Scientific Paper

Nanoscale dosimetric consequences around bismuth, gold, gadolinium, hafnium, and iridium nanoparticles irradiated by low energy photons

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Abstract

In the current study, nanoscale physical dose distributions around five potential nanoparticles were compared. Five potential nanoparticles including bismuth, gold, gadolinium, hafnium, and iridium nanoparticles in the form of a sphere with a diameter of 50 nm were simulated in a water medium. The MCNPX (2.7.0) Monte Carlo code with updated libraries was used for calculations of electron dose deposition and electron flux in water from 25 nm up to 4000 nm with a step of 25 nm. Also, secondary electron spectra after irradiation of nanoparticles with mono-energetic photons with energies of 30, 60, 100 keV were derived. The nano-scale distance-dose curves showed a very steep gradient with distance from nanoparticle surface up to 60 nm and after this point, a gradual decrease was seen. The dose deposition characteristics in the nano-scale were dependent on the type of nanoparticle as well as photon energy. Our results concluded that for each photon energy in the energy range of 30-100 keV, a suitable nanoparticle can be selected to boost the effect of energy deposition by low energy photon beams used in brachytherapy.

Key words: nanoparticle; radiation therapy; electron spectra; heavy atoms.

Introduction

Application of nanoparticles in medical radiation physics, medical imaging, and radiation therapy of cancer has been reported by enormous studies.¹⁻¹⁰ Several nanoparticles have been used and studied for application in nanoparticle-aided radiation therapy (NART) with the photons in the energy range of tens to hundreds of keV.^{2,5,11-17} The studies showed that photoelectrons produced through photoelectric interaction of photons with high Z atoms of nanoparticles are the major players in the extra dose delivered around the nanoparticles.^{15,18} However, after the photoelectric phenomenon, in addition to photoelectrons, the auger electrons, characteristics x-rays, other secondary electrons are released from nanoparticles and deliver a high dose near the surface of nanoparticles.^{18,19} The contribution of photoelectrons and auger and other secondary electrons in absorbed dose around a nanoparticle depends strongly on the nanoparticle size, photon energy, and atomic composition of the nanoparticle. Investigations reported that for nanoparticles with a diameter less than 10 nm the auger electron contribution in absorbed dose can be very significant but for larger nanoparticles, the auger electrons can be highly absorbed inside of nanoparticle and only high energy photoelectrons will be able to deposit their energy at several tens of nanometer from particle surface and are responsible for observed dose enhancement effect.^{6,20-25}

As it is evident the secondary electrons produced by photon beams after hitting the nanoparticle are responsible for the dose enhancement effect of NART, thus knowing their dosimetric features in the nano-scale including secondary electron energy spectra, distance-dose relationship, and secondary electrons flux variations with distance from nanoparticle can provide useful information for more optimized NART of cancers. However, it should be noticed here that the final clinical consequence of NART will be dependent on several biochemical and biological phenomena that are beyond the scope of the current paper. Only the radiation physics aspect of the dose deposition effect of some nanoparticles will be studied here.

Numerical studies including analytical and MC studies have shown the importance of photon energy and the atomic number of nanoparticles in dose enhancement factor (DEF). There are many papers on gold and bismuth dose enhancement effect. Also, gadolinium which is used extensively as an MRI contrast agent has been investigated as a radiosensitizer in radiation therapy.^{11,26,27} Moreover, hafnium oxide was used as a radiosensitizer in radiation therapy by several investigations.^{14,28} Several reliable publications state that the total dose enhancement effect of nanoparticles, in reality, is composed of three components of physical, chemical, and biological enhancement.^{19,22,29-32} It can help us to interpret the

considerable discrepancy observed between calculated DEF and observed experimental DEF for high energy photons in the MeV range where the photoelectric phenomenon reduces significantly and the Compton effect dominates. On the other hand, if only physical DEF is considered, there are many investigations with a widespread range of nanoparticle size, type, concentration, and photon energy which make the estimation of physical DEF very difficult.

Experimental electron spectroscopy for nanoparticles is a very cumbersome and sophisticated procedure. Thus, Monte Carlo (MC) modeling of single nanoparticle from the different types and for applied photon energy in brachytherapy can give more information on the nano-scale dose estimations.

