distances of 160–180 nm greater than the typical therapeutic value. With increasing NP diameter, the absorbed dose near its surface decreases, but at distances from the NP center of more than 200 nm, the radial distributions of the absorbed dose for NPs of different diameters become practically identical.

Calculated dependences of DER on the distance from the NP center for gold NPs with diameters of 20, 50 and 100 nm at an incident

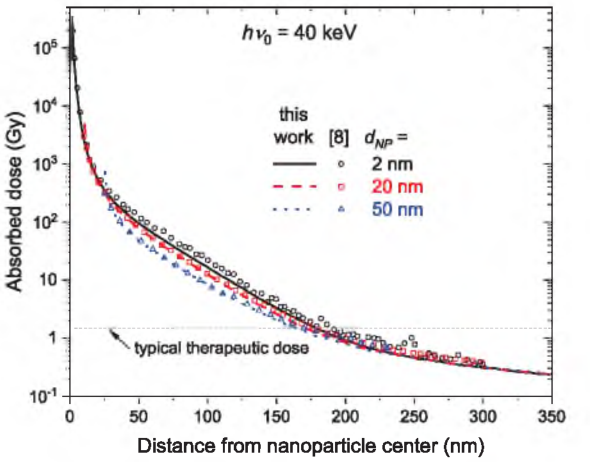

Fig. 2. Dependencies of local absorbed dose in water near the surface of gold NPs with diameters of 2, 20, and 50 nm upon absorption of one 40 keV photon. Lines – calculation of this work, symbols – results of Monte Carlo simulation [8] using Geant4-DNA code

photon energy of 40 keV (above the threshold AuL_1 ≈ 14.4 keV, but below AuK ≈ 81 keV) are shown in Fig. 3.

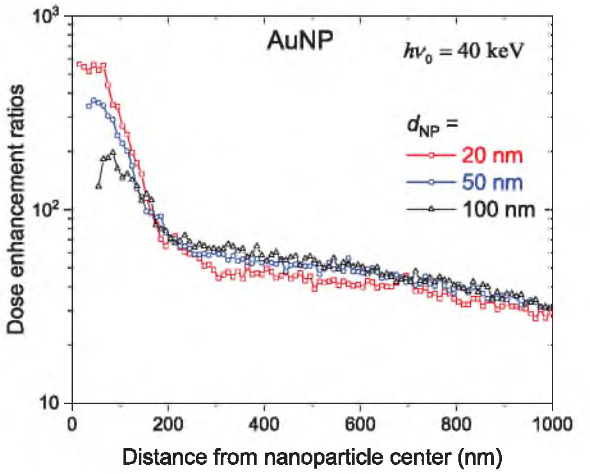

Fig. 3. Dose enhancement ratios depending on the distance from the center of a gold NP at an incident photon energy of 40 keV for NPs with diameters of 20, 50, and 100 nm. The results are normalized to the same mass ratio of gold NPs in water (0.114%)

It can be seen that the absorbed dose increases several hundred times near the NP, at distances up to 150 nm from its center. In this region the main transmitters of energy from the NP to the medium are Auger electrons emitted by ionized gold atoms during cascade decays of inner-shell vacancies. It is also seen that the NPs of smaller diameter are more effective.

Conclusion

Using Monte Carlo simulation, the dose enhancement ratios were calculated depending on the distance from the gold NP center when irradiated with X-ray photons. The obtained results may be useful in the development of methods of photon activation therapy.

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