Monte Carlo Simulation on the Imaging Contrast Enhancement in Nanoparticle-enhanced Radiotherapy

Ferdos Albayedh, James C. L. Chow[1,2]

Department of Physics, Ryerson University, [1]Princess Margaret Cancer Centre, UHN, [2]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

Abstract

This study focused on the imaging in radiotherapy by finding the relationship between the imaging contrast ratio and appropriate gold, iodine, iron oxide, silver, and platinum nanoparticle concentrations; the relationship between the imaging contrast ratio and different beam energies for the different nanoparticle concentrations; the relationship between the contrast ratio and various beam energies for gold nanoparticles; and the relationship between the contrast ratio and different thicknesses of the incident layer of the phantom including variety of gold nanoparticles (GNPs) concentration. Monte Carlo simulation was used to model the gold, iodine, iron oxide, silver, and platinum nanoparticle concentration which were infused within a heterogeneous phantom (50 cm × 50 cm × 10.5 cm) choosing different concentrations (3, 7, 18, 30, and 40 mg), and beams (100, 120, 130, and 140 kVp) correspondingly that were delivered into the phantom. The results showed obvious connection between the high concentration and having a high imaging contrast ratio, low energy and a high contrast ratio, small thickness, and a high contrast ratio. The superior nanoparticle obtained was GNP, the better concentration was 40 mg, the better beam energy was 100 kVp, and the better thickness was 0.5 cm. It is concluded that our study successfully proved that medical imaging contrast could be improved by increasing the contrast ratio using GNP as the finest choice to accomplish this improvement considering a high concentration, low beam energy, and a small thickness.

Keywords: Nanoparticle concentration, contrast ratio, medical imaging, Monte Carlo simulation, nanoparticle, photon and electron beams, tumor thickness

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Introduction

In radiation dose delivery, the primary aim is to maximize the dose conformity at the tumor, while at the same time, sparing the surrounding normal tissues. This aim can be achieved using heavy atom radiosensitizer/contrast agent such as nanoparticles. This agent enhances the contrast of the tumor in medical imaging, and hence increases the accuracy of radiation beam targeting. In addition, the agent enhances the dose absorption in the tumor and therefore the cancer cells will be destroyed as an outcome. The timely development of heavy atom radiosensitizer improves the imaging contrast between the healthy and cancerous cells as well as the tumor control following radiotherapy. It has been shown that the dosage transmitted to a tumor among photon-based radiotherapy can be improved by loading high atomic number (Z) materials, for example, gold (Au, Z = 79) into the tumor.[1-4] It brings about more prominent photoelectric absorption inside the tumor than in encompassing tissues, in such the result will have a lower risk of normal tissue damage. Gold nanoparticles (GNPs) can increase the contrast of the tumor in medical imaging.[5-7] This helps target the cancer cells, and enhances the accuracy of the process. In addition, it increases the dose absorption in the tumor, which kills the cancer cells as an outcome.[8-10]

The GNP can enhance radiation dose according to the energies of ionizing photons, which can produce different types of interactions arise between the photons and GNPs and the most effective process in medical imaging is the photoelectric effect with energy from 10–500 keV. In the photoelectric interaction between photons and GNPs, a vacancy in a K, L, or M shell following photoelectric absorption results in de-excitation of the atomic system either by characteristic X-ray or Auger

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Address for correspondence: Dr. James C. L. Chow, Princess Margaret Cancer Centre, UHN, Toronto, ON, Canada. Department of Radiation Oncology, University of Toronto, 700 University Avenue, Toronto, ON M5G 1Z5, Canada. E-mail: james.chow@rmp.uhn.on.ca

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electron emission. The fluorescence yield gives the relative probability of these de-excitation processes. The fluorescence yield depends on the atomic number, being small for light atoms and large for heavy atoms such as gold.[11,12]

For the development of nanoparticle-enhanced radiotherapy, Hainfeld *et al.*[1] carried out *in vivo* test using mice and 250 kVp X-rays which exhibited that GNPs could be securely controlled and utilized. GNPs were infused into mice bearing mammary carcinomas, and it was found that the addition of GNPs greatly increased the survival rate of mice by 86%, compared to 20% with the irradiation alone and 0% with the GNP addition alone. Hainfeld *et al*.[13] then further demonstrated that GNPs were effective while treating exceedingly forceful squamous cell carcinoma utilizing the little creature display. Therefore, GNP-enhanced radiotherapy uses GNPs taken up by a tumor under radiation beam to improve the physiological active, viable measurements, or treatment result. Cho[14] estimated dose enhancements with different photon beam energies. He created a mixture of gold and tissue as per results from Hainfeld *et al.*[13] and found that the dose enhancement over the tumor volume was over a factor of two for the 140 kVp photon beam. Cho concluded that further study using a more sophisticated computational model would be necessary.