To the best of our knowledge, there is no comparative study on the dosimetric properties of these nanoparticles in the literature. In the current study, five potential nanoparticles were selected based on the literature and their physical dose deposition was calculated in nano-scale for comparison purposes. We think that the results can provide new information in the selection and the design of alternative nanoparticles for radiation therapy applications. On the other hand, to provide more detailed physical information concerning the potential nanoparticles, optimize DEF, and consequently cell toxicity in conjunction with X-rays, the current study was conducted. In the current study, using MCNPX MC code a single nanoparticle made of bismuth, Gold, Gadolinium, Hafnium, and iridium was simulated and the secondary electron dose, flux, and spectra were calculated for three photon energies of 30, 60, 100 keV. Based on the provided data, the nano-scaled dose deposition of the studied nanoparticles was compared and analyzed.

Materials and Methods

In the current study, we used MCNPX (2.7.0) Monte Carlo code for scoring electron fluence, electron energy spectra, and dose deposition around a single spherical nanoparticle made of different elements including bismuth, gold, gadolinium, Hafnium, Iridium. The MCNPX code can simulate the transportation and tracking of secondary electrons down to 1 keV energy. The range of 1 keV electron could be around 10 nm in water. The simulation geometry was based on the study of Leung et al.²⁴ depicted in **Figure 1**. To ensure the geometry accuracy and monitoring the electron and photon tracks the visual editor of MCNPX code was used. A spherical nanoparticle with a radius of 25 nm was located at the center of the simulation space. Then, multiple concentric spherical surfaces with 25 nm increments were simulated around nanoparticle to score electron fluence and provide shell-like cells for dose scoring around it. A circular-planar photon source with a radius of 25 nm to irradiate the nanoparticle uniformly was defined at the distance of 5 nm from the nanoparticle. The photons trajectories were set to be parallel and impinging on nanoparticles homogeneously.

Three quantities were tallied for each nanoparticle type and three energies of mono-energetic beams of 30, 60, 100 keV. The selection of the nanoparticle types was based on the previous studies, which reported potentials and advantages for these nanoparticles. However, iridium with the highest density was selected by this research for the first time due to its atomic number and density. Studied nanoparticles comprised of Bismuth ($Z = 83$, density = 9.78 g/cm^3), Gold ($Z = 79$, density = 19.32 g/cm^3), Gadolinium ($Z = 64$, density = 7.89 g/cm^3), Hafnium ($Z = 72$, density = 13.31 g/cm^3), Iridium ($Z = 77$, density = 22.56 g/cm^3).

For photoelectrons and auger electrons coming out from the nanoparticle, fluence and energy spectra scoring were performed using F2 tally which calculates electron crossing a surface in terms of number per cm^2 for the surface of the nanoparticle as well as other concentric spherical surfaces with radii starting from 50 nm with an increment of 25 nm up to 4000 nm. Also, the dose delivered to the peripheral cells around the nanoparticles was calculated using *F8:e tally. for excluding the dose deposition from primary and scattered photons, the importance of photons was set to be zero for all scoring cells except the first cell where the photon source was located. The concentric cells were filled with water with a density of 1 g/cm^3 in dose deposition calculations.

Figure 1. Schematic diagram of Monte Carlo simulated geometry

Results

Figures 2-4 show the absorbed dose variation with distance from nanoparticle's surface with a step of 25 nm for five studied nanospheres and three photon energies. In **Figure 2** absorbed dose from electrons with distance has been depicted for the photon energy of 30 keV. In **Figure 2A** as it can be seen the dose drops exponentially which shows itself as a straight line on a semi-log plot. It starts from around 10^{-3} at a distance of 37.5 nm and decreases to 10^{-9} - 10^{-10} scale at 62.5 nm. At the distance of 62.5 nm, there is a breaking point for all nanoparticles. And, the absorbed dose is reduced at a slower pace with distance as it was shown in **Figure 2B**. In **Figure 2B**, the absorbed dose from 100 to 4000 nm has been shown. For example, the dose falls from 4.73×10^{-9} Gy at 100 nm to 2.52×10^{-12} Gy at 4000 nm. Comparing the nanoparticles, iridium and gold deliver the higher doses and the same dose-distance pattern, while the bismuth is very close to them but it gets lower especially at long distances from nanoparticles surface. After them, hafnium and gadolinium nanoparticles deliver dose in descending order.

