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Monte Carlo study on the gold and gadolinium nanoparticles radio-sensitizer effect in the prostate ^{125}I seeds radiotherapy

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Abstract

Monte Carlo and TL dosimetry applied to the characterization of ^{125}I brachytherapy with a different design with other ^{125}I seeds. In a water phantom, lattice configuration simulated with ^{125}I seed in the center and 10 nm gold and gadolinium nan-particle filed voxels. This simulation conducted to the characterization of the nano-particles DEF in low energy and prostate tissue. To study of the prostate brachytherapy, a humanoid computational phantom developed by CT slices applied. KTMAN-2 computational phantom contains 29 organs and 19 skeletal regions and was produced from cross-sectional x-ray computed tomography (CT slices) images. The simulated seed was ^{125}I seed having an average energy of 28.4 keV for photons, a half-life of 59.4 days. DEF factor in the seed radiation energy (28.4 keV) DEF factor was found to be two times higher for the gold nano-particles. It was revealed than gold-nano-particles posing Z about 1.24 times higher than gadolinium led to around 200% DEF increasing in the same conditions and the nano-particles size. It was concluded that in low energy sources brachytherapy, photoelectric is dominant in the presence of relative high element nanoparticles. This leads to a high dose increasing in some micro-meters and causes a dramatic dose gradient in the vicinity of a nano-particle. This dose gradient effectively kills the tumor cells in continuous low energy irradiation in the presence of a high Z material nano-scaled particle. Application of gold nano-particles in low energy brachytherapy is recommended.

Key words: Monte Carlo; gold nano-particles radiotherapy, brachytherapy; TLD; brachytherapy seed; Dose Enhancement Factor.

Introduction

Brachytherapy in cancer treatment, palliation on cure is an important modality of radiation therapy. It is associated with some advantages; low energy special design, continuous irradiation and rapid dose drop at a low distance from the source. Different brachytherapy sources with own design have been studied utilizing Monte Carlo (MC) simulation and experimentally by different dosimeters [1-7]. Among the sources, ^{125}I seed also has designed and used to cancerous tissue treatment [8-12]. Villagas et al. [9] conducted a study to characterize the magnitude of the spread in specific energy deposition per cell and reported increasing in micro-dosimetric value with decreasing target size and decreasing energy of the radiation quality. They also reported that in clinical relevant dose the maximum spread dose 6% for ^{125}I . On the other study, Teles et al. [13] characterized two ^{125}I and ^{103}Pd brachytherapy seeds at different depths in the water. Bradley et al. [9] in a study on the prostate low dose rate (LDR) radiotherapy reported it with excellent outcome and reported it superior

radiation dose escalation and conformity compared to external beam radiation therapy (EBRT). Davis et al. [14] chose ^{125}I LDR brachytherapy because of their reported reason; the notable difference between the sources is the longer half-life ($t_{1/2}$), or rate of radioactive decay for ^{125}I ($t_{1/2} = 59.4$ days) relative to ^{103}Pd ($t_{1/2} = 17$ days) or ^{131}Cs ($t_{1/2} = 9.7$ days). The lower physical doses that are commonly prescribed with ^{103}Pd and ^{131}Cs are primarily a consequence of their shorter half-lives and are based on consensus review of the clinical literature [14]. Application of the radio-sensitization agents may make the method better. Some others studied ^{125}I brachytherapy in different organs seated malignancies [15-17]. Our aim in this study was to the characterization of ^{125}I brachytherapy seed radiation and dose in the prostate brachytherapy in the presence of some gold and gadolinium nano-particles. This investigation conducted to the radio-sensitizer effect of the nano-particles in the ^{125}I prostate brachytherapy as well as the seed radiation characterization.

Figure 1. The schematic representation of geometry used for dose scoring around the ^{125}I seed. The lattice card of MCNP5 code was used to produce $2 \times 2 \times 2 \text{ mm}^3$ voxels around the seed. Dimensions of the seed were explained in this figure and readers can find the data applied to simulate the ^{125}I seed. The seed is positioned at the center of the water phantom.

Materials and Methods

MCNP5 MC code (Los Alamos National Laboratory) was applied for the simulations and calculations entire this work. The simulated ^{125}I seed radiation and geometry simulated and schematically shown in **Figure 1**. Titanium cylindrical capsule including Silver rod in the center with 0.050 cm diameter and length of 0.280 cm with a radioactive layer and capsule length and diameter simulated in 0.455 cm and 0.080 cm respectively simulated for problem calculations. The radiation spectrum of ^{125}I and cross-section of TG43U1 publication [18] were used for source definition in the MC model. The ^{125}I seed had an average energy of 28.4 keV for photons, the half-life of 59.4 days. Our calculations and simulations were done according to the updated AAPM task group report No. 43. Using the MCNP5 MC code calculation and its capability of the radiation characteristics estimation (Tallies), dosimetric characterization of the simulated seed such as dose rate constant (DRC), geometry function $g(r)$, radial dose function and anisotropy function conducted in presence and absence of the nano-particles. A water phantom with a dimension of $10 \times 10 \times 10 \text{ cm}^3$ including some nanoparticles (7 mg per gr of water in the voxels, separate modeling for gold and gadolinium) and seed in its center were modeled. The modeled water phantom including source was shown in **Figure 2**. In order to calculate deposited dose and dose enhancement by the nano-particles around the seed, the lattice card was used and the water phantom was divided into some voxels with a dimension of $2 \times 2 \times 2 \text{ mm}^3$. *F8 tally of Mc code used in data card to scoring the dose deposition which calculates the energy in terms of MeV per initial source photon or particle in each scoring cell. All data for dosimetric characterization was extracted from dose distribution data around the modeled seed in the water in the presence and in the absence of the nanoparticles.