The utilization of GNPs as dosage enhancer appears to be more encouraging than microspheres and other materials for two essential reasons. In the first place, gold has a higher *Z* number than iodine (I, Z = 53) or gadolinium (Gd, Z = 64), while indicating little toxic quality, up to no less than 3% by weight, in either the rat or human tumor cells. Since the atomic photoelectric cross-section is roughly corresponding to $Z^4 \sim Z^{4.6}$, the photoelectric communication likelihood connected with a gold-stacked tumor, for instance, is higher by not less than an element of 2 than that linked to a gadolinium-stacked tumor, accepting a similar concentration of materials in the tumor and a similar radiation quality. Along these lines, gold unmistakably prompts to a higher tumor dose compared to other materials such as iodine or gadolinium. Second, nanoparticles give a superior system than microspheres, as far as delivering high-*Z* materials to the tumor, conquering a portion of the troubles found among an earlier attempt utilizing gold microspheres.[15] It would be tough to produce high-*Z* materials consistently all through the tumor with microspheres, fundamentally due to the more prominent size of the particles. Then again, nanoparticles are smaller by characterization (e. g., 1 – 10 nm) than a distinctive cutoff size of the pores (e. g., up to 400 nm) in the tumor vasculature, so they can take the full favorable position of the purported “leaky” vasculature of tumors. Accordingly, nanoparticles may have an excellent opportunity to enter into the tumor and to be all the more consistently disseminated all through the tumor.[14,16]

As yet, the usage of GNPs has not been all around considered, especially for necessary radiotherapy conditions considering medical imaging. Although imaging contrast enhancement is predictable according to the atomic number of the contrast agent and photon beam energy, using Monte Carlo method can show the relationship between the contrast enhancement and nanoparticle parameters in much greater detail. The aims of this study are as follows: (1) To determine the relationship between the imaging contrast ratio and appropriate gold, iodine, iron oxide, silver and platinum nanoparticle concentrations; (2) to assess the relationship between the imaging contrast ratio and different beam energies for the various nanoparticle concentrations; (3) to evaluate the relationship between the imaging contrast ratio and various beam energies for GNPs; and (4) to investigate the relationship between the contrast ratio and different thicknesses of the incident layer of the phantom including the variety of GNP concentration.

Materials and Methods

Monte Carlo simulation (the EGSnrc code) was used to predict the imaging contrast enhancement in this study.[17] The EGSnrc can be applied to carry out Monte Carlo simulations of joined photon–electron transport, for particle energies that range from 1 keV to 10 GeV.[18] The EGSnrc-based BEAMnrc code included is a component that involves the dose scoring utility DOSXYZnrc to approximate radiation dose in a voxel geometry.[19] DOSXYZ is an all-purpose Monte Carlo EGSnrc user-code for three-dimensional immersed dose calculations.[20] The present examination was directed with a few phantom test cases that simulated average computed tomography imaging utilizing 100, 120, 130, and 140 kVp photon beams. For most situations, it was established that GNPs were in a layer which assumable to be the tumor. The geometry used for the external beam cases simulated a tumor infused with GNPs within a tissue phantom (50 cm × 50 cm × 10.5 cm).