Figure 2. The calculated absorbed dose variation with distance from a single spherical nanoparticle with the diameter of 50 nm for impinging photons with energy of 30 keV. (A) At distances from 37.5 to 137.5 nm (B) at distances from 100 to 4000 nm.

Figure 3. The calculated absorbed dose variation with distance from a single spherical nanoparticle with the diameter of 50 nm for impinging photons with energy of 60 keV. (A) at distances from 37.5 to 137.5 nm (B) at distances from 100 to 4000 nm.

In **Figure 3**, the absorbed dose from electrons with distance has been depicted for the photon energy of 60 keV. In **Figure 3A** for the distance of 37.5 to 62.5 nm where a steep gradient of dose fall-off exists and like the 30 keV case, the turning point for dose reduction locates at 62.5 nm. The highest dose is seen for gadolinium and then bismuth nanoparticles. And the lowest dose was found for hafnium nanospheres. In **Figure 3B** the dose was depicted for 100 to 4000 nm and the curves follow a different pattern after 2000 nm compared to 30 keV. As can be seen that the bismuth and gadolinium, have comparable dose deposition properties till 2000nm. But after 2000 nm it reduces sharply and reaches hafnium at 2500 nm.

In **Figure 4**, the calculated absorbed doses from secondary electrons with distance have been depicted for the photon energy of 100 keV. As can be seen in **Figure 4A** in short distances, gold and iridium nanospheres have the highest values which are very close together in terms of dose deposition with distance. While the lowest dose deposition was found for gadolinium.

Figure 4. The calculated absorbed dose variation with distance from a single spherical nanoparticle with the diameter of 50 nm for impinging photons with energy of 100 keV. (A) at distances from 37.5 to 137.5 nm (B) at distances from 100 to 4000 nm.

However, the same turning point of 62.5 nm was seen for this energy of photons like the previous energies. For long distances, gold and iridium keep their ranks compared to other nanospheres. But the dose deposition curves exhibits not a smooth and continuous reduction with distance and they fluctuate with distance for each nanoparticle.

Figure 5 illustrates the secondary electron flux per initial photon impinging on Bismuth, Gold, Gadolinium, Hafnium, and Iridium nanospheres. In **Figure 5A** where the results of 30 keV photons were shown, the electron flux for iridium and gold nanospheres was the highest among the studied atoms. While the electron flux for gadolinium showed the lowest value. For photon energy of 60 keV, the gadolinium had the highest secondary electron flux up to 1800 nm. Then it went down rapidly and at the distance of 2200 nm has the lowest electron flux among the studied nanospheres. But for other nanospheres, the electron flux decreased continuously without sudden variations like gadolinium with distance. Up to 2000 nm, hafnium and bismuth have the lowest secondary electron flux among studied nanoparticles.

Figures 6-8 show electron energy spectra for photon energies of 30, 60, 100 keV respectively. In **Figure 6**, the secondary electron spectra were illustrated for 30 keV photons. As can be seen there three groups of electrons in the energy spectra. The first group consists of the auger and multiply scattered electrons from 1 keV to 12 keV, and the second and third groups are photoelectrons from M- and L- shells. In **Figures 7 and 8**, the energy spectra of secondary electrons have been depicted for 60 and 100 keV photons. The location of low-energy auger electrons does not change considerably, but due to higher photon energy, the energy of photoelectrons is increased and other peaks such as auger electrons from K-shell are seen in the spectra.

Figure 5. The calculated electron fluence with distance from the nanoparticle for three different energies of photons. (A) 30 keV (B) 60 keV (C) 100 keV

Figure 6. Energy spectra of secondary electrons exiting the nanoparticle surface for photon beam of 30 keV.

Figure 7. Energy spectra of secondary electrons exiting the nanoparticle surface for photon beam of 60 keV.

Figure 8. Energy spectra of secondary electrons exiting the nanoparticle surface for photon beam of 100 keV.

Discussion

Our results were in line with the results of McMahon et al.³³ as it was reported that secondary electrons were composed of photoelectrons and auger electrons with an energy around 10 keV with many less than 1 keV. However, due to the electron energy cutoffs of 1 keV for the MCNPX code, we did not score auger less than 1 keV in our simulations. On the other hand, their study indicated that compared to photoelectrons, auger electrons were more effective components in dose enhancement around nanoparticles up to 200 nm for gold nanoparticle with a diameter of 20 nm and photon energy of 40 keV. Our finding was in accordance with their results. In **Figures 2-4**, there was a higher dose deposition region up to 60 nm, which can be attributed to low energy auger electrons, which diminished rapidly with distance, and then high energy photoelectrons are the prominent component of dose deposition around nanoparticles. And, according to McMahon et al only auger electrons of L-shell contribute to the dose deposition beyond 200 nm distance from nanoparticle surface. The observed differences in dose deposition around nanoparticles can be attributed to the electron energy cutoffs used in two studies and also differences in electron transport algorithms and libraries between MCNPX and GEANT codes.