For dose enhancement calculations, the modeled seed was positioned in the center of the prostate gland of the phantom (Korean man computational phantom). Additionally, a concentration of 7 mg of the nanoparticle per gr of water in diameter of 10 nm was uniformly simulated in the prostate tissue using lattice and universe card properties in MCNP5 MC code separately for the gold and gadolinium nano-particles. MC calculated doses considered as relative and also for

Figure 2. The schematic representation of geometry used for dose scoring around the ^{125}I seed. The lattice card of MCNP5 code was used to produce $2 \times 2 \times 2 \text{ mm}^3$ voxels around it. the seed. Dimensions of the seed were explained in this figure and readers can find the data applied to simulate the ^{125}I seed. The seed is positioned at the center of the water phantom.

absolute dose calculations, a prescribed dose of 145 Gy was considered. The initial dose rate of a $21.0 \text{ cGy} \cdot \text{h}^{-1}$ also was considered.

Applied humanoid computational phantom in the current study named as Korean man or (KTMAN-2) was used to simulate the seed implementation inside its prostate cell. **Figure 3** shows the used phantom in this study. The KTMAN-2 computational phantom contains 29 organs and 19 skeletal regions and was produced from cross-sectional x-ray computed tomography (CT slices) images. It is made of $300 \times 150 \times 344$ voxels (3D cells) with a spatial resolution of $2 \times 2 \times 5 \text{ cm}^3$ and, height and weight of 1.71 m and 70 kg respectively. For dose enhancement calculations, the tissue inside the voxels of the prostate gland was filled with GNPs using Lattice card in MCNP5 code. The dose calculations were conducted for voxels of prostate gland including two types of nano-particles (gold and gadolinium) and without nano-particle. Derived data are presented and compared to make a conclusion.

Figure 3. (a) utilized humanoid KTMAN-2 (Korean Man) computational phantom lateral view. The prostate gland of the phantom marked. (b) The cross-sectional plot from Korean man voxel phantom (KTMAN-2 Plot in MCNP5). The densities of prostate tissue considered as 1.025 g/cm^3 in the KTMAN-2 humanoid phantom (Korean Man phantom) development using the CT slices. Prostate gland showed with “P” character.

Results and Discussion

Modeling the ^{125}I seed with described design and utilizing MCNP5 MC code, dose rate constant, geometry and radial dose functions were calculated for the modeled seed. Our modeled seed DRC is closer to luxton corrected [19] of Chiu-Tsoa et al. [20] measurement of ^{125}I (6702) seed DRC. Chiu-Tsoa et al. [20] corrected luxton measured 6702 model of ^{125}I and reported $0.955 \text{ cGy}\cdot\text{h}^{-1}\cdot\text{U}^{-1}$ instead of $0.932 \text{ cGy}\cdot\text{h}^{-1}\cdot\text{U}^{-1}$ as DRC (Λ) of the 6702 modeled seed of ^{125}I . Comparing our study results in the code calculation for the seed dosimetric characterization with the other published results confirmed the accuracy of the MC modeling for dose calculations and data estimation. In the absence of nanoparticle, the prostate tissue absorbed $16.84 \text{ mSv}\cdot\text{Ci}^{-1}$. 10 nm gold nanoparticles increased the dose as 24.93% while gadolinium nano-particles in the same concentration and size increased the dose as 10.01%. Dose enhancement factor (DEF) was also calculated for a distance of 1 to $30 \mu\text{m}$ around a single nano-particle. Calculated DEF in the first μm in the vicinity of a single gold nano-particle was 48% and dropped to 5% in $30 \mu\text{m}$ from the nano-particle while in case of gadolinium the result showed drop from 20% to 1%. The average DEF in the presence of all gold and gadolinium nanoparticles were approximately 23% and 8%. The results in DEF by both gold and gadolinium nano-particles from the center of a single nano-particle to $30 \mu\text{m}$ was shown in **Figure 4** and a rapid drop of DEF can be seen in the figure which demonstrates a high dose gradient in the vicinity of a nano-particle. This phenomenon may be attributed to a high dose gradient in the vicinity of the nano-particles which can be more effective in the vicinity of the malignant cells. The calculated dosimetric parameters of the simulated source were described in the Tables in this work. Difference between our

results and TLD measurement of dose constant for the same model source was 16%. Experimental measurements conducted only for 3 distances and water only and in perspex medium to radial dose function data comparing to our MCNP5 modeling. Measurements conducted in the medium with density higher than water. This higher difference with measurement can arise from the measurement conditions such as the used medium. It should be stated that our estimation was conducted in a humanoid phantom and a density of 1 g/cm^3 was used for prostate gland, while in the measurement study the perspex phantom with a density of 1.18 g/cm^3 was used.