The medium in the phantom is defined by choosing the first layer to be water and the second layer has a material of a particular concentration level of the GNP plus water. The source parameters consist of the incident particles, which is a photon beam and the type of source will be a full phase-space file, and in that file, the energy will be chosen between 100 and 140 kVp. First, data were collected from only the first layer without the second layer of the phantom, and it was accounted as the background absorbed dose given the four different beam energies. Second, data were collected from the second layer of the phantom with the addition of GNP, Iodine (I), iron oxide (Fe_3O_4), platinum (Pt), and silver (Ag) considering different beam energies and different concentrations, then considering different thicknesses with the addition of GNP.[21] The aim of this procedure is to collect the absorbed dose so that the contrast ratio can be calculated afterward. For the first section of the process, the materials of the phantom selected were only water. The second part of the procedure consists running a simulation with the addition of different nanoparticles to the second volume choosing (3, 7, 18, 30, and 40 mg), and accounting 100, 120, 130, and 140 kVp correspondingly. The target value was obtained for each case, and then the imaging contrast ratio was calculated.

The imaging contrast ratio was found using the equation by C = (target value − background value)/background value. In labels, $C = (I_t - I_b)/I_b$, where I_t is the transmitted X-ray intensity and I_b is the transmitted background intensity. These intensities are calculated by Monte Carlo simulation using the Beer–Lambert Law: $I_t = I_o\, e^{-\mu x}$, where I_o is the incident intensity and x represents the thickness of the matter. The mass attenuation coefficient (μ) is the sum of the three interactions between X-ray photons and traversed matter in the proper energy range.[22]

It is observed that the mass attenuation coefficient increases with increasing atomic number of elements in a periodic table and decreases with increasing energy of X-ray. Numerous hypothetical and trial studies have additionally demonstrated that higher atomic number elements show superior X-ray attenuation ability at typical or significantly higher working tube voltages because of the higher K-edges of heavy elements. The K-edges of heavy elements are within the diagnostic X-ray energy range which can be seen as sudden increases in attenuation coefficient curves at those discrete energies. Along these lines, a contrast medium in light of elements with a higher atomic number will be more profitable as far as inherent contrast, bring down measurement prerequisite, and lower radiation exposure to patients. Even though, long-term exposure and high doses can be endeavored to expand X-ray contrast, it is not recommended for therapeutic application. Rather, infusing a high-contrast material into the imaged specimen can develop the imaging contrast.

Results

Relationship between imaging contrast ratio and concentration of different nanoparticles

Under the delivery of 100 kVp beam, Figure 1 illustrates that the imaging contrast ratio for all nanoparticles was observed to be different for each. The GNP showed the highest contrast ratio compared to all the nanoparticles, and the closest value of contrast ratio to GNP calculated was platinum nanoparticle but the GNP was observed to be slightly higher than platinum nanoparticle. For iodine nanoparticle and silver nanoparticle, their values of imaging contrast ratio were not as close as platinum to gold. However, the difference was not huge compared to iron oxide nanoparticle. In Figure 1, it was noticed that the iron oxide had the lowest imaging contrast ratio compared to all.

Relationship between imaging contrast ratio and beam energy

Figure 2 demonstrates the assessment of the imaging contrast ratio of 40 mg concentration for distinctive nanoparticles and changed beam energies. It was observed that once again the contrast ratio of all nanoparticles was different from one another. The GNP conquests again in this evaluation and it was observed that the contrast ratio was higher than all of the various nanoparticles in all cases except for one case, in which it was less than platinum nanoparticle by a minor difference of 0.0004 for 120 kVp. Correspondingly, the GNP was greater than silver nanoparticle by roughly 1 for 100, 120, 130, and 140 kVp. In addition, Figure 2 showed that iodine nanoparticle had the lowest imaging contrast ratio.

Relationship between imaging contrast ratio and gold nanoparticles with various concentrations

Figure 3 shows that the highest imaging contrast ratio obtained was for 40 mg concentration in all cases considering all beam energies. To demonstrate, it was observed that the contrast ratio of 40 mg concentration with the delivery of 100 kVp was higher than the contrast ratio of 30 mg concentration by almost one. Moreover, for 120 kVp, the contrast ratio of 40 mg concentration was seen to be higher than the contrast ratio of 30 mg concentration.

Relationship between imaging contrast ratio and beam energy with gold nanoparticles in various concentrations

In Figure 4, the imaging contrast ratio was found to be higher for 100 kVp among all concentrations. Considering the imaging contrast ratio for 120 kVp, the contrast ratio for 100 kVp beam was observed to be higher by about 0.05 for 3 mg as well as higher by 0.1 for 7 mg. Then, considering the imaging contrast ratio of 130 kVp, the contrast ratio of 100 kVp beam was found to be higher by around 0.08 for 3 mg as well as more by 0.2 for 7 mg.