The atomic number of an element impacts on K- and L-shell binding energy of its electrons and if the photon energy is slightly higher than electron binding energy, the probability of photoelectric interaction will be significantly high. However, photoelectric interaction with other shells such as M has a lower probability. Our results indicated that the deposition of energy around the NP is higher near its surface and within the distance of 100 nm, it hastily drops by nearly an order of magnitude.

In **Figures 2-4**, it was shown the very strong dose gradients around nanoparticles up to 60 nm from nanoparticle surface, which was independent of photon energy and slightly varied with nanoparticle type. For gadolinium, it is in agreement with the finding of Delorme et al.¹¹ which showed the same steep gradient for small nanoparticles as small as 1 nm and it was extended to less than 100 nm for nanoparticle with a diameter of 50 nm.

The electron flux with distance curves indicated a close similarity between dose-distance and electron flux-distance for all energies and nanoparticles. Thus, the electron flux variation with distance had the same scenario as dose deposition concerning the nanoparticle type and photon energy.

We obtained the electron energy spectra for five studied nanoparticles, in which the energy spectrum for gadolinium was consistent with the results of published articles.^{11,12,34} The origin of peaks in all calculated electron energy spectra was identified using atomic relaxation tables and their binding energies. In an in silico and in vitro study by Delorme et al.,¹¹ the gadolinium nanoparticles were used for radio-sensitization in a range of photon energies from 30 keV to 1.25 MeV. The

simulations' results were not in agreement with the in vitro finding considering the photon energy effect. However, in silico results showed that maximum DEF found at 65 keV and 58 keV for nucleus and cytoplasm respectively. Besides, optimal X-ray energy above Gd K-edge was a key factor for increased dose around nanoparticle for photons in the keV range. Our finding was in complete agreement with their modeling results and gadolinium showed higher dose deposition for the photon energy of 60 keV.

In another study by Maggiorella et al.¹⁴ which was done on hafnium oxide nanoparticles and their application in radiation therapy, they used photons in keV and MeV ranges for both MC, in vitro and in vivo studies. They did not provide any information regarding the nano-scaled dosimetric features of hafnium oxide nanoparticles, but they showed its considerable DEF for the 200 keV photon beam. We were not able to compare our results with their findings.

As it was stated by other studies the Auger electrons are effective components in dose deposition around small nanoparticles. In the current study, for the nanoparticle with the diameter of 50 nm, the effect of auger electrons in dose deposition was significant around nanoparticle which was in agreement with the results of McMahon et al.³³, but in contrast with another study by Douglass et al.³⁵ which showed that auger electron contribution in dose was insignificant. This discrepancy arises from the size of nanoparticle of 400 nm which was used in their study.

Comparing the nanoparticles showed promising potentials for iridium nanoparticles in enhancing the dose of low energy photons which was comparable to gold and bismuth in some photon energies. Bismuth and gold had a higher dose deposition for the energies of 30 and 100 keV photon beams due to the proximity of photon energies to their L- and K-electrons and the higher probability of photoelectric effect in these energies.

Conclusion

The application of high atomic number (Z) nanoparticles in radiation therapy has been proposed as a promising method for the treatment of solid cancers. Our finding showed a promising potential for iridium nanoparticles in dose enhancement of low energy photons which was comparable to gold and bismuth. Also, the gadolinium nanoparticle was very effective in dose enhancement for the photon energy of 60 keV. The dose deposition in the nano-scale was dependent on the atomic number of nanoparticle as well as photon energy. Thus, it can be concluded that for each photon energy, a suitable nanoparticle based on K-edge or L-edge binding energy of orbital electrons can augment the dose enhancement of nanoparticles irradiated by low energy photon beams used in brachytherapy.

Acknowledgments

The project was conducted in the Molecular Medicine Research Center and Department of Medical Physics of Tabriz University of Medical Sciences.

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