Figure 4. MCNP5 MC code estimation of DEF by gold and gadolinium nanoparticles in the field of simulated ^{125}I seed in the center of the water phantom. The curve data derived with MC simulation in separate input file runs.

Geometric parameters were estimated by MC code calculation in different radii including 0.25 cm, 0.5 cm, and 5 cm. Our results were in good agreement with the reported measured data with TL dosimetry data. **Table 2** shows our MC estimations and experimental measurements three distances. In the presence of gold and gadolinium nano-particles the values different as 12.1% and 5.7% comparing the nano-particles absence. In addition, radial dose function was tabulated in **Table 2** which includes TLD-100 measured and MC estimated values for the same source of ^{125}I . the measurement conducted in water and results tabulated in **Table 2** for comparison the experimental data with MC derived results. Normalized geometry function factor for the simulated brachytherapy seed was also obtained and tabulated in **Table 3**. Our results were compared with the MC study of other work [19-22]. It was seen a close agreement between our results and their reported values.

In the case of DEF of gold and gadolinium nano-particles in the brachytherapy, some paper has been published [3-16]. The studies show that for low energy sources, DEF of nanoparticles is higher than high energy sources. Because the Atomic number of elements plays a significant role in photo-electric interaction, we can conclude the high DEF by gold nano-particles rather than gadolinium nano-particles related to higher Z of the gold (Gold and Gadolinium Z are 79 and 64 respectively). Then, the difference in DEF may be attributed to the photoelectric phenomenon which is dominant in low energies, high Z materials and also the photo-electrons from the interaction deposit their energy in short range from the production site. 1.24 times higher Z of gold rather than gadolinium led to around 2 times increase in DEF on average and in **Figure 4** this difference can be seen. Studying the dose distribution around a single GNP showed a dramatic DEF in a few μm distance from the nano-particles was seen in the current study which results to a dose inhomogeneity and higher cell killing effect in the vicinity of the nano-particle.

Conclusion

We concluded that using the nano-particles and low energy-high dose rate radiation source in brachytherapy leads to significant DEF. Furthermore, a dramatic dose gradient in micro-scale was found in the vicinity of GNPs which can cause higher cells kill effect in malignant tissue compared to the treatment without using nano-particles. Our study showed LDR brachytherapy seed with the nano-particles application can be considered as an applicable choice for good brachytherapy outcome.

Table 1. MCNP5 derived anisotropy function for different angles and distances for the seed in water without nano-particle ^{125}I .

r (cm)	1 cm	1 cm	2 cm	2 cm	5 cm	5 cm	7 cm	7 cm
θ (degree)	Wang [22]	This work	Wang [22]	This work	Wang [22]	This work	Wang [22]	This work
0	0.814	0.831	0.763	0.762	0.760	0.764	0.773	0.779
5	0.811	0.825	0.753	0.762	0.760	0.765	0.770	0.776
10	0.816	0.810	0.777	0.781	0.780	0.784	0.781	0.800
15	N/A	0.812	N/A	0.810	N/A	0.793	N/A	0.809
20	0.844	0.870	0.811	0.819	0.820	0.815	0.815	0.819
30	0.872	0.902	0.849	0.871	0.860	0.863	0.863	0.871
40	0.900	0.901	0.895	0.900	0.900	0.897	0.903	0.909
45	N/A	0.910	N/A	0.928	N/A	0.949	N/A	0.921
50	0.930	0.927	0.930	0.934	0.940	0.946	0.938	0.934
60	0.960	0.956	0.958	0.959	0.970	0.967	0.968	0.971
70	0.983	0.986	0.989	0.984	0.990	0.988	0.993	0.995
75	N/A	0.990	N/A	0.990	N/A	0.990	N/A	0.996
80	0.996	0.986	0.995	0.997	1.00	1.00	1.004	0.100
90	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Table 2. Radial dose function for the simulated ^{125}I seed and comparison with the experimental TLD measurement for the real same seed.

r (cm)	Our study In phantom	Line geometry function; Measurement medium was Perspex	Line geometry function; MC derived in Perspex	Point geometry function derived by MC simulation in liquid water
0.5	1.002	1.054	1.009	1.161
1	1.002	1.00	1.00	1.00
5	0.189	0.19	0.109	0.092

Table 3. Normalized geometry function for the simulated seed in present work calculated by MCNP5 MC code calculation and comparison with other work on the same model. Data derived at 0.25 cm from the seed ^{125}I .

r (cm)	$\alpha=0^\circ$	$\alpha=15^\circ$	$\alpha=30^\circ$	$\alpha=45^\circ$	$\alpha=60^\circ$	$\alpha=90^\circ$
Derived data at 0.25 cm from the seed	3.12	2.30	1.41	1.01	0.89	0.71

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