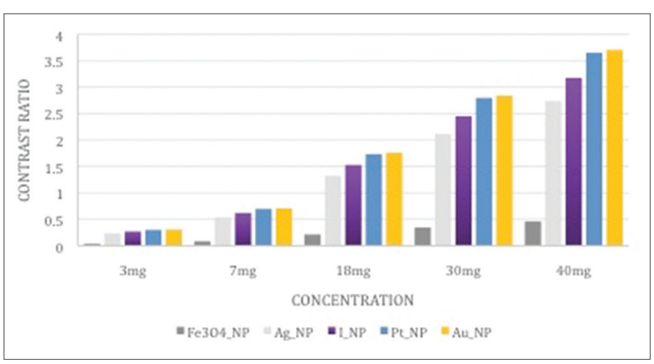

Figure 1: Relationship between contrast ratio and different nanoparticles concentration (mg) with the delivery of 100 kVp beam

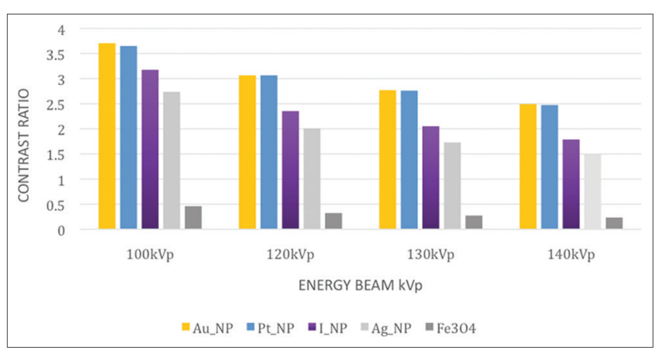

Figure 2: The relationship between contrast ratio and different kVp energies delivered to a phantom with 40 mg concentration of nanoparticles

Relationship between imaging contrast ratio and different thicknesses of the incident layer of the phantom including gold nanoparticle with various concentrations

Figure 5 shows that the highest imaging contrast ratio observed was for 0.5 cm thickness in all cases considering all different concentrations. The contrast ratio for 0.5 cm thickness with 3 mg was seen to be higher than that for 1 cm thickness by about 0.006. For 7 mg, the contrast ratio for 0.5 cm thickness was higher by 0.02. The imaging contrast ratio for 3 mg concentration was found to be higher for 0.5 cm thickness than for the 1.5 cm thickness by about 0.02.

Discussion

From Figures 1-2, it is evident that the imaging contrast ratio of GNPs is the highest among all the materials for all cases, even though corresponding the values for platinum nanoparticles are not much different since their atomic numbers are similar being 79 and 78 for GNPs and paltinum nanoparticles respectively. As explained in the beginning, the photoelectric interaction between photons and GNPs results in a vacancy in K, L, or M shell in the atom which in turn results in de-excitation of the atomic system by characteristic X-ray or Auger electron emission. The comparative chance of this de-excitation process is specified by the fluorescence yield, which is the emission of light from a material that has absorbed light or radiation in this study. The fluorescence yield highly depends on the atomic number; higher the atomic number is, the higher the fluorescence will be. Therefore, the imaging contrast will increase if the emission of the light increases.

It can be noticed from Figure 4 that the largest value of GNP concentration, which was 40 mg, provided the highest imaging contrast ratio compared to all concentrations in all cases taking into account all beam energies. Specifically, the contrast ratio for the 40 mg of GNP was the highest among all nanoparticles. According to the above explanation, it can be understood that higher the concentration of GNP, the more photoelectric absorption there will be, and therefore, the more emission of fluorescence. Hence, the contrast ratio will increase.

For relationship between the imaging contrast ratio and beam energy considering various nanoparticle concentrations, it was discussed previously that the highest contrast ratio was observed for 40 mg concentration, specifically for GNPs. It can be added to it, that it was shown in Figure 3 when finding the relationship between the imaging contrast ratio and energy, the highest contrast ratio was obtained in the case of 100 kVp beam as compared to all other energies.

The thickness of the second layer of the phantom, where the absorbed dose is detected was altered from 0.5 to 2.5 cm. The study aimed to know the relationship between the imaging contrast ratio and the thickness considering different concentrations as well as various beam energies. GNP was chosen in this assessment due to its better imaging contrast ratio among all the nanoparticles. According to the previous estimates in this study, 40 mg proved to provide the highest contrast ratio in all cases in addition to the various thicknesses. Moreover, 0.5 cm thickness was found to give a better imaging contrast ratio in all circumstances. On top of it, with the delivery of 100 kVp, 0.5 cm thickness provided the best imaging contrast ratio in comparison to all cases. The reason is smaller the thickness, the better the contrast ratio because GNP will be highly concentrated in a smaller thickness than in a larger thickness. According to the explanations above, it is expected to have a higher imaging contrast ratio when the concentration increases and when the beam energy decreases. Since the 100 kVp beam had the best contrast ratio, especially for 40 mg concentration, Figure 5

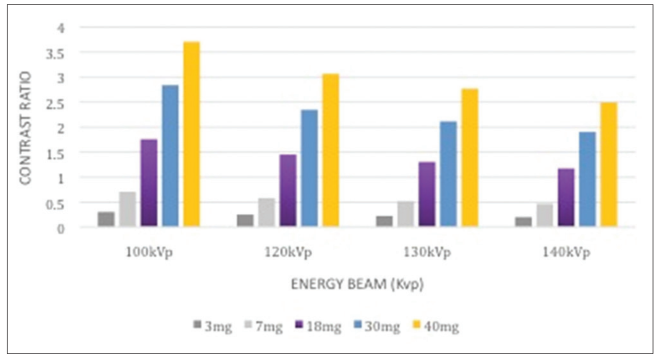

Figure 3: The relationship between contrast ratio and gold nanoparticle concentration (mg) with the delivery of different beam energies (kVp)

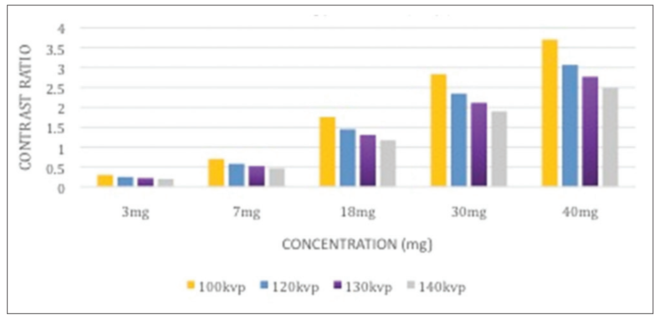

Figure 4: The relationship between imaging contrast ratio and different (kVp) energies delivered to a phantom with different gold nanoparticle concentrations (mg)

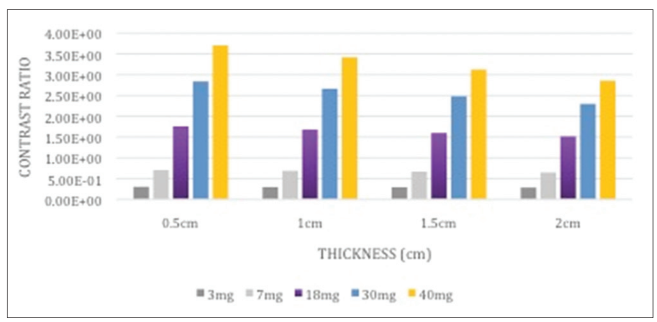

Figure 5: The relationship between imaging contrast ratio and different thicknesses (cm) with different gold nanoparticle concentrations (mg) with the delivery of 100 kVp beam energy

shows the best obtainable relationship between imaging contrast ratio and thickness.

Conclusions

It is concluded that GNP is the best option to be chosen as an imaging contrast agent due to the results obtained. Monte Carlo results showed that GNPs had the highest imaging contrast ratio compared to all other nanoparticles used in this study. In addition, it was proven that the higher the concentration, the higher contrast there will be; the lower the beam energy, the higher the contrast obtained; and the smaller the thickness of the tumor, the higher the contrast observed as well. This study provided new information on imaging contrast enhancement dependent on different parameters of nanoparticles such as concentration and nanoparticle materials. The results in this study should be very useful for researchers in GNP-enhanced radiotherapy in conducting the preclinical and clinical experiment and model.